No. 25-

IN THE

Supreme Court of the United States

MSN PHARMACEUTICALS, INC., *ET AL.*,

Petitioners,

v.

NOVARTIS PHARMACEUTICALS CORPORATION,

Respondent.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

PETITION FOR A WRIT OF CERTIORARI

AMIT R. VORA
Counsel of Record
HUNTER S. PEARL
ANNALIESE CHO BRELLIS
KASOWITZ LLP
1633 Broadway
New York, New York 10019
(212) 506-1834
avora@kasowitz.com

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QUESTION PRESENTED

In a patent case, "after-arising technology" is technology that was not invented until after the patent's filing. Neither this Court nor the Federal Circuit en banc has addressed the disclosure rules for after-arising technology. One line of Federal Circuit case law holds that when a patentee secures a claim construction that ensnares, as infringing, an accused device that features after-arising technology, the patentee risks invalidating its own patent under 35 U.S.C. § 112(a), which requires a patentee to describe and teach the claimed invention. A contradictory line of Federal Circuit decisions, including the decision below, carves out an exception for after-arising technology. This line holds that "later-existing state of the art … may not be properly considered" in the validity analysis. After-arising technology, that is, may not "reach back and invalidate" a patent. Yet that proposition conflicts with *The Incandescent Lamp Patent*, 159 U.S. 465 (1895). Edison's after-arising bamboo-filament technology exposed the invalidity of Sawyer and Man's patent for an electric lightbulb.

The question presented is: Whether, in a patent-infringement suit, a court may consider after-arising technology to hold that the patent is invalid under § 112(a) of the Patent Act.

PARTIES TO THE PROCEEDING

Petitioners MSN Pharmaceuticals, Inc., MSN Laboratories Private Ltd., and MSN Life Sciences Private Ltd. are the defendants-appellees below.

Respondent Novartis Pharmaceuticals Corp. is the plaintiff-appellant below.

CORPORATE DISCLOSURE STATEMENT

Petitioners MSN Pharmaceuticals, Inc. and MSN Life Sciences Private Limited are wholly owned subsidiaries of Petitioner MSN Laboratories Private Limited. Petitioner MSN Laboratories Private Limited has no parent corporation and no publicly held company owns 10% or more of its stock.

RELATED PROCEEDINGS

U.S. District Court for the District of Delaware:

In re Entresto (Sacubitril/Valsartan) Pat. Litig., No. 19-cv-1979-RGA. Judgment entered on July 7, 2023.

In re Entresto (Sacubitril/Valsartan) Pat. Litig., No. 19-cv-2021-RGA. Judgment entered on July 7, 2023.

In re Entresto (Sacubitril/Valsartan) Pat. Litig., No. 19-cv-2053-RGA. Judgment entered on July 7, 2023.

In re Entresto (Sacubitril/Valsartan) Pat. Litig., No. 20-mdl-2930-RGA. Judgment entered on July 7, 2023.

U.S. Court of Appeals for the Federal Circuit:

In re Entresto, No. 2023-2218. Judgment entered on Jan. 10, 2025.

In re Entresto, No. 2023-2220. Judgment entered on Jan. 10, 2025.

In re Entresto, No. 2023-2221. Judgment entered on Jan. 10, 2025.

TABLE OF CONTENTS

Page

TABLE OF APPENDICES

Page

TABLE OF AUTHORITIES

Page(s)

Cases

Constitutional Provision

Statutes

Other Authorities

PETITION FOR A WRIT OF CERTIORARI

Petitioners MSN Pharmaceuticals, Inc., MSN Laboratories Private Ltd., and MSN Life Sciences Private Ltd. (collectively, "MSN") respectfully request a writ of certiorari to review the judgment of the U.S. Court of Appeals for the Federal Circuit.

OPINIONS BELOW

The Federal Circuit's opinion is available at 125 F.4th 1090. App. 1a-21a. The Federal Circuit's order denying panel rehearing and rehearing en banc is unpublished. App. 98a-100a. The opinion of the U.S. District Court for the District of Delaware is unpublished and available at 2023 WL 4405464. App. 22a-81a.

JURISDICTION

The Federal Circuit entered judgment on January 10, 2025, App. 1a, and denied the timely petition for panel rehearing and rehearing en banc on March 25, 2025, App. 98a. Chief Justice Roberts extended the time to file a petition to August 22, 2025. This Court has jurisdiction under 28 U.S.C. § 1254(1).

RELEVANT STATUTORY PROVISIONS

35 U.S.C. § 112(a)-(b) provides:

(a) In General.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated

by the inventor or joint inventor of carrying out the invention.

(b) Conclusion.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

INTRODUCTION

Although *Incandescent Lamp* did not employ the term, it was an early "after-arising technology" case. William Sawyer and Albon Man had invented a fragile electric lightbulb with a filament made of "carbonized paper." 159 U.S. 465, 472 (1895). Their patent, however, broadly claimed all "carbonized fibrous or textile material." *Id.* at 468. The breadth was by design. They boldly lassoed a sweeping claim to ensnare an invention that arose after their patent's filing: Thomas Edison's electric lightbulb, which featured a bamboo filament, and which was a great success. *Id.* at 473-76. True, bamboo was, like "carbonized paper," a "carbonized fibrous or textile material." *Id.* So Sawyer and Man's patent claim had indeed captured Edison's invention on infringement grounds. *Id.* The problem, though, was that their infringement strategy ran headlong into bedrock prerequisites for patent validity. Their patent disclosures did not describe the broadly claimed invention or teach Edison's after-arising bamboo technology. Having failed to pay the quid of proper public disclosures, they were properly denied the quo of a monopoly right. Edison's invention had exposed their patent's invalidity, and they lost their patent-infringement case. *Id.* at 475-76.

Today, however, a distinct line of Federal Circuit

case law conflicts with *Incandescent Lamp*. These decisions exempt, from ordinary patent disclosure rules, cases involving after-arising technology—that is, technology that was invented after the patent's filing. But other Federal Circuit decisions involving after-arising technology follow *Incandescent Lamp*. They adhere to the ordinary rules.

Outside the context of after-arising technology, all courts agree that patentees must face the validity consequences of their infringement strategies. In a patent-infringement suit, if a patentee secures a broad construction of its patent claim, and through that strategy demonstrates that the accused device falls within the claim's scope and infringes the patent, the patentee's victory could be Pyrrhic. That is because, for a patent to remain valid, it must satisfy 35 U.S.C. § 112(a), which requires the patent's disclosures to (i) convey that the inventor actually invented the claimed invention (the written-description requirement) and (ii) enable fellow skilled artisans to make and use the invention (the enablement requirement). Further, the claim's scope must stay the same for infringement and validity. So if a patent's claim sweeps broadly to ensnare an accused device and establish infringement, but the patent fails to describe and teach the full scope of the claimed invention, the patentee will have invalidated its own patent. "The motto, 'beware of what one asks for,' might be applicable here." *Liebel-Flarsheim Co. v. Medrad, Inc.*, 481 F.3d 1371, 1380 (Fed. Cir. 2007).

Within the context of after-arising technology, however, "doctrinal chaos" reigns. Robin Feldman, *Rethinking Rights in Biospace*, 79 S. Cal. L. Rev. 1, 16 (2005). Some Federal Circuit decisions—such as

Idenix, *Plant Genetic*, and *Chiron*—apply the usual rules. They hold that when a patentee secures a claim construction that ensnares, as infringing, an accused device that features after-arising technology, the patentee risks invalidating its own patent on written-description and enablement grounds. Under this line, patents are invalidated when they claim after-arising technology that they neither describe nor teach.

But other Federal Circuit decisions—such as *Hogan* and the decision below—hold that when a patentee secures a claim construction that ensnares, as infringing, an accused device that features after-arising technology, the patent may survive a validity attack—even if the patent does not describe or teach the after-arising technology. These decisions presume that after-arising technology "may not be properly considered" in the validity analysis and cannot "reach back and invalidate" a patent. App. 18a-19a. Put differently, this line carves out an exception for after-arising technology from the hornbook rule of claim-scope symmetry across infringement and validity.

Still other cases, like *Schering* and *SuperGuide*, adopt inconsistent approaches by narrowly or broadly construing claims to avoid or embrace after-arising technology—despite analogous facts.

Neither this Court nor the Federal Circuit en banc has addressed the disclosure rules for after-arising technology. While *Amgen* held that a patent must enable the full scope of its claims, *see Amgen Inc. v. Sanofi*, 598 U.S. 594, 616 (2023), *Amgen* did not address the "puzzle[]" of after-arising technology, *see* Jonathan S. Masur & Lisa Larrimore Ouellette, *Disclosure Puzzles in Patent Law*, 92 U. Chi. L. Rev. (forthcoming 2025), at 1 ("Are the rules different for

after-arising technologies? Federal Circuit caselaw provides few clear answers.").[1] Orthogonal approaches have filled the vacuum, leaving inventors, competitors, and courts without clear guidance.

The dispute here exemplifies the problem. Respondent Novartis filed its '659 patent in 2002, claiming a "combination" of valsartan and sacubitril to treat heart failure. (Cf. Sawyer and Man's patent for fibrous or textile material.) Four years later, scientists discovered a way to "complex" the two compounds together as a single entity with superior therapeutic effects. The complex was after-arising technology. (Cf. Edison's bamboo.) In fact, Novartis separately patented the complex. Yet Novartis's weapon of choice in its patent-infringement suit against respondent MSN's generic valsartan-sacubitril *complex* was its '659 patent for a valsartan-sacubitril *combination*. To capture MSN's product, Novartis sought a construction of "combination" to cover the complex. (Cf. Sawyer and Man's strategy.) The district court adopted Novartis's construction, found MSN's product infringing, and invalidated the '659 patent under § 112. But the Federal Circuit reversed, reasoning that complexes were "not what is claimed" for validity purposes—while leaving intact the infringement finding that hinged on the broader construction. According to the court, because after-arising technology "may not be properly considered" in the validity analysis, the after-arising complex could not "reach back and invalidate" the patent. App. 18a-19a; *but see Idenix Pharms. LLC v. Gilead Scis.*

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[1] https://perma.cc/A6HB-HU3M.

Inc., 941 F.3d 1149, 1156 n.3 (Fed. Cir. 2019) (holding that after-arising technology exposed the patent's invalidity, and rejecting the dissent's view—as "no way to conduct an appeal"—that the panel should have found "a hypothetical narrower claim valid").

This approach runs counter to *Incandescent Lamp*. More fundamentally, it undermines the bargain that animates the Progress Clause and the Patent Act. The patent system confers an extraordinary monopoly in exchange for the inventor's disclosure of what the inventor actually invented. If patentees may reap the benefits of broad claims that cover after-arising technologies while avoiding the disclosure obligations that those claims entail, the public is denied its side of the bargain. In this way, the *Hogan-Entresto* approach is a loophole in our patent system. It stifles innovation and invites gamesmanship—not only in the pharmaceutical industry, where brand-name companies can leverage broad claims to delay generic entry and extend monopoly profits, but across the technology, life sciences, and manufacturing sectors. This Court should thus reject the *Hogan-Entresto* approach and confirm that after-arising technology is properly part of the § 112(a) validity analysis.

Amgen, decided in 2023, did not address the question presented, and its recency further militates for review. Granting review of the question presented now, while courts are implementing *Amgen*, will ensure that patent disclosure doctrine *overall* develops uniformly and coherently, within and outside the context of after-arising technology.

This Court should grant review and reverse.

STATEMENT OF THE CASE

I. Background Patent Principles

In a patent application, the "claims" define the subject matter that the inventor regards as the invention. *See* 35 U.S.C. § 112(b). To support the claims, the application's disclosures must: (i) convey to a person of ordinary skill in the art (a POSA) that the inventor possessed—that is, actually invented—the claimed subject matter at the time of the application's filing (the written-description requirement); and (ii) explain the invention in clear enough terms to enable a POSA to make and use the invention (the enablement requirement). *See* 35 U.S.C. § 112(a); *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1346 (Fed. Cir. 2010) (en banc).

These requirements are central to the "bargain" that animates our patent system. In exchange for a term of protection against competition, the inventor must provide disclosures that teach others how to make and use the invention so that "the public may have the full benefit of the invention … after the expiration of the patent term." *Amgen Inc. v. Sanofi*, 598 U.S. 594, 604-05 (2023) (citation modified). Further, allowing the public to understand what the inventor actually invented empowers others to improve on the invention while avoiding the boundaries of the patentee's exclusive rights. *See Ariad*, 598 F.3d at 1345-47. A system that permits inventors to patent inventions that they had not actually invented would force society to bear the costs of monopoly rights (e.g., higher prices) without receiving the benefits of innovation. It also would be fundamentally unfair. *See Evans v. Eaton*, 20 U.S.

356, 434 (1822) (observing that the requirement to "put the public in possession of what the party claims as his own invention" serves to "tak[e] from the inventor the means of practising upon the credulity or the fears of other persons, by pretending that his invention is more than what it really is"). The Constitution's Progress Clause thus sensibly vested Congress with the power to "promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to *their* respective Writings and Discoveries." U.S. Const. art. I, § 8, cl. 8 (emphasis added).

When a patentee sues a competitor for infringing its patent claims, the district court ordinarily conducts a *Markman* hearing to construe the claims' scope. "Victory in an infringement suit requires a finding that the patent claim covers the alleged infringer's product or process, which in turn necessitates a determination of what the words in the claim mean." *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 374 (1996) (citation modified).

"It is axiomatic that a claim must be interpreted the same way in determining infringement and invalidity for it would be fundamentally unfair to give a claim a narrow interpretation to uphold its validity … and then give it a broad interpretation to establish infringement." 5A Chisum on Patents § 18.03 (2025). Thus, if a patentee seeks and secures an overbroad claim construction to ensnare an accused product and prevail on infringement, the victory is Pyrrhic. An overbroad claim may (i) fail to convey that the inventor possessed the claimed subject matter, thus resulting in a finding of invalidity for lack of written description, or (ii) fail to adequately teach the

invention, thus resulting in a finding of invalidity for non-enablement. *See Trs. of Bos. Univ. v. Everlight Elecs. Co.*, 896 F.3d 1357, 1365 (Fed. Cir. 2018).

In *Amgen*, this Court reaffirmed that an overbroad claim risks invalidity. If a patent's claim sweeps so broadly as to capture "an entire class of … compositions of matter, the patent's specification must enable a skilled artist to make and use the entire class." 598 U.S. at 610. The rationale for this principle is that "if an inventor claims a lot, but enables only a little, the public does not receive its benefit of the bargain." *Id.* at 616. Correspondingly, if an inventor claims a lot, but describes only a little, the inventor will reap the reward of a monopoly while skirting "the difficult work of invention." *Ariad*, 598 F.3d at 1353 (citation modified).

It remains unclear, however, whether these disclosure obligations apply in the context of after-arising technology, i.e., technology invented after the patent's filing. In that context, some decisions apply the ordinary rules, while other decisions do not. Neither this Court nor the Federal Circuit en banc has reconciled the divergent approaches.

II. Factual and Procedural Background

In January 2002, Novartis, a brand-name pharmaceutical corporation, filed the '659 patent, whose sole independent claim (Claim 1) recited a pharmaceutical composition comprising: (i) valsartan; (ii) sacubitril; and (iii) a pharmaceutically acceptable carrier; (iv) where the valsartan and sacubitril are "administered in combination in about a 1:1 ratio." U.S. Patent 8101659; App. 6a-7a. The valsartan-sacubitril combinations were effective in treating

heart failure. App. 7a. But four years after Novartis filed the '659 patent, scientists discovered that valsartan and sacubitril could co-crystallize as a "complex"—a single compound linked by weak, non-covalent bonds. App. 4a. This complex yielded greater efficacy in treating heart failure and reduced ejection fraction. App. 4a. MSN, a generic medicine manufacturer, holds one of the first Abbreviated New Drug Applications for a generic valsartan-sacubitril complex. App. 7a. Novartis sells the brand-name valsartan-sacubitril complex as Entresto. App. 4a. Although Novartis separately patented the complex, App. 83a, only Novartis's '659 patent is at issue.

A. District Court Proceedings

In 2019, Novartis filed a complaint in the U.S. District Court for the District of Delaware alleging that MSN and other generic manufacturers had infringed its patents. App. 7a. During claim construction in 2021, MSN argued that Claim 1 of the '659 patent—which describes valsartan and sacubitril administered "in combination"—was limited to the active agents "as two separate components." App. 89a. But the district court sided with Novartis's proposed claim construction, rejecting a limitation that would have excluded valsartan and sacubitril linked in a single complex. App. 89a-91a. The district court relied on the plain meaning of the term "combination" and on Novartis's representation to the U.S. Patent and Trademark Office (P.T.O.) that the '659 patent "cover[s] Entresto," which contained a valsartan-sacubitril complex. App. 87a-91a. Novartis had made that representation to secure a patent-term extension, and it succeeded. App. 90a. Still, the district court warned: "there will be a non-frivolous issue of written

description and/or lack of enablement as this case proceeds on Novartis's preferred construction." App. 91a. Given the district court's conclusion, and to expedite a trial on validity, MSN stipulated to infringement of the as-construed claim. *See* App. 9a; *see also, e.g.*, *Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149, 1153 (Fed. Cir. 2019) (discussing analogous stipulation).

Two years later, the district court's warning proved prescient. In July 2023, after a three-day bench trial, the court issued its findings of fact and conclusions of law on the '659 patent. App. 22a-23a. The court rejected MSN's argument that the '659 patent failed to meet § 112's enablement requirement, as the court saw itself bound by a particular strand of Federal Circuit case law stating that "later-existing state of the art may not be properly considered in the enablement analysis." App. 70a (citing, *e.g.*, *In re Hogan*, 559 F.2d 595 (C.C.P.A. 1977)). But the court held that the complex's after-arising nature proved fatal for written description. App. 77a-80a. Novartis could not show that it possessed the claimed complex at the time of the patent's filing. App. 77a-80a. The court thus invalidated Novartis's '659 patent and entered judgment for MSN. App. 80a-81a.

B. Circuit Court Proceedings

Novartis appealed to the Federal Circuit, and in January 2025, a Federal Circuit panel reversed the district court's finding of invalidity for lack of written description. App. 1a-21a. Although neither party had appealed the claim construction, the panel held that the valsartan-sacubitril complex "is not what is claimed," App. 15a, and that because "valsartan-

sacubitril complexes were undisputedly unknown at the time of the invention," "the '659 patent could not have been construed as claiming those complexes as a matter of law," App. 16a n.5. The panel further held that "later-existing state of the art … may not be properly considered in the enablement analysis," App. 18a (citing the district court's decision and *Hogan*), and that "[t]he later-discovered valsartan-sacubitril complexes, which arguably may have improved upon the 'basic' or 'underlying' invention claimed in the '659 patent, cannot be used to 'reach back' and invalidate the asserted claims," App. 18a-19a.

Having narrowed the '659 patent's claim to exclude the complexed form, the panel held that it was enough for the patent specification to have described and enabled valsartan and sacubitril solely as a physical mixture, and not as a complexed form. App. 15a. The panel thus deemed the patent valid. App. 15a-17a.

Despite narrowing the claim's scope in its validity analysis, the panel did not vacate—or address—the infringement judgment that was based on the district court's broader claim construction. *See* App. 15a-17a. In other words, the panel construed the claim narrowly for validity, but it left intact the claim's broad construction for infringement. *See* App. 16a n.5.

As a result of the district and circuit court proceedings, MSN was deemed to have infringed Novartis's patent under a broad construction of the claim, while Novartis's patent was deemed valid under a narrow construction of the claim.

MSN petitioned for panel rehearing and rehearing en banc. App. 98a-100a. The petition was denied. App. 100a. This petition followed.

REASONS FOR GRANTING THE WRIT

I. Review Is Needed to Reconcile Incoherent Doctrinal Lines on the Patent Disclosure Rules for After-Arising Technology.

A. The Doctrinal Chaos Has Persisted Despite Longstanding Criticism.

In some decisions—unlike here—the Federal Circuit recognizes that after-arising technology is relevant to whether a patent has satisfied the validity requirements for written description and enablement. Under these decisions, if a patentee secures a claim construction that ensnares, as infringing, an accused product that features after-arising technology, the patentee risks invalidating its own patent on written-description and enablement grounds. This line holds that patents are invalid when they claim after-arising technology that they do not describe or teach.

Other decisions—including the decision below—depart from this approach. They presume that after-arising technology is irrelevant to the validity analysis. Under these decisions, if a patentee secures a claim construction that ensnares, as infringing, a competitor's product that features after-arising technology, the patent may survive a validity attack—even if the patent does not describe or teach the after-arising technology. The *Entresto* line thus carves out an exception for after-arising technology from the hornbook rule that claim scope is the same for infringement and validity.

Patent practitioners and scholars have long deplored the doctrinal confusion. In 2005, Professor Feldman noted the "doctrinal chaos." Robin Feldman, *Rethinking Rights in Biospace*, 79 S. Cal. L. Rev. 1, 16

(2005); *see also id.* at 28 ("Across a broad range of doctrines, the courts have adopted entirely inconsistent visions of the proper footprint of the invention and how far an inventor can reach toward things that come after the invention."). Twenty years later, that description still rings true. As Professors Masur and Oullette ask: "Are the rules different for after-arising technologies? Federal Circuit caselaw provides few clear answers." Jonathan S. Masur & Lisa Larrimore Ouellette, *Disclosure Puzzles in Patent Law*, 92 U. Chi. L. Rev. (forthcoming 2025), at 1 (adding that *Amgen* did not solve "longstanding puzzles");[2] 5A Chisum on Patents § 18.03(2)(g) (2025) ("The time framework for construing patent claims is the subject of surprisingly sparse judicial authority."); Joshua D. Sarnoff, *Correcting Misunderstandings of Literal Infringement Scope Regarding After-Arising Technologies Protected by the Doctrine of Equivalents*, 53 Akron L. Rev. 767, 768 (2019) (describing "the conflicting cases that have led to … confusion" on "the U.S. law of literal infringement's temporal scope"); Timothy R. Holbrook, *Patent Disclosures and Time*, 69 Vand. L. Rev. 1459, 1461 (2016) ("the relationship between time and patent disclosures is surprisingly underdeveloped"); Kevin Emerson Collins, *Enabling After-Arising Technology*, 34 J. Corp. L. 1083, 1087 (2009) ("The Federal Circuit's cases addressing the enablement of claims encompassing AAT [i.e., after-arising technology] are commonly viewed as inconsistent and chaotic."); Kevin Emerson Collins, *The Reach of Literal Claim Scope into After-Arising*

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[2] https://perma.cc/A6HB-HU3M.

Technology: On Thing Construction and the Meaning of Meaning, 41 Conn. L. Rev. 493, 496 (2008) ("very little attention has been paid to … how far beyond the technology constructively disclosed by an inventor and into future technology a claim can reach"); Eileen M. Kane, *Patent-Mediated Standards in Genetic Testing*, 2008 Utah L. Rev. 835, 858 (2008) ("The Federal Circuit has not developed a coherent approach to later-developed technology that might fall within the scope of a generally broad claim."); Mark A. Lemley, *The Changing Meaning of Patent Claim Terms*, 104 Mich. L. Rev. 101, 122 (2005) ("The Federal Circuit must choose between the benefits of integrated claim construction and the niceties of time-differentiated claim construction.").

The Federal Circuit has declined to bring order to the chaos through en banc review. It denied the en banc petition here, just as it denied prior en banc petitions that sought clarity on the disclosure rules for after-arising technology. *See, e.g.*, *Idenix Pharms. LLC v. Gilead Scis. Inc.*, No. 18-1691, Doc. 95 (Fed. Cir. Apr. 24, 2020); *Chiron Corp. v. Genentech, Inc.*, No. 03-1158, Doc. 34 (Fed. Cir. June 8, 2004); *SuperGuide Corp. v. DirecTV Enters., Inc.*, No. 02-1561, Doc. 42 (Fed. Cir. Apr. 13, 2004).

B. The Divergent Approaches to After-Arising Technology

1. The *Idenix* Line: Decisions holding that after-arising technology is relevant to validity, and that ensnaring after-arising technology for infringement risks invalidity.

This Court should embrace *Idenix*'s approach.

Idenix Pharms. LLC v. Gilead Scis. Inc., 941 F.3d 1149 (Fed. Cir. 2019). Idenix patented a method to treat the hepatitis C virus (HCV) with a nucleoside compound. *Id.* at 1154. Although Gilead's accused product—an HCV treatment with a 2'-fluoro-down nucleoside—fell within the literal scope of Idenix's broadly construed claim, it was undisputed that the 2'-fluoro-down embodiment did not exist until "a year or so after the application was filed." *Id.* at 1164. Gilead thus stipulated to infringement but argued that Idenix's patent was invalid—and the Federal Circuit agreed: "In light of the conspicuous absence of that compound, a POSA would not visualize or recognize the members of the genus as including 2'-fluoro-down, and the specification could not demonstrate to a POSA that the inventor had possession of that embodiment at the time of filing." *Id.* at 1165 (citation modified).

Judge Newman dissented, urging that "[t]he majority's holding that validity under section 112 is determined based on whether unclaimed subject matter is described and enabled" was "flawed" and created "a new path of uncertainty and unreliability of the patent grant." *Id.* at 1166 (Newman, J., dissenting). But the *Idenix* majority countered that the dissent had reached a contrary conclusion "only by disregarding the district court's binding claim construction, ignoring the resulting stipulation of infringement, and analyzing a case that is not the one presented to us." *Id.* at 1156 n.3. As the majority reasoned, although "under a narrower construction, the claims … might well be enabled, and the accused product would not infringe," neither party had appealed the issue of claim construction, which

"tasked" the panel with "deciding whether the claims, *as construed*, are enabled." *Id.* The majority continued: "[R]ather than answer that question, the dissent has applied its newly invented claim construction to find a hypothetical narrower claim valid but not infringed. Respectfully, that is no way to conduct an appeal." *Id.* Yet that is how the decision below conducted this appeal.

Consistent with *Idenix*, *Plant Genetic Systems (PGS)* rejected the proposition that a patent is "entitled to both a broad scope of coverage and a lower standard of enablement." *Plant Genetic Sys., N.V. v. DeKalb Genetics Corp.*, 315 F.3d 1335, 1341 (Fed. Cir. 2003). PGS "concede[d]" that its patent claimed transgenic plant cells that covered stably transformed monocot cells. *Id.* "Only by doing so can PGS sue DeKalb, which makes monocot products, for infringement." *Id.* And "[h]aving agreed that the cell claims encompass monocot cells, a later development," PGS could not escape the consequence that its patent was invalid for non-enablement: "stably transformed monocot cells were difficult to produce" when PGS filed its patent, and the patent "gave no instruction how" to produce them. *Id.* at 1340-41.

In *Chiron*, likewise, Chiron's claim for monoclonal antibodies was "broadly construed" to embrace chimeric antibodies—which doomed the patent's validity. *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247, 1252 (Fed. Cir. 2004). "[C]himeric antibody technology did not even exist at the time of the 1984 filing," which meant that "the Chiron scientists, by definition, could not have possession of, and disclose, the subject matter of chimeric antibodies that did not even exist at the time of the 1984 application." *Id.* at

1255. As the Federal Circuit held: "Thus, axiomatically, Chiron cannot satisfy the written description requirement for the new matter appearing in the … patent, namely chimeric antibodies." *Id.*

To be sure, *Chiron* separately held that the after-arising technology was "outside the bounds of the enablement requirement." *Id.* at 1254; *but see id.* at 1262-63 (Bryson, J., concurring) (disagreeing that "the enablement requirement is inapplicable," and urging that because "Chiron is arguing that the 1984 application provides support for claims covering technology that was not in existence at that time," "the 1984 application does not enable the asserted claims"). This *Chiron* holding falls into the next line, underscoring the doctrinal disarray.

2. The *Hogan-Entresto* Line: Decisions holding that after-arising technology is irrelevant to validity, and that ensnaring after-arising technology for infringement does not risk invalidity.

In another line of cases, the Federal Circuit has taken the polar opposite approach, presuming that after-arising technology is irrelevant to the validity analysis.

Here, for example, Novartis secured a claim construction for its '659 patent that covered not only valsartan-sacubitril physical mixtures, but also valsartan-sacubitril complexes, even though scientists had not discovered complexes until four years after Novartis had filed the '659 patent. Only by doing so could Novartis sue MSN, which produced complexed valsartan-sacubitril generic medicine, for

infringement. MSN stipulated to infringement; the district court invalidated the patent. App. 9a-13a.

On appeal, however, the panel reversed under the theory that "later-discovered valsartan-sacubitril complexes … cannot be used to 'reach back' and invalidate the asserted claims." App. 18a-19a. The panel presumed: "later-existing state of the art … may not be properly considered in the enablement analysis." App. 18a (citing the district court's decision and *Hogan*). Thus, although claim construction was not on appeal, the panel narrowed the claim for validity while leaving intact a broad claim for infringement. *See* App. 16a n.5.

The *Entresto* panel's approach traces to *Hogan*, a 1977 decision by the Federal Circuit's predecessor, the Court of Customs and Patent Appeals. *In re Hogan*, 559 F.2d 595 (C.C.P.A. 1977). There, a patent filed in 1953 claimed a solid polymer of propylene. *Id.* at 605-06. Although the claims encompassed crystalline and amorphous forms, amorphous forms did not exist until 1962. *Id.* On appeal from a P.T.O. decision that the patent was invalid for non-enablement because it did not teach how to prepare amorphous propylene, the C.C.P.A. held that the agency had erred in relying on the after-arising technology in assessing enablement: "To now say that appellants should have disclosed in 1953 the amorphous form which on this record did not exist until 1962, would be to impose an impossible burden on inventors and thus on the patent system." *Id.* The court defended "the right to broad claims," observed that pioneering inventions "deserve broad claims to the broad concept," and warned against "utiliz[ing] the patenting or publication of later existing improvements to 'reach back' and preclude or

invalidate a patent on the underlying invention." *Id.*

The C.C.P.A. ultimately remanded for the P.T.O. to reconsider enablement. *Id.* at 609; *see also U.S. Steel Corp. v. Phillips Petroleum Co.*, 865 F.2d 1247, 1251 (Fed. Cir. 1989) ("That the [claim] may cover a later version of the claimed composition … relates to infringement, not to patentability."); *In re Koller*, 613 F.2d 819, 825 (C.C.P.A. 1980) (extending *Hogan* to written description).

Notably, Judge Miller's partial concurrence faulted the *Hogan* majority for "advocat[ing] a double standard." 559 F.2d at 610 (Miller, J., concurring in part); *see also Chiron*, 363 F.3d at 1262 (Bryson, J., concurring) (noting risks of *Hogan*'s literal implications); *PGS*, 315 F.3d at 1340 (same).

3. The *Schering* Line: Decisions narrowly construing patents to exclude after-arising technology and finding no infringement.

In a separate line of cases, which does not neatly map onto the first two, the Federal Circuit has narrowly construed claims to exclude after-arising technology—and, on that basis, it has held that the accused device did not infringe the patent. In *Schering*, for example, Schering claimed that Amgen had infringed its patent for "interferon alpha," which was based on Dr. Charles Weissmann's work and which, at the time of filing, scientists believed was the only interferon of its kind. *Schering Corp. v. Amgen Inc.*, 222 F.3d 1347, 1353 (Fed. Cir. 2000). "Only later did scientists learn that interferon has many subtypes." *Id.* Upon limiting the claim scope to the interferon subtype that Dr. Weissmann had

discovered, the district court held that Amgen's after-arising interferon product did not infringe the patent. *Id.* The Federal Circuit affirmed, noting that "[t]o grant broader coverage would reward Dr. Weissmann for inventions he did not make." *Id.* at 1354; *see also Kopykake Enters., Inc. v. Lucks Co.*, 264 F.3d 1377, 1384 (Fed. Cir. 2001) (holding that claim for "screen printing" images on foodstuffs excluded "ink jet printing," which was not a convention for printing images on foodstuffs at the time of filing, and affirming non-infringement).

4. The *SuperGuide* Line: Decisions broadly construing patents to cover after-arising technology and finding infringement.

In yet another line of cases, the Federal Circuit has taken the polar opposite approach of the third line. Consider *SuperGuide*, where the patent claimed systems that "regularly received television signal[s]." *SuperGuide Corp. v. DirecTV Enters., Inc.*, 358 F.3d 870, 876 (Fed. Cir. 2004). At the time of filing in 1985, televisions could receive only analog signals—not digital ones. *Id.* In accordance with *Schering*, the district court reasoned that because the claim could cover only "the type of television signals that were broadcast in 1985"—i.e., analog signals—the advanced systems of DirecTV and the other defendants, which were invented nearly a decade later and could receive digital signals, did not infringe the patent. *Id.* But the Federal Circuit vacated that holding, observing that the district court had "improperly" concluded that "later or 'after-arising technologies' cannot fall within the literal scope of the claim at issue." *Id.* at 878; *see also Innogenetics, N.V.*

v. Abbott Labs., 512 F.3d 1363, 1371-72 (Fed. Cir. 2008) ("Our case law allows for after-arising technology to be captured within the literal scope of valid claims that are drafted broadly enough.").

Although Judge Michel concurred (on the alternative basis that the doctrine of equivalents could protect the patentee), he criticized the majority for "expand[ing] the scope of the … patent far beyond what the named inventors say they actually invented in their application, and what it describes and enables." *Id.* at 896-98 (Michel, J., concurring in the result). In doing so, according to Judge Michel, the majority had flouted two principles: "first, that the applicant must be the 'inventor' of the things covered by the patent claims, and second, that the right to exclude will be no broader than the inventor's enabling disclosure. The inventors here most assuredly did not invent a system that receives digital signals; their patent cannot therefore cover such systems." *Id.* at 898.

5. The doctrinal lines are incoherent.

To recap: The *Idenix* line holds that after-arising technology is relevant to the validity analysis. Because Idenix's patent for a nucleoside HCV treatment was construed to cover 2'-fluoro-down nucleoside—an invention that was not discovered until "a year or so" after the patent's filing and that was featured in Gilead's accused HCV treatment—Idenix's patent was invalid: it could not describe or enable the after-arising technology. *Idenix*, 941 F.3d at 1164. So too with PGS's patent for transgenic plant cells and plant products. Because it was construed to cover monocot cells—a "later development" that was featured in DeKalb's accused monocot products—

PGS's patent was invalid: it did not teach how to produce the after-arising technology. *PGS*, 315 F.3d at 1340-41. Chiron's patent for monoclonal antibodies suffered the same fate. Because it was construed to cover chimeric antibodies—which "did not even exist at the time of" the patent's filing, and which Genentech's accused product featured—Chiron's patent was "axiomatically" invalid: "Chiron scientists, by definition, could not have possession of, and disclose, the subject matter of chimeric antibodies that did not even exist at the time of the 1984 application." *Chiron*, 363 F.3d at 1255.

Put differently, the *Idenix* line recognizes that, even in the context of after-arising technology, if a patentee secures a claim construction that captures a competing product and establishes infringement, the same construction applies to the validity analysis. There is no after-arising technology exception to the settled patent-law principles (i) that claim scope is symmetrical for infringement and validity, and (ii) that patentees must live with the validity consequences of their infringement strategies. Idenix sought and secured a broad claim construction to ensnare Gilead's product, and Gilead thus stipulated to infringement—but Idenix consequently lost on validity. *Idenix*, 941 F.3d at 1164-65. Similarly, PGS sought and secured a broad claim construction to ensnare DeKalb's product. The *PGS* decision does not shy away from calling out PGS's infringement strategy. "Only by doing so can PGS sue DeKalb, which makes monocot products, for infringement." 315 F.3d at 1341. But "[h]aving agreed that the cell claims encompass monocot cells, a later development," PGS could not escape the result that it had

invalidated its own patent. *Id.*

The *Idenix* line harmonizes with the *Schering* line (which clashes with the *SuperGuide* line) in that they eschew patent claims that "reward" inventors "for inventions [they] did not make." *Schering*, 222 F.3d at 1354. But the *Idenix* line goes further than the *Schering* line in acknowledging that where, as here, the patentee has secured a broad construction covering after-arising technology, and this construction is not on appeal, the appellate court may not narrow the claim solely for the validity inquiry merely because after-arising technology is involved.

In diametric opposition to the *Idenix* line, the *Hogan-Entresto* line holds that after-arising technology is irrelevant to the validity analysis. Championing the "right to broad claims," *Hogan* held that accused infringers may not "utilize the patenting or publication of later existing improvements to 'reach back' and preclude or invalidate a patent on the underlying invention." 559 F.2d at 606. Echoing *Hogan*, the *Entresto* panel below held: "later-existing state of the art … may not be properly considered in the enablement analysis." App. 18a.

Put another way, the *Hogan-Entresto* line permits a "double standard." *See Hogan*, 559 F.2d at 610 (Miller, J., concurring in part). The patentee may both (i) draw a broad claim to ensnare after-arising technology and prevail on infringement and (ii) treat the claim narrowly to exclude after-arising technology and avoid invalidity. In this line, then, there is an after-arising technology exception to the settled patent-law principles (i) that claim scope is symmetrical for infringement and validity, and (ii) that patentees must live with the validity

consequences of their infringement strategies. *See* Jorge A. Goldstein, U.S. Biotechnology Patent Law § 6:26 (Aug. 2025) ("The *Entresto* rule overrules *sub silentio* the conclusion reached in *Chiron* … ."); *but see Robert Bosch, LLC v. Pylon Mfg. Corp.*, 719 F.3d 1305, 1316 (Fed. Cir. 2013) (en banc) (the prior panel precedent rule).

Indeed, the *Entresto* panel below conducted the appeal in the way that the *Idenix* majority rejected and the *Idenix* dissent endorsed. Although the *Idenix* dissent would have afforded Idenix's patent a validity-specific construction on appeal that would have excluded the after-arising technology, the *Idenix* majority rejected, as "no way to conduct an appeal," the idea of applying a "newly invented claim construction to find a hypothetical narrower claim valid." 941 F.3d at 1156 n.3.

The *Hogan-Entresto* line harmonizes with the *SuperGuide* line (which clashes with the *Schering* line) in that they tolerate patent claims that reward inventors for inventions they did not make—to Judge Michel's consternation. The *SuperGuide* patentee was not the "'inventor' of the things covered by the patent claims," and the patentee's "right to exclude" was "broader than the inventor's enabling disclosure." 358 F.3d at 898 (Michel, J., concurring in the result).

There is doctrinal tension along another dimension, as well. While the *Hogan-Entresto* and *Schering* lines discourage courts from construing claims to embrace after-arising technology, the *Idenix* and *SuperGuide* lines recognize that courts may interpret claims to embrace after-arising technology, depending on the claim's language.

Despite the doctrinal confusion, and despite the disapproving concurrences in *Hogan* (Miller, J.), *SuperGuide* (Michel, J.), and *Chiron* (Bryson, J.) and the dissent in *Idenix* (Newman, J.), the Federal Circuit en banc has declined to enter the fray.

II. This Court Should Embrace the *Idenix* Line and Reject the *Hogan-Entresto* Line.

This Court should embrace the *Idenix* line's view that after-arising technology is a proper consideration in the validity inquiry for written description and enablement under 35 U.S.C. § 112(a). Thus, when a patentee secures a claim construction that captures after-arising technology for infringement, the patent must describe and enable the full scope of the construed claim, including the after-arising technology, to remain valid. Both inside and outside the after-arising technology context, claim scope must remain constant for validity and infringement. This approach coheres with the *Schering* line's principle that inventors should not be rewarded for things they did not invent, and with the *SuperGuide* line's principle that claims can encompass after-arising technology.

Meanwhile, the *Hogan-Entresto* loophole—which, from the flawed premise that after-arising technology is irrelevant to the validity analysis, incorrectly holds that a claim may capture after-arising technology for infringement without describing or enabling that technology for validity—should be closed.

A. Fundamental Patent Principles Militate for *Idenix*'s Approach and Against the *Hogan-Entresto* Loophole.

1. Outside the context of after-arising technology,

"claims are construed the same way for both invalidity and infringement." *Source Search Techs., LLC v. LendingTree, LLC*, 588 F.3d 1063, 1075 (Fed. Cir. 2009) (collecting cases). To construe a claim broadly for infringement but narrowly for validity would afford an unfair advantage to patentees and allow courts to treat a patent "like a nose of wax, which may be turned and twisted in any direction." *See White v. Dunbar*, 119 U.S. 47, 51 (1886). So when the as-constructed claims are broader than the supporting disclosure, the solution is to deem the claims invalid, not to imagine narrower claims that would have been supported.

Consider Boston University's fate: "Having obtained a claim construction that included a purely amorphous layer within the scope of the claim, BU then needed to successfully defend against an enablement challenge as to the claim's full scope. Put differently: if BU wanted to exclude others from what it regarded as its invention, its patent needed to teach the public how to make and use that invention. That is part of the quid pro quo of the patent bargain." *Trs. of Bos. Univ. v. Everlight Elecs. Co.*, 896 F.3d 1357, 1365 (Fed. Cir. 2018) (citation modified). Because BU's patent failed to teach the purely amorphous layer, its patent was invalid, and it lost its infringement suit. *Id.*

Liebel, too, learned the hard truth that claim scope for infringement and validity is symmetrical: "The irony of this situation is that Liebel successfully pressed to have its claims include a jacketless system, but, having won that battle, it then had to show that such a claim was fully enabled, a challenge it could not meet. The motto, 'beware of what one asks for,'

might be applicable here." *Liebel-Flarsheim Co. v. Medrad, Inc.*, 481 F.3d 1371, 1380 (Fed. Cir. 2007).

The black-letter rule of claim-scope equivalence for infringement and validity is why patent-law practitioners warn against pursuing overbroad claims. "Patent owners often advocate for broad interpretations of claim terms in order to capture the accused product. But in doing so, they may find themselves hoisted by their own petard. … In their quest for litigation advantage, patent owners may stretch claim scope just far enough to capture the target and right into the jaws of invalidity." Shashank Upadhye, *The Perils of Broad Patent Claims: From Issuance to Invalidity*, Upadhye Tang LLP (July 1, 2025) (collecting cases).[3]

2. There is no sound reason to deviate from this established framework in the context of after-arising technology. The *Hogan-Entresto* loophole should be closed.

To begin, it lacks textual support. Neither the Progress Clause nor § 112 of the Patent Act hints at an after-arising-technology exception from the disclosure requirements for validity. Congress granted great advantages to patentees but was equally insistent on limiting those advantages. "Judges may no more subtract from the requirements for obtaining a patent that Congress has prescribed than they may add to them." *Amgen*, 598 U.S. at 612.

The *Hogan-Entresto* loophole also vitiates the bargain at the heart of patent law. The loophole

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[3] https://perma.cc/J9XU-5HVB.

permits patentees to enjoy claims that cover after-arising technology for infringement purposes without the corresponding need to describe or enable it for validity purposes. Patentees thus get the quo of a monopoly right without paying the quid of describing and teaching their claimed invention for society's benefit. Judge Miller's *Hogan* concurrence decried this "double standard," 559 F.2d at 610, a view that Judge Michel's *SuperGuide* concurrence shared: the "right to exclude" should be "no broader" than the disclosure, even in the after-arising-technology context. 358 F.3d at 898.

As Professors Masur and Oullette urge, the "*Hogan* approach is misguided," as it "violates the principle that a patent right should be commensurate with its disclosure" and allows patentees to "have it both ways." Masur & Oullette, *supra*, at 36. In the same vein, Professor Sarnoff maintains: "[I]f claims are drafted broadly using future-regarding terminology or employ terminology that does not convey a future sense but nevertheless is construed to include after-arising technology, such claims should be held invalid for lack of enablement and of written description." Sarnoff, *supra*, at 792.

Worse still, the *Hogan-Entresto* loophole conflicts with this Court's precedents. This Court has never held that after-arising technology is irrelevant to whether a patent's disclosure is sufficient to validate the patent. Instead, this Court has held that a patent must "enable the full scope of the invention as defined by its claims." *Amgen*, 598 U.S. at 610. Although *Amgen* did not address the written-description requirement, there is no reason to believe that a patent must not describe the full scope of the

invention as defined by its claims as well. *See Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 736 (2002) ("[T]he patent application must describe, enable, and set forth the best mode of carrying out the invention."); *Evans v. Eaton*, 20 U.S. 356, 434 (1822) ("The other object of the specification is, to put the public in possession of what the party claims as his own invention.").

In *The Incandescent Lamp Patent*, for example, William Sawyer and Albon Man had patented an "electric lamp" made of "carbonized fibrous or textile material." 159 U.S. 465, 466, 468 (1895). "Instead of confining themselves to carbonized paper, as they might properly have done … they made a broad claim for every fibrous or textile material." *Id.* at 472. Only later—through "painstaking experimentation"—did Thomas Edison invent an electric lamp that employed, with great success, a bamboo filament. *Id.* at 475-76. Because bamboo was a "fibrous or textile material," Sawyer and Man sued Edison for infringement. *Id.* at 471-72. But this Court held that Sawyer and Man's patent was invalid, as the patent had claimed but failed to describe and enable Edison's after-arising technology. *Id.* at 475-76. Nowhere did this Court suggest, as *Hogan*'s logic would dictate, that "[t]o now say that [Sawyer and Man] should have disclosed [the bamboo filament] which on this record did not exist until [later], would be to impose an impossible burden on inventors and thus on the patent system." *See Hogan*, 559 F.2d at 606. Nor did this Court suggest, as *Entresto*'s logic would dictate, that Edison's after-arising technology could not, as a matter of law, "reach back and invalidate" Sawyer and Man's patent. *See* App. 18a-19a.

This Court has also never held that if a patentee broadly claims after-arising technology, and claim construction is not on appeal, the appellate court may save the patentee from the invalidity outcome of its overbroad claim by pushing after-arising technology outside claim scope "as a matter of law," *see* App. 16a n.5. Sawyer and Man lost against Edison.

Contrary to Judge Newman's dissent, the *Idenix* line will not create a "new path of uncertainty" in the patent system. 941 F.3d at 1166. Upon granting review, this Court can fashion limiting principles and refine related doctrines to guard against the risks of equating the disclosure rules for after-arising-technology cases and other cases. For example, the doctrine of equivalents allows a patentee to obtain an infringement judgment against copycats who make trivial changes to the patent. *See Festo*, 535 U.S. at 733; *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 37 (1997) (rejecting the proposition that doctrine of equivalents "should not extend to after-arising equivalents").

Despite precedents such as *Amgen* and *Incandescent Lamp*, because neither this Court nor the Federal Circuit en banc has addressed whether the disclosure rules are the same inside and outside the context of after-arising technology, doctrinal confusion remains—paving the way for decisions like the one below.

B. The Decision Below Is Incorrect.

Under a framework that applies equivalent disclosure rules to after-arising-technology cases and other cases, the panel below erred. Novartis used its '659 patent for a heart-failure medication claiming

valsartan-sacubitril combinations to ensnare, as infringing, MSN's generic product featuring a valsartan-sacubitril complex—a structure where the valsartan and sacubitril compounds are non-covalently bonded into a single structure. App. 4a. Scientists did not invent the valsartan-sacubitril complex until four years after the '659 patent's filing. App. 15a. Valsartan-sacubitril complexes are thus after-arising technology.

Crucially, the plain-meaning construction of the patent's claim for a combination was broad enough to include the complex. *See* App. 56a. Because that construction meant that MSN's product had infringed Novartis's patent, MSN stipulated to infringement. *See* App. 9a. But as the district court properly held, that broad construction also invalidated the patent, as the patent had claimed technology that, at the time of its filing, Novartis had not actually invented. App. 77a-80a. Although Novartis appealed that ruling, neither party challenged the claim construction on appeal. *See* App. 7a-13a.

The Federal Circuit panel, though, allowed Novartis to have it both ways. The panel narrowly construed the patent for validity purposes, holding that the patent did not claim complexes under the view that "later-existing state of the art may not be properly considered" in the validity analysis. App. 12a (citing, e.g., *Hogan*). The panel thus deemed the patent valid. App. 17a. At the same time, the panel did not vacate—or address—the infringement judgment, even though it hinged on the broad construction that the panel had rejected and narrowed for validity. *See* App. 13a-17a.

In light of *Incandescent Lamp*—as well as *Idenix*,

PGS, *Chiron*, and other decisions—the decision below should have concluded that Novartis's claim-construction and infringement strategy rendered its patent invalid.

Novartis insisted on a broad construction to ensnare MSN's competing product—just as Sawyer and Man had done against Edison, and just as PGS had done against Gilead. "Instead of confining" itself to a claim that excluded valsartan-sacubitril complexes, it "made a broad claim" that encompassed valsartan-sacubitril complexes. *See Incandescent Lamp*, 159 U.S. at 472. "Only by doing so can [Novartis] sue [MSN], which makes [complexes], for infringement." *See PGS*, 315 F.3d at 1341. MSN then stipulated to infringement—just as Gilead had done in *Idenix*, 941 F.3d at 1153. And because the patent neither described nor taught the "full scope" of its claims, *see Amgen*, 598 U.S. at 616, which encompassed the complexes that arose after the patent's filing, the patent was "axiomatically" invalid, as in *Chiron*, 363 F.3d at 1254-55.

As in *Idenix* and *PGS*, moreover, claim construction was not on appeal. Yet the Federal Circuit did what the *Idenix* majority dubbed "no way to conduct an appeal." 941 F.3d at 1156 n.3. It "applied its newly invented claim construction to find a hypothetical narrower claim valid." *Id.* And while the panel premised its holding on the view that after-arising technology cannot "'reach back' and invalidate" a patent as a matter of law, *see* App. 18a-19a, Edison's after-arising invention did just that.

Given the principle that "claims are construed the same way for both invalidity and infringement," *Source Search*, 588 F.3d at 1075, if the panel believed

that it was appropriate to conduct a de novo claim construction even though neither party had appealed the issue of claim construction, it should have held that the narrower construction applies not only to its assessment of validity under § 112, but also to the scope of the claim generally, including for infringement. Instead, Novartis was gifted a construction that twisted like a nose of wax: broad enough to ensnare MSN's product for infringement, yet narrow enough to avoid invalidity under § 112.

The panel was also wrong to characterize the complex as an "unclaimed feature[]." App. 18a. Although an "unclaimed element," by definition, need not be described or enabled, that term of art applies to a feature that is severable from an invention's essence. *See* Collins, *Enabling*, *supra*, at 1114. While a casing for Sawyer and Man's lightbulb could have been an unclaimed element, Edison's bamboo-filament lightbulb could not have been. To validly claim it, Sawyer and Man had to describe and enable it, which they did not do. So too with the valsartan-sacubitril complex. The valsartan-sacubitril complex is an *embodiment*—indeed, a *species*—of valsartan-sacubitril combinations. App. 79a-80a.

III. This Case Presents an Ideal Opportunity to Address an Important, Recurring Question.

A. This case tees up an unresolved, recurrent, and critical issue: whether the same disclosure rules apply within and outside the context of after-arising technology. The issue is longstanding (*see* Feldman, *supra*, at 16 (seeing "doctrinal chaos" in 2005)), and it has grown in salience as the Federal Circuit's treatment of after-arising technology has drifted further from its constitutional, statutory, and logical

mooring. The issue also gains salience as courts begin to apply *Amgen*, which addressed enablement but not written description or the puzzle of after-arising technology. Granting review here, on the heels of *Amgen*, will ensure that the disclosure principles for after-arising-technology cases and other cases develop uniformly and coherently. *Cf. McDonald v. Chicago*, 561 U.S. 742, 791 (2010) (addressing Second Amendment incorporation after *District of Columbia v. Heller*, 554 U.S. 570 (2008)).

The discord in the disclosure rules for after-arising technology shakes the stability of patent law on which scientific progress depends. As this Court has observed, the scope of patent rights "must be known" not only to protect "the patentee," but also to spur "the inventive genius of others." *See Markman*, 517 U.S. at 390 (citation modified). Indeed, a shared comprehension of what is, and what is not, protected intellectual property enables inventors to focus their research-and-development efforts on productive pursuits, allows for effective business planning, encourages investment in new technologies, reduces barriers to entry, and supports a fair competitive environment. *See Hunter Douglas, Inc. v. Harmonic Design, Inc.*, 153 F.3d 1318, 1331 (Fed. Cir. 1998) (listing uniformity's benefits). But the Federal Circuit's decisions—including the decision below—have introduced serious uncertainty into the patent system by ruling, with contradictory reasoning and results, that the presence of after-arising technology creates exceptions to the rules of claim construction, infringement, and validity.

B. More specifically, this Court's intervention is needed to abrogate the *Hogan-Entresto* line. *Hogan* and its progeny reflect an overreaction to the notion that advances in technology will unfairly wipe out patents. The ordinary rules account for that risk. The system fairly rewards patentees who do not overclaim and who do the relevant inventive work. *See* Masur & Oullette, *supra*, at 35-36. The problem with the *Hogan-Entresto* loophole is that by removing after-arising technology from the validity equation entirely, it allows patentees to weaponize sweeping claims and block after-arising technologies without having done the relevant inventive work.

Unless the *Hogan-Entresto* loophole is closed, pharmaceutical companies can deploy aging patents to delay the entry of generic medications. *See, e.g.*, S. Sean Tu & Charles Duan, *Pharmaceutical Patent Two-Step: The Adverse Advent of Amarin v. Hikma Type Litigation*, 12 NYU J. Intell. Prop. & Ent. L. 1, 4-5 (2022).[4] Technology companies can use vague disclosures to stifle genuine innovation. *See, e.g.*, Colleen V. Chien, *The Inequalities of Innovation*, 72 Emory L.J. 1, 59-61 (2022). And the Sawyers can block the Edisons.

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[4] *See also* Roy H. Wepner, *An Enablement Defense Is Disabled by the Federal Circuit*, IPWatchdog (Jan. 29, 2025), https://perma.cc/8B8J-QQZR (observing that *Entresto*'s holding allows "the patentee to extend its monopoly to drug products for which the patentee did not provide the required quid pro quo").

CONCLUSION

The petition for writ of certiorari should be granted.

Respectfully submitted,

Amit R. Vora
Counsel of Record
Hunter S. Pearl
Annaliese Cho Brellis
Kasowitz LLP
1633 Broadway
New York, New York 10019
(212) 506-1834
avora@kasowitz.com

August 22, 2025

APPENDIX

TABLE OF APPENDICES

APPENDIX A — OPINION OF THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT FILED JANUARY 10, 2025

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

2023-2218, 2023-2220, 2023-2221

IN RE: ENTRESTO (SACUBITRIL/VALSARTAN)

NOVARTIS PHARMACEUTICALS CORPORATION,

Plaintiff-Appellant,

v.

TORRENT PHARMA INC., TORRENT PHARMACEUTICALS LTD.

Defendants.

NOVARTIS PHARMACEUTICALS CORPORATION,

Plaintiff-Appellant,

v.

ALEMBIC PHARMACEUTICALS LIMITED, ALEMBIC PHARMACEUTICALS INC.,

Defendants.

Appendix A

NOVARTIS PHARMACEUTICALS CORPORATION,

Plaintiff-Appellant,

v.

MSN PHARMACEUTICALS, INC., MSN LABORATORIES PRIVATE LTD., MSN LIFE SCIENCES PRIVATE LTD.,

Defendants-Appellees,

HETERO USA, INC., HETERO LABS LIMITED, HETERO LABS LIMITED UNIT-III,

Defendants.

Decided: January 10, 2025

OPINION

Appeals from the United States District Court for the District of Delaware in Nos. 1:19-cv-01979-RGA, 1:19-cv-02021-RGA, 1:19-cv-02053-RGA, 1:19-cv-02053-RGA, 1:20md-02930-RGA, Judge Richard G. Andrews.

Before LOURIE, PROST, and REYNA, *Circuit Judges.*

LOURIE, *Circuit Judge.*

Following a three-day bench trial, the United States District Court for the District of Delaware determined that claims 1-4 of U.S. Patent 8,101,659

("the '659 patent") were not shown to be invalid for obviousness, lack of enablement, or indefiniteness, but were shown to be invalid for lack of written description. *In re Entresto (Sacubitril/Valsartan) Pat. Litig.*, No. 20-md-2930, 2023 WL 4405464, at *13, *21, *22 (D. Del. July 7, 2023) ("*Decision*"). Judgment was entered on those grounds. Appellant Novartis Pharmaceuticals Corporation ("Novartis") challenges the district court's written description determination. Appellees MSN Pharmaceuticals, Inc., MSN Laboratories Private Ltd., and MSN Life Sciences Private Ltd. (collectively, "MSN")[1] argue that the judgment of invalidity should be affirmed, either by affirming the district court's written description determination or, alternatively, by reversing the district court's obviousness or enablement determinations.

For the following reasons, we reverse the district court's determination that the claims lack an adequate written description, and we affirm its determinations that the claims were not shown to be invalid as either non-enabled or obvious.

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1. Of the presently named defendants, only MSN participates in this appeal. Each of Hetero USA Inc., Hetero Labs Limited, Hetero Labs Limited Unit-III (collectively, "Hetero"), Torrent Pharma Inc., Torrent Pharmaceuticals Ltd. (collectively, "Torrent") have since settled their disputes with Novartis. *See* ECF Nos. 57, 58, 61, 78. Moreover, Novartis indicated that it noted an appeal in its case against Alembic Pharmaceuticals, Ltd. and Alembic Pharmaceuticals, Inc. (collectively, "Alembic") only "[o]ut of an abundance of caution." ECF No. 15 at 2 n.1. But because the case against Alembic is stayed and because Alembic did not participate in the trial on the merits, "Alembic is not an appellee here." *Id.*

Appendix A

BACKGROUND

I

In 2015, the U.S. Food and Drug Administration ("FDA") approved the New Drug Application ("NDA") for a combination therapy of valsartan and sacubitril, which Novartis markets and sells under the brand name Entresto®. Entresto includes valsartan and sacubitril in a specific form known as a "complex," which combines the two drugs into a single unit-dose-form through weak, non-covalent bonds. Valsartan is an angiotensin receptor blocker ("ARB") that prevents angiotensin II from binding to its receptor, thereby reducing the blood-vessel-constricting effects of angiotensin II, a naturally occurring hormone. Sacubitril is a neutral endopeptidase ("NEP") inhibitor that, like valsartan, reduces blood vessel constriction, but does so through a mechanism-of-action not involving angiotensin. At the time of its initial approval, Entresto was indicated to treat heart failure with reduced ejection fraction. In 2019, Entresto was additionally approved for the treatment of heart failure in children, and, in 2021, it was approved for the treatment of heart failure with a preserved ejection fraction. In 2023 alone, sales of Entresto in the United States totaled more than $3 billion.

Entresto is protected by a number of patents, including the '659 patent, which was timely listed in the Orange Book. The '659 patent has a priority date of January 17, 2002, and will expire on January 15, 2025, due to the grant of Patent Term Extension ("PTE"). The

'659 patent explains that, at the time of the invention, "the most widely studied" drugs to treat hypertension and heart failure were a class of drugs called angiotensin converting enzyme ("ACE") inhibitors. '659 patent, col. 1 ll. 55-61. Like valsartan and other ARBs, ACE inhibitors' function involves angiotensin. But instead of preventing angiotensin II from binding to its receptor, ACE inhibitors reduce vasoconstriction by blocking the initial formation of angiotensin II. *See Decision,* at *4. The '659 patent explains that, although ACE inhibitors prevent the formation of vasoconstrictive angiotensin II, research showed that the effects of those drugs may be attributed to other pathways. '659 patent, col. 2 ll. 6-9. The patent also sets forth that, at the time of the invention, research showed that NEPs, like sacubitril, can lower blood pressure and exert effects such as diuresis. *Id.* col. 2 ll. 39-41. Sacubitril had been discovered and patented by a predecessor to Novartis in 1992, but as of the time of the invention, it "had never been administered to humans or tested in an animal model of hypertension and heart failure." *Decision,* at *7.

The patent explains that, because "the nature of hypertensive vascular diseases is multifactorial[,] . . . drugs with different mechanisms of action have been combined." '659 patent, col. 2 ll. 65-67. But "just considering any combination of drugs having different modes of action does not necessarily lead to combinations with advantageous effects." *Id.* col. 2 l. 67-col. 3l. 3. Accordingly, the inventors of the '659 patent sought to discover a "more efficacious combination therapy which has less deleterious side effects." *Id.* col. 3 ll. 3-5. And as the

specification explains, it was "surprisingly [ ] found that[ ] a combination of valsartan and a NEP inhibitor achieves greater therapeutic effect than the administration of valsartan, ACE inhibitors or NEP inhibitors alone." *Id.* col. 6 ll. 41-44.

The '659 patent has four claims, all of which are asserted here. Claim 1, the sole independent claim, recites:

> 1. A pharmaceutical composition comprising:
>
> > (i) the AT 1-antagonist valsartan or a pharmaceutically acceptable salt thereof;
> >
> > (ii) the NEP inhibitor [sacubitril] or [sacubitrilat][2] or a pharmaceutically acceptable salt thereof; and
> >
> > (iii) a pharmaceutically acceptable carrier;
>
> wherein said (i) AT 1-antagonist valsartan or pharmaceutically acceptable salt thereof and said (ii) NEP inhibitor [sacubitril] or

2. Sacubitrilat is the active metabolite of the prodrug sacubitril, which means that, when sacubitril is ingested into the body, it is metabolized to sacubitrilat. *Decision,* at *1 n.3. The parties and district court used the term "sacubitril" to refer collectively to sacubitril, sacubitrilat, and their pharmaceutically acceptable salts. *Id.* Unless it is otherwise clear from context, we follow that convention here.

> [sacubitrilat] or a pharmaceutically acceptable salt thereof, are administered in combination in about a 1:1 ratio.

'659 patent, col. 16 ll. 17-33. Claim 2 recites that the valsartan and the NEP inhibitor "are administered in amounts effective to treat hypertension or heart failure," *id.* col. 16 ll. 34-41; claim 3 recites that the NEP inhibitor is sacubitril, *id.* col. 16 ll. 42-45; and claim 4, which depends from claim 3, recites that the composition is in the form of a capsule or tablet, *id.* col. 16 ll. 46-47. On appeal, the validity of all of the claims rests on the same bases, so we will not treat them separately.

II

In 2019, MSN, among other generic manufacturers, submitted an Abbreviated New Drug Application ("ANDA") seeking FDA approval to market and sell a generic version of Entresto. Novartis sued MSN and the other generic manufacturers, alleging that the filing of the ANDA directly infringed claims 1-4 of the '659 patent. Those cases were consolidated in multidistrict litigation in Delaware and proceeded to discovery.

A. Claim Construction

At claim construction, the parties disputed only a single term of the '659 patent: "wherein said [valsartan and sacubitril] are administered *in combination*." *See In re Entresto (Sacubitril/Valsartan) Pat. Litig.*, No. 20-md-2930, 2021 WL 2856683, at *3 (D. Del. July 8, 2021)

("*Claim Construction Decision*") (emphasis added). MSN argued that the term limited the claim to administration of the active agents valsartan and sacubitril "as two separate components." *Id.* As context for that position, according to MSN, the accused generic product, like Entresto, comprises a complex of non-covalently bonded valsartan and sacubitril. MSN Br. 1. Accordingly, if the claims were read to require the valsartan and sacubitril to be administered as separate components (*i.e.*, in a non-complexed form, such as a physical mixture), then MSN's generic product would not infringe the '659 patent. For its part, Novartis argued that the claim was not so limited, and that the term should be given its plain and ordinary meaning. *See Claim Construction Decision,* at *3.

The district court agreed with Novartis and gave the term its plain and ordinary meaning: "wherein said [valsartan and sacubitril] are administered in combination." *Id.* In rejecting MSN's proposal, the court observed that the intrinsic record "is silent on whether sacubitril and valsartan must be separate (and not complexed)." *Id.* It explained that "the absence of any indication in the written description that the patentee limited its invention solely to separate compounds means, in context, that a person of ordinary skill in the art [ ] would not read the claims as so limited." *Id.* The court found that the representations Novartis had made to the U.S. Patent and Trademark Office ("the Patent Office") to obtain PTE further bolstered that conclusion. *Id.* Specifically, Novartis told the Patent Office that the claims of the '659 patent recite compositions that include Entresto, a drug that includes "non-separate, complexed valsartan and sacubitril." *Id.*; *see* Novartis Br. 16. The

court found that a person of ordinary skill in the art would have given that evidence at least some weight in understanding the meaning of the disputed term. *Claim Construction Decision,* at *3.

Based in part on those representations to the Patent Office, MSN argued that Novartis's position – that the plain and ordinary meaning of the claim scope encompasses valsartan-sacubitril complexes – would render the claims invalid for lack of written description and enablement because the specification nowhere describes such complexes. *Id.* at *4. The court rejected this argument, finding "no basis to believe that the construction [the court] adopt[ed was] necessarily consigning the asserted claims to a judgment of invalidity." *Id.* After claim construction, MSN stipulated to infringement of the asserted claims. *Decision,* at *1.

B. Bench Trial

The case proceeded to a three-day bench trial on the issues of obviousness, lack of written description, and non-enablement.[3] *Id.*

1. Obviousness

At trial, MSN set forth two theories of obviousness. First, it argued that a person of ordinary skill in the art

3. MSN also argued the claims were invalid as indefinite. Finding that MSN raised that argument only in a footnote of its opening post-trial brief, the district court deemed the argument forfeited. *Id.* at *22. Neither party addresses indefiniteness on appeal, so we too do not consider it.

would have been motivated to modify a prior art ARB-NEP inhibitor combination therapy – specifically, one using the ARB irbesartan and an NEP inhibitor named "SQ 28,603" – with valsartan and sacubitril to arrive at the claimed invention. *Id.* at *10. Alternatively, MSN argued that a person of ordinary skill in the art would have been motivated to individually select and combine sacubitril and valsartan from two different prior-art references to arrive at the claimed invention. *Id.* The court was unpersuaded by both theories.

Although the court found persuasive MSN's argument that a person of ordinary skill in the art would have understood "that the combination of an ARB (irbesartan) and a NEP[inhibitor] (SQ 28,603) achieved synergistic results," the court ultimately concluded that, even if a person of ordinary skill in the art would have been motivated to pursue an ARB-NEP inhibitor combination, MSN "fail[ed] to provide clear and convincing evidence that a [person of ordinary skill in the art] would have been motivated to select the ARB valsartan and the NEP[inhibitor] sacubitril specifically." *Id.* Indeed, the court found that, as of 2002, sacubitril "had never been administered to humans or tested in an animal model of hypertension and heart failure," and that, of the NEP inhibitors that had been so tested, the results had been "discouraging." *Id.*

In rejecting MSN's challenges, the court further noted that none of the prior art "combined valsartan with sacubitril, sacubitril with an ARB, or valsartan with a[n] NEP[inhibitor]." *Id.* at *12. It also observed

that neither valsartan nor sacubitril were considered promising treatments for cardiac conditions in 2002. *Id.* Most importantly, in the court's view, was "the fact that a large number of hypertension and heart failure drugs and drug classes were known in 2002 – including multiple ARBs and a myriad of NEP[inhibitors] – with no clear hierarchy within the ARB and NEP[inhibitor] classes and no available information pointing directly at the claimed valsartan-sacubitril combination." *Id.* The court further rejected MSN's "obvious-to-try" theory on the grounds that there was a "surfeit of potentialities with respect to drug combinations for heart failure and hypertension treatment," such that MSN's obviousness theory hinged on impermissible hindsight. *Id.* at *13.

Accordingly, the court determined that MSN had not shown by clear and convincing evidence that the claims of the '659 patent were invalid as obvious. *Id.*

2. Written Description and Enablement

The court then turned to the issues of written description and enablement. Guided by the understanding that the court had "construed the asserted claims to cover valsartan and sacubitril as a physical combination and as a complex," *id.* at *17, the parties' dispute centered on whether the '659 patent was required to enable and describe such complexes. MSN argued that it was, since a patent must enable and describe the full scope of the claims. *E.g., id.* at *17, *21. Novartis disagreed, arguing that a complex of valsartan and sacubitril was an after-arising invention that need not have been enabled or described.

E.g., id. at *18-19. More specifically, Novartis contended that its "later, nonobvious discovery of valsartan and sacubitril in the form of a complex should not invalidate the '659 patent claims to Novartis's earlier invention: the novel combination of valsartan and sacubitril." J.A. 4219. The court agreed with Novartis on the issue of enablement, but with MSN on the issue of written description.

With respect to enablement, the court determined that, because enablement is judged as of the priority date, later-existing state of the art may not be properly considered in the enablement analysis. *Decision,* at *19 (relying on *In re Hogan,* 559 F.2d 595 (CCPA 1977); *Plant Genetic Sys., N.V. v. DeKalb Genetics Corp.,* 315 F.3d 1335 (Fed. Cir. 2003); *Chiron Corp. v. Genentech, Inc.,* 363 F.3d 1247 (Fed. Cir. 2004)). And because complexes of valsartan and sacubitril were unknown in the art in 2002, the court determined that they need not have been enabled in the '659 patent. *Id.* at *20. The court further found that MSN had failed to establish that pharmaceutical complexes, more generally, were known or were nascent technology as of the 2002 priority date. *Id.* at *20-21. Accordingly, the court determined that MSN had failed to establish that the claims of the '659 patent were invalid for lack of enablement.

The court reached the opposite conclusion with respect to written description. Relying primarily on *Chiron,* the court found that "the facts that helped [Novartis] with respect to enablement proved fatal for written description." *Id.* at *21. Specifically, because it was undisputed that complexes were unknown to a

person of ordinary skill in the art, "'[Novartis] scientists, by definition, could not have possession of, and disclose, the subject matter of [such complexes]' in 2002, and therefore, 'axiomatically, [Novartis] cannot satisfy the written description requirement' for such complexes." *Id.* at *22 (quoting *Chiron,* 363 F.3d at 1255 (first and second alteration in original)). Thus, the court found the claims invalid for lack of written description and entered judgment on that basis.

Novartis timely appealed. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

Novartis challenges the district court's findings on written description. MSN counters that, even if the claims are supported by adequate written description, the judgment of invalidity should be affirmed by reversing the district court's determinations on obviousness and enablement. We address each issue in turn.

I

We begin with written description. The issue on appeal is whether the '659 patent describes what is claimed, viz., a pharmaceutical composition comprising valsartan and sacubitril administered "in combination." The issue is *not* whether the '659 patent describes valsartan-sacubitril complexes. Because the '659 patent does not claim valsartan-sacubitril complexes, those complexes need not have been described.

As we have long recognized, "[t]he invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" *Vas-Cath Inc. v. Mahurkar,* 935 F.2d 1555, 1564 (Fed. Cir. 1991). "A specification adequately describes an invention when it 'reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.'" *Juno Therapeutics, Inc. v. Kite Pharma, Inc.,* 10 F.4th 1330, 1335 (Fed. Cir. 2021) (quoting *Ariad Pharms., Inc. v. Eli Lilly & Co.,* 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc)). The scope of what is claimed (and must be adequately described) is, in turn, determined through claim construction. *Phillips v. AWH Corp.,* 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) ("It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled a right to exclude." (internal quotation marks and citation omitted)).

Recall that, at claim construction, MSN sought – as accused infringers often do – a construction that would exclude from infringement the accused product: a valsartan-sacubitril complex. The court ultimately rejected MSN's proposed construction because the '659 patent "is silent on whether sacubitril and valsartan must be separate (and not complexed)." *Claim Construction Decision,* at *3. The term was therefore given its plain and ordinary meaning: "wherein said [valsartan and sacubitril] are administered in combination." *Id.*

That invention is plainly described throughout the specification. For example, the opening sentence of the detailed description provides that "the present invention

relates to pharmaceutical *combinations comprising valsartan* . . . and *a NEP inhibitor* . . . and pharmaceutical compositions comprising them." '659 patent col. 3 ll. 20-25 (emphases added); *see also id.* col. 6 ll. 65-67 ("It can be shown that *combination therapy with valsartan and a NEP inhibitor* results in a more effective anti-hypertensive therapy[.]" (emphasis added)). The patent further specifies that the NEP inhibitor used in combination with valsartan can be sacubitril. *Id.* col. 7 ll. 33-36 ("Representative studies are carried out with a *combination* of valsartan and [sacubitril.]" (emphasis added)). And it further teaches that "[a] therapeutically effective amount of each of the component[s] *of the combination of the present invention* may be administered simultaneously or sequentially in any order." *Id.* col. 10 ll. 57-59 (emphasis added). Those disclosures (and more) plainly show that the inventors had possession of a pharmaceutical composition comprising valsartan and sacubitril administered "in combination." Indeed, even MSN's expert conceded that the '659 patent adequately discloses administration of valsartan and sacubitril in combination as a physical mixture. *See* J.A. 3322. Thus, the claims are supported by an adequate written description.[4]

The fact that the '659 patent does not describe a complexed form of valsartan and sacubitril does not affect the validity of the patent. That complex – not discovered until four years after the priority date of the '659 patent – is not what is claimed. By stating that the claims were

4. MSN does not argue that the other limitations of the asserted claims are not adequately described. Accordingly, we focus our inquiry on only the disputed claim term: "in combination."

"*construed to cover* complexes of valsartan and sacubitril," the district court erroneously conflated the distinct issues of patentability and infringement, which led it astray in evaluating written description. *Decision,* at *15 (emphasis added). Written description asks whether that which is claimed is adequately described. As we have explained:

> [C]laims are not construed "to cover" or "not to cover" the accused [product]. That procedure would make infringement a matter of judicial whim. It is only *after* the claims have been *construed without reference to the accused device* that the claims, as so construed, are applied to the accused device to determine infringement.

SRI Int'l v. Matsushita Elec. Corp. of America, 775 F.2d 1107, 1118 (Fed. Cir. 1985).

Here, after claim construction, MSN stipulated to infringement of the as-construed claims.[5] In light of that

5. To the extent MSN maintains that the claims were construed to *claim* valsartan-sacubitril complexes (*i.e.,* to the extent MSN alleges that its stipulation of infringement was made on that basis), that construction would have been error. "Claim interpretation requires the court to ascertain the meaning of the claim to one of ordinary skill in the art *at the time of invention.*" *SmithKline Beecham Corp. v. Apotex Corp.,* 403 F.3d 1331, 1338 (Fed. Cir. 2005) (emphasis added); *see Phillips,* 415 F.3d at 1313. Because valsartan-sacubitril complexes were undisputedly unknown at the time of the invention, *see Decision,* at *20, the '659 patent could not have been construed as claiming those complexes as a matter of law.

stipulation and the fact that the '659 patent does not claim valsartan-sacubitril complexes, any further issue regarding such complexes is not before us.

For those reasons, we hold that the district court clearly erred in finding that claims 1-4 of the '659 patent are invalid for lack of written description. The patent has an adequate written description of what is claimed.

II

We affirm the district court's enablement determination for reasons similar to those that led us to reverse its written description determination: a specification must only enable the *claimed* invention. *See Amgen Inc. v. Sanofi,* 598 U.S. 594, 610, 143 S.Ct. 1243, 215 L.Ed.2d 537 (2023).

The invention of the '659 patent, as construed by the district court, is a composition in which valsartan and sacubitril are administered "in combination." As explained above, the patent does not claim as its invention valsartan-sacubitril complexes. Indeed, Novartis obtained separate, later patents to such complexes. *See Claim Construction Decision,* at *1 (noting that "[s]everal years" after filing the '659 patent, "Novartis developed a novel compound comprising non-covalently bound valsartan and sacubitril salts," which are disclosed in U.S. Patents 8,877,938 and 9,388,134).

The district court correctly recognized that valsartan-sacubitril complexes, which include the claimed invention along with additional unclaimed features, are part of a "later-existing state of the art" that "may not be properly considered in the enablement analysis." *Decision,* at *19; *see In re Hogan,* 559 F.2d 595, 606 (CCPA 1977) (holding that enablement must be judged in light of the state of the art at the time of filing); *Plant Genetic,* 315 F.3d at 1340 ("[O]ne [can]not use a later-existing state of the art to invalidate a patent that was enabled for what it claimed at the time of filing."). As our predecessor court explained:

> The use of a subsequently-existing improvement to show lack of enablement in an earlier-filed application on the basic invention would preclude issuance of a patent to the inventor of the thing improved, and in the case of issued patents, would invalidate all claims (even some "picture claims") therein. Patents are and should be granted to later inventors upon unobvious improvements. Indeed, encouragement of improvements on prior inventions is a major contribution of the patent system and the vast majority of patents are issued on improvements. It is quite another thing, however, to utilize the patenting or publication of later existing improvements to "reach back" and preclude or invalidate a patent on the underlying invention.

Hogan, 559 F.2d at 606. That is precisely the case here. The later-discovered valsartan-sacubitril complexes,

which arguably may have improved upon the "basic" or "underlying" invention claimed in the '659 patent, cannot be used to "reach back" and invalidate the asserted claims.

Thus, because the '659 patent does not expressly claim complexes, and because the parties do not otherwise dispute that the '659 patent enables that which it does claim, we affirm the district court's determination that MSN failed to show that the claims are invalid for lack of enablement.

III

Finally, we turn to obviousness. "Obviousness is a question of law based on underlying findings of fact." *Adapt Pharma Operations Ltd. v. Teva Pharms. USA, Inc.*, 25 F.4th 1354, 1364 (Fed. Cir. 2022) (citations omitted). Whether a person of ordinary skill in the art would have been motivated to combine the prior-art references to arrive at the claimed invention is a factual question we review for clear error. *Id.*

We see no clear error warranting reversal of the district court's obviousness analysis. The district court found that, even if a person of ordinary skill in the art had been motivated to provide an ARB-NEP inhibitor combination therapy, there was no motivation in the relied-upon prior art to combine valsartan and sacubitril, let alone with any reasonable expectation of success. As of 2002, sacubitril was one of over 100 known NEP inhibitors, it had never been administered to humans or

animals, and the clinical results of other NEP inhibitors in hypertension and heart failure patients had been "discouraging." *See Decision,* at *7.

Those facts, as the district court acknowledged, distinguish this case from *Nalpropion Pharmaceuticals, Inc. v. Actavis Laboratories FL, Inc.*, 934 F.3d 1344 (Fed. Cir. 2019), and *BTG International Ltd. v. Amneal Pharmaceuticals LLC,* 923 F.3d 1063 (Fed. Cir. 2019), on which MSN relies. In each of those cases, the prior art showed that the claimed drugs "were both together and individually considered promising . . . treatments at the time [of the invention]." *BTG,* 923 F.3d at 1074; *see Nalpropion Pharms.*, 934 F.3d at 1354 (concluding that, because the prior art taught that each drug could cause weight loss effects, "a person of ordinary skill would have been motivated to combine them" to promote weight loss). That is not the case here, at least with respect to sacubitril. We therefore agree with the district court that MSN's obviousness theories impermissibly use valsartan and sacubitril as a starting point and "retrace[ ] the path of the inventor with hindsight." *Decision,* at *13 (citation omitted).

Accordingly, because we see no errors in the district court's factual findings or application of the law, we affirm the district court's determination that MSN failed to establish that the claims would have been obvious.

Appendix A

CONCLUSION

We have considered the parties' remaining arguments and find them unpersuasive. For the foregoing reasons, we reverse the district court's finding that the claims lack adequate written description, and we affirm its determinations that the claims were not shown to have been obvious or non-enabled.

AFFIRMED IN PART, REVERSED IN PART.

COSTS

Costs to Novartis.

APPENDIX B — OPINION OF THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF DELAWARE, FILED JULY 7, 2023

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

MDL Nos. 20-2930-RGA
C.A. Nos. 19-1979-RGA
19-2021-RGA
19-2053-RGA

IN RE ENTRESTO (SACUBITRIL/VALSARTAN) PATENT LITIGATION

Filed July 7, 2023

TRIAL OPINION

/s/ Richard G. Andrews
ANDREWS, U.S. DISTRICT JUDGE:

This case is part of the multi-district litigation of patent infringement claims regarding Entresto® (sacubitril/valsartan). *In re Entresto (Sacubitril/Valsartan) Patent Litigation*, C.A. No. 20-md-02930 ("*In re Entresto*"). Novartis brought this action against Defendants for infringement of U.S. Patent 8,877,938 (the "'938 Patent"), 9,388,134 (the "'134 Patent"), 8,101,659 (the "'659 Patent") and 8,796,331 (the "'331 Patent"). Only the '659 Patent is at issue in this opinion.

The parties dispute whether claims 1–4 of the '659 Patent (collectively, "the asserted claims") are invalid for obviousness, lack of written description, non-enablement,

and indefiniteness. On September 12, 2022, I held a three-day bench trial.[1] (D.I. 595–597).[2]

I have considered the parties' post-trial submissions (D.I 599, 600, 618, 619, 620). Having considered the documentary evidence and testimony, I make the following findings of fact and conclusions of law pursuant to Federal Rule of Civil Procedure 52(a).

I. BACKGROUND

Novartis is the holder of New Drug Application ("NDA") No. 207620 for Entresto®, a tablet containing the active ingredients sacubitril[3] and valsartan.[4]

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1. The '331 Patent was also asserted in that trial. (D.I. 521-1, Ex. 1 at 11; D.I. 537). The '331 Patent's expiration date is January 14, 2023, and the '331 Patent is subject to pediatric exclusivity until July 14, 2023. (D.I. 601 at 3). The parties agreed that I need not reach a decision regarding the validity of that patent. (*Id.*). I held separate trials addressing the '938 Patent and the '134 Patent. (D.I. 604–607 (infringement), D.I. 608–609 (invalidity)).

2. Unless otherwise specified, the docket referred to is C.A. No. 1:19-cv-01979.

3. The chemical name for sacubitril is N-(3-carboxy-1-oxopropyl)-(4S)-(p-phenylphenylmethyl)-4-amino-2R-methylbutanoic acid ethyl ester. (D.I. 521-1, Ex. 1 at 6). Sacubitrilat—also referred to by the chemical name (2R,4S)-5-biphenyl-4-yl-4- (3-carboxypropionyl amino)-2-methyl-pentanoic acid—is the active metabolite of the prodrug sacubitril. (*Id.*). The term "sacubitril" herein includes both sacubitril and sacubitrilat unless otherwise specified.

4. The chemical name for valsartan is (S)—N-(1-carboxy-2-methylprop-1-yl)-N-pentanoyl-N-[2'-(1H-tetrazol-5-yl)-biphenyl-4-yl-methyl]amine. (D.I. 521-1, Ex. 1 at 6).

(D.I. 521-1, Ex. 1 at 5–6). The FDA has approved Entresto® "to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction," "for treatment of symptomatic heart failure with systemic left ventricular systolic dysfunction in pediatric patients aged one year and older," and "to reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure." (*Id.*).

The '659 Patent is listed in the FDA's Orange Book for Entresto®. (*Id.* at 11). The '659 Patent's undisputed priority date is January 17, 2002. (*Id.* at 11). The patent generally relates to compositions of valsartan and sacubitril and the use of such compositions to treat hypertension and heart failure. Defendants submitted Abbreviated New Drug Application ("ANDAs") for approval to market generic versions of Entresto®. (*Id.* at 7–11). Plaintiff initiated this lawsuit, asserting infringement of claims 1–4 of the '659 Patent ("the asserted claims") against all Defendants. (*Id.* at 2, 11). Defendants stipulated to infringement of the asserted claims (*id.* at 17–18), but Defendants assert that the claims are invalid.

II. ASSERTED CLAIMS

The claims at issue are claims 1–4 of the '659 Patent ("the asserted claims"). (D.I. 521-1, Ex. 1 at 11).

Appendix B

Claim 1 reads:

1. A pharmaceutical composition comprising:

   (i) the AT 1-antagonist valsartan or a pharmaceutically acceptable salt thereof;

   (ii) the NEP inhibitor N-(3-carboxy-1-oxopropyl)-(4S)-(p-phenylphenylmethyl)-4-amino-2R-methylbutanoic acid ethyl ester or (2R,4S)-5-biphenyl-4-yl-4(3-carboxy-propionyl amino)-2-methyl-pentanoic acid or a pharmaceutically acceptable salt thereof; and

   (iii) a pharmaceutically acceptable carrier;

   wherein said (i) AT 1-antagonist valsartan or pharmaceutically acceptable salt thereof and said (ii) NEP inhibitor N-(3-carboxy-1-oxopropyl)-(4S)-(p-phenylphenylmethyl)-4-amino-2R-methylbutanoic acid ethyl ester or (2R,4S)-5-biphenyl-4-yl-4(3-carboxy-propionyl amino)-2-methyl-pentanoic acid or pharmaceutically acceptable

> salt thereof, are administered in combination in about a 1:1 ratio.

(*Id.* at 11–12).

Claim 2 depends from claim 1 and reads:

> 2. The pharmaceutical composition of claim 1, wherein said (i) AT 1-antagonist valsartan or a pharmaceutically acceptable salt thereof and said (ii) NEP inhibitor N-(3-carboxy-1-oxopropyl)-(4S)-(p-phenylphenylmethyl)-4-amino-2R-methylbutanoic acid ethyl ester or (2R,4S)-5-biphenyl-4-yl-4(3-carboxy-propionyl amino)-2-methyl-pentanoic acid or pharmaceutically acceptable salt thereof are administered in amounts effective to treat hypertension or heart failure.

(*Id.* at 12).

Claim 3 depends from claim 1 and reads:

> 3. The pharmaceutical composition of claim 1 wherein (ii) said NEP inhibitor is N-(3-carboxy-1-oxopropyl)-(4S)-(p-phenylphenylmethyl)-4-amino-2R-methylbutanoic acid ethyl ester.

(*Id.*)

Claim 4 depends from claim 3 and reads:

> 4. The pharmaceutical composition of claim 3 in the form of a capsule or tablet.

(*Id.*)

III. OBVIOUSNESS

A. Legal Standard

A patent claim is invalid as obvious under 35 U.S.C. § 103 "if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains." 35 U.S.C. § 103; *see also KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406–07, 127 S. Ct. 1727, 167 L. Ed. 2d 705 (2007). "As patents are presumed valid, a defendant bears the burden of proving invalidity by clear and convincing evidence." *Shire, LLC v. Amneal Pharms., LLC*, 802 F.3d 1301, 1306 (Fed. Cir. 2015) (citations omitted). "Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined." *KSR*, 550 U.S. at 406 (internal citation and quotation marks omitted).

A court is required to consider secondary considerations, or objective indicia of nonobviousness, before reaching an obviousness determination, as a "check against hindsight bias." *See In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1078–79 (Fed. Cir. 2012). "Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17–18, 86 S. Ct. 684, 15 L. Ed. 2d 545 (1966).

B. Findings of Fact

1. Level of Ordinary Skill in the Art

The parties dispute whether a person of ordinary skill in the art ("POSA") would have knowledge and experience in solid-state chemistry. (*See* D.I. 599 at 5; D.I. 600 at 2–3; D.I. 618 at 35–38; D.I. 619 at 30–31; D.I. 620 at 11). The parties do not argue that the outcome of the obviousness analysis would change depending on whose position I adopt. Instead, the parties assert that their dispute is relevant to the enablement and written description analyses. (*See, e.g.*, D.I. 619 at 30–31 (framing POSA definition as § 112 issue); D.I. 620 at 10 (same)). Accordingly, I discuss the parties' disagreement, and my conclusions, in that portion of this opinion. *See infra* Section IV.A.2.

Ultimately, I think that Plaintiff's definition of a POSA is the correct definition. I therefore conclude that a

POSA with respect to the '659 Patent is "a medical doctor or Ph.D. in medicinal chemistry or a related field who is interested in developing new drugs for heart failure and hypertension, and would not have had experience, familiarity, or interest in solid-state chemistry." (D.I. 619 at 30–31; Tr. at 47:17–23 (Dr. Fintel); *Id.* at 279:24–280:8 (Dr. Spinale); *Id.* at 399:8–21, 401:8–402:9 (Dr. Klibanov)).

2. Scope and Content of the Prior Art

a. Background

i. Heart Failure and Hypertension

Hypertension is "abnormally high arterial blood pressure"—a disease of the arteries. (Tr. at 281:4–10 (Dr. Spinale); JTX-133 at 308). Heart failure is a "condition in which the heart is unable to pump blood at an adequate rate or an adequate volume"—a disease of the heart muscle. (Tr. at 11–14 (Dr. Spinale); JTX-133 at 278). I agree with Plaintiff that, in 2002, a POSA understood these disease states to be distinct from each other. (D.I. 619 at 2; Tr. at 282:4–10 (Dr. Spinale)). Hypertension and heart failure were studied using different research methodologies (Tr. at 282:21–283:9 (Dr. Spinale)); entailed different goals and guidelines with respect to treatment (*id.* at 284:6–10 (Dr. Spinale)); and were sometimes treated using drugs that ameliorate one condition, but not the other. (*Id.* at 283:22–284:5 (Dr. Spinale)).

I also agree with Defendants, however, that a POSA would also have understood that these disease states are

related to each other in significant ways. (*See* D.I. 600 at 15). Hypertension is the most common clinical condition closely associated with and leading to heart failure. (Tr. at 50:19–51:8 (Dr. Fintel); JTX-211 at 1557). Over the decades prior to the priority date, it was known that controlling blood pressure helps to prevent heart failure (*id.* at 51:9–22 (Dr. Fintel)). Multiple drug categories developed to treat hypertension were prescribed to treat heart failure as well. (*Id.* at 52:5–24 (Dr. Fintel)).

ii. Combination Treatment for Heart Failure and Hypertension

Defendants argue that, in 2002, combination treatment for hypertension and heart failure was standard. (D.I. 600 at 17). Plaintiff argues to the contrary. (D.I. 619 at 3–4). Plaintiff cites Dr. Spinale's testimony that certain combination treatments could be ineffective or result in adverse effects. (Tr. 304:4–17 (Dr. Spinale)). Dr. Spinale admitted, however, that combining drugs from different classes to treat hypertension (Tr. at 378:6–10 (Dr. Spinale)) and heart failure (*id.* at 378:2–5 (Dr. Spinale)) was standard.[5] Thus, I generally agree with Defendants that

5. Plaintiff emphasizes that neither Dr. Fintel nor Dr. Spinale testified that it was standard to treat either condition with a combination that included drugs that were not FDA-approved for a condition. (D.I. 619 at 3–4). Plaintiff does not point to any part of the trial transcript in which Dr. Fintel or Dr. Spinale were asked to opine on this subject, and I have not independently located any such testimony. Dr. Spinale testified to combination treatment, generally. (Tr. at 378:2–10 (Dr. Spinale)). Thus, I am not convinced by Plaintiff's argument with respect to FDA approval.

combination treatment was established in the field with respect to both hypertension and heart failure.

The size of the universe of potential drugs that a person skilled in the art would encounter when seeking an effective combination is relevant to the obviousness analysis. *See In re Kubin*, 561 F.3d 1351, 1361 (Fed. Cir. 2009). The more potentialities, the less likely that a particular combination is obvious. *Id.* The fewer potentialities, the more likely that a particular combination is obvious. *Id.*

Plaintiff argues that the possibilities were vast in number. (D.I. 619 at 2). I agree. If a POSA were interested in pursuing a new treatment for hypertension or heart failure as of 2002, there was a myriad of potential combinations that could be considered, including both clinically approved drugs and those that were the subject of clinical research. (Tr. at 307:16–308:12 (Dr. Spinale); *see also id.* at 52:5–24 (Dr. Fintel (listing drug categories used to treat hypertension and heart failure)); PTX-1017 (FDA-approved products to treat hypertension included multiple ACE inhibitors, alpha-blockers, ARBs, beta-blockers, calcium antagonists, diuretics, and direct vasodilators); PTX-1018 (FDA-approved products to treat heart failure included multiple ACE inhibitors, beta-blockers, diuretics, and positive inotropic agents)). Thus, this factor weighs against a finding of obviousness.

Defendants do not dispute the number of possibilities at play here. Defendants maintain, however, that good reasons existed for a POSA to pursue the combination of valsartan—an ARB—and sacubitril—a NEPi—for

heart failure and hypertension. According to Defendants, a POSA would have pursued this combination because: (1) the ARB-NEPi combination was known as of the priority date and was reported to have synergistic effects for the treatment of both conditions (D.I. 599 at 7–8); (2) ACEi-NEPi combinations were known, and the prior art suggested that replacing the ACEi with an ARB would reduce side effects associated with the ACEi (*id.*); (3) the prior art suggested that an ARB-NEPi combination could unmask the benefits of the NEPi (*id.*); (4) valsartan was a preferred ARB for heart failure and hypertension (*id.* at 8-9); and (5) sacubitril was a preferred NEPi for heart failure and hypertension (*id.* at 9–10). I address these arguments in detail below.

b. Angiotensin-Converting Enzyme Inhibitors (ACEis)

As of 2002, ACEis were used to treat hypertension and heart failure. (Tr. at 52:5–24 (Dr. Fintel)). Plaintiff contends that ACEis were the "gold standard of heart failure therapy" (D.I. 619 at 17), a characterization fairly supported by Dr. Spinale's testimony (*e.g.*, Tr. at 303:21–24) and by standard-of-care guidelines from the American College of Cardiology and the American Heart Association. (*See* JTX-366 (2001 Guidelines) at 3002 (giving ACEis a Class I recommendation—the strongest possible recommendation—for treatment of symptomatic left ventricular systolic dysfunction)).

In 2002, ACEis were understood to treat hypertension and heart failure in the following ways. Angiotensin-converting enzyme (ACE) converts the protein angiotensin

I into angiotensin II, which causes vasoconstriction and thereby raises blood pressure. (Tr. at 57:12–22 (Dr. Fintel)). ACEis block this conversion, thereby lowering blood pressure. (*Id.* at 57:14–58:12 (Dr. Fintel)). ACEis also prevent ACE from breaking down bradykinin, which can lead to an accumulation of bradykinin. (*Id.* at 59:12–18 (Dr. Fintel)). Bradykinin accumulation was believed to contribute to the beneficial effects of ACEis. (*Id.* at 131:1–131:2 (Dr. Fintel); *id.* at 315:23–316:17 (Dr. Spinale)).

Defendants assert that the accumulation of bradykinin can also lead to side effects, including a serious condition called angioedema. (D.I. 600 at 16; Tr. at 59, 12–23 (Dr. Fintel)). Plaintiff responds that a POSA would not have understood this, as the cause of angioedema was unknown as of 2002, and thus the connection between bradykinin accumulation and angioedema was inconclusive. (D.I. 619 at 17 (citing Tr. at 313:12–314:7 (Dr. Spinale); JTX-57; JTX-194)). I would not go so far. The evidence that Plaintiff cites indicates that POSA would have understood that bradykinin accumulation may play a role in angioedema. (*See, e.g.*, JTX-194 at 172 ("A great part of all reviewed reports suggest a relationship between . . . angioedema and increased levels of bradykinin.")).

In any event, I think that, even absent a clear understanding of the role of bradykinin, a POSA would understand that ACEis are associated with angioedema. While I credit Dr. Spinale's testimony that ACEis were well tolerated, with low estimated incidence of angioedema (Tr. at 312:20–313:10 (citing JTX-138, JTX-151)), the record reflects that a POSA would have been aware that

angioedema is a serious possible adverse effect of ACEi therapy, and that this was a problem that persons skilled in the art were seeking to solve. (*See, e.g.*, JTX-194 at 172 ("The incidence of angioedema is low . . . but can be considered as a potentially life-threatening adverse effect of ACE inhibitor therapy. . . . The estimated incidence is quite underestimated.")).

c. Angiotensin Receptor Blockers (ARBs) and Valsartan

ARBs were developed in the 1990s. (Tr. at 60:15–17 (Dr. Fintel)). ARBs act by blocking the interaction of angiotensin II with the ATI receptor, which ultimately decreases blood pressure. (*Id.* at 60:15–67:1 (Dr. Fintel)). In 1995, the forerunner to Novartis, Ciba-Geigy, was issued U.S. Patent No. 5,399,578 ("the '578 Patent"). (JTX-23). That patent disclosed and claimed the use of the ARB valsartan for hypertension and for "cardiac insufficiency," which a POSA would have understood to be heart failure. (Tr. at 76:3–9 (Dr. Fintel); JTX-23). In 1996, the FDA approved valsartan (Diovan®) for hypertension. (JTX-67 (Diovan® Label)). By 2002, there was "great interest" in studying ARBs for use in heart failure treatment. (Tr. at 376:16–20 (Dr. Spinale)). The emerging data was promising; for example, the 2001 Val-HeFT clinical trial concluded that the ARB valsartan "significantly reduces the combined end point of mortality and morbidity and improves clinical signs and symptoms in patients with heart failure." (JTX-60 at 1667). I credit Dr. Fintel's testimony that such studies generated "buzz" among cardiologists, who used ARBs increasingly often to

treat heart failure. (Tr. at 74:21–75:5; *see also* DTX-686 at 2:12–20 (stating that ARBs can be used for the treatment of congestive heart failure)).

A central disagreement concerns angioedema. Defendants assert that ARBs do not lead to bradykinin accumulation and therefore lack bradykinin-induced side effects, such as angioedema, that were associated with ACEis. (D.I. 600 at 17 (citing Tr. at 61:8–13 (Dr. Fintel))). I don't think this characterization is entirely accurate; as Plaintiff points out (D.I. 618 at 18), it was known that ARBs could potentially cause angioedema. (Tr. at 315:9–16 (Dr. Spinale); PTX-198 at 2167). ARBs were, however, associated with a lower relative incidence of angioedema. (JTX-151 at 831; JTX-164 at 80). Defendants contend that doctors preferred ARBs to ACEis on this basis. (D.I. 620 at 3). I do not think that ARBs were poised to surpass ACEis altogether—as Plaintiff says (D.I. 619 at 17), ACEis remained the "gold standard" in 2002. (*See* JTX-366 at 3002). But I think that a POSA would have viewed a reduced risk of angioedema as one of the benefits of the ARB class. (*See* JTX-366 at 3002 (recommending ARBs in patients who cannot be given an ACE inhibitor because of cough or angioedema)).

Six ARBs were FDA-approved for hypertension in 2002. (PTX-1017 (including, e.g., irbesartan and valsartan)). Defendants argue that valsartan was a preferred ARB for heart failure and hypertension.[6] (D.I.

6. Counter to Defendants' argument (e.g., D.I. 599 at 8), I don't think that U.S. Patent No. 6,211,217 ("the '217 Patent," which identifies Dr. Spinale as an inventor) (DTX-686) confirms that

600 at 18–20). Defendants assert that three properties distinguish valsartan from the other ARBs: potency, selectivity, and liver enzyme affinity. For potency, Defendants rely on Shetty (JTX-169), which investigated the relative potency of four ARBs and reported that valsartan was, numerically, the most potent. (*Id.* at 185). But as Plaintiff notes (D.I. 619 at 14–15), the reported difference in potency between valsartan and the second-most-potent ARB, irbesartan, was not statistically significant. (*Id.*). Furthermore, I agree with Plaintiff (*id.* at 15) that Defendants did not provide clear and convincing evidence linking potency to any clinical advantage. Thus, I do not think that Defendants' potency argument is particularly persuasive.

Neither am I convinced by Defendants' argument regarding valsartan's selectivity. Defendants rely on Malacco (JTX-118), which compared valsartan and irbesartan and reported that valsartan is more selective for the AT_1 receptor as opposed to the AT_2 receptor. (*Id.* at 790). This is a clinically advantageous property, say Defendants, because the target of an ARB is the AT_1 receptor—the receptor responsible for, e.g., the control of blood pressure—whereas the AT_2 receptor counteracts the effects of the AT_1 receptor. (D.I. 600 at 19 (citing Tr.

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valsartan was a preferred ARB for these conditions. Defendants say that the '217 Patent disclosed the use of valsartan to treat hypertension and heart failure. (D.I. 600 at 19). I disagree. That patent identified valsartan as a preferred ARB "for use in the methods of the present invention"—"reducing pericardial fibrosis and adhesion formation," not treating hypertension or heart failure. (DTX-686 at Abstract, 8:66–67).

at 66:21–67:13 (Dr. Fintel); JTX-118 at 795)). Maybe so. But as Plaintiff points out (D.I. 618 at 16), Malacco taught that this difference in selectivity did not appear to result in any differences between irbesartan and valsartan with respect to the magnitude and duration of antihypertensive efficacy. (JTX-118 at 790). The clinical relevance of Malacco's selectivity finding is therefore unclear.

As for liver enzyme affinity, Defendants point to Taavitsainen (JTX-218), which investigated potential interactions of five ARBs with various drug-metabolizing enzymes. (*Id.* at 135). Dr. Fintel explained that lower rates of interaction are clinically advantageous, as lower interaction rates suggest a lower potential for drug-drug interactions. (Tr. at 70:6–13; JTX-218 at 135). Taavitsainen reported that, compared to losartan and irbesartan, valsartan demonstrates a 5- to 30-fold lower rate of interaction with the CYP2C9 enzyme. (*Id.* at 137 (concluding that losartan and irbesartan are "the most obvious candidates to cause potentially significant interactions" with respect to this enzyme)). Counter to Defendants' assertions (D.I. 600 at 13), I do not think that Taavitsainen broadly teaches that valsartan has a lower potential for drug-drug interactions as compared to other ARBs. Indeed, it is unclear to me what a POSA would conclude from Taavitsainen, as Defendants decline to discuss Taavitsainen's findings with respect to the other ARBs and enzymes investigated.

In sum, I agree with Plaintiff (D.I. 618 at 16) that Defendants have failed to show that a POSA would view valsartan as a "preferred ARB" by virtue of its potency,

selectivity, or liver enzyme affinity. There was no clear hierarchy of ARBs. Indeed, as Plaintiff points out (D.I. 619 at 16), when valsartan and irbesartan were explicitly compared to each other in a clinical context, valsartan ranked beneath irbesartan; for example, Mancia (JTX-119) taught that irbesartan demonstrated superior results with respect to blood pressure reduction in hypertension patients. (JTX-119; Tr. at 301:19–23 (Dr. Spinale)).

d. Neutral Endopeptidase Inhibitors (NEPis) and Sacubitril

NEPis are another class of agent that can result in vasodilation. (Tr. at 62:8–17 (Dr. Fintel)). In 2002, the universe of candidate NEPis was large. Over 100 NEPis had been identified, and approximately 50 NEPis had been studied in animal models and demonstrated preclinical activity. (Tr. at 440:10–441:6 (Dr. Klibanov); PTX-1021 (summary exhibit of NEPis disclosed in the prior art); Tr. at 297:21–298:9 (Dr. Spinale); *id.* at 126:23–127:1 (Dr. Fintel)). One such NEPi was sacubitril. Sacubitril had not, as of 2002, been administered to humans. (Tr. at 125:22–126:6 (Dr. Fintel)).

Defendants argue that sacubitril was a preferred NEPi for heart failure and hypertension. (D.I. 600 at 20; D.I. 599 at 9–10). In support of this position, Dr. Fintel relied on two prior art references: U.S. Patent No. 5,217,996 ("the '996 Patent") (JTX-362) and Ksander (JTX-352). (Tr. at 126:7–9). The '996 Patent was filed in 1992 by Ciba-Geigy. (Tr. at 91:2–4 (Dr. Fintel); *Id.* at 299:20–24 (Dr. Spinale)). That patent disclosed the NEPi

sacubitril and its recommended doses, claimed the use of sacubitril for "treating cardiovascular disorders," and explained that such disorders include hypertension and heart failure. (JTX-362 at 1:22–28, 11:7–12, claim 11). It did not compare sacubitril to the other NEPis that were known at the time. (Tr. at 297:21–298:9 (Dr. Spinale)).

Ksander disclosed Ciba-Geigy's efforts "to identify novel NEP inhibitors with superior pharmacologic properties" compared to candidate NEPis that had already been studied. (JTX-352 at 1689). To this end, Ksander synthesized and evaluated 31 NEPis and reported that, of these compounds, sacubitrilat[77] was the most potent. (*Id.* at 1692). Ksander also reported that sacubitrilat's potency is similar to that of two known NEPis (thiorphan and CGS 24,592). (Tr. at 441:8–442:15 (Dr. Klibanov); JTX-352 at 1693). Ksander cited an article concerning the hypertensive and renal activity of another known NEPi—SQ 28,603 (JTX-352 at 1689, 1699), which is the NEPi used in the single ARB-NEPi combination disclosed in the prior art. *See infra* Section III.B.2.e.i. This article was one of dozens of references that Ksander cited. (*See* JTX-352 at 1699–700). Neither Dr. Fintel nor Dr. Spinale testified that SQ 28,603 was one of the NEPis that Ksander compared to sacubitril or sacubitriliat, nor have the parties cited any prior art suggesting that sacubitril or sacubitrilat is more potent than SQ 28,603.

In 1997, Novartis abandoned the '996 Patent, and no one pursued further research with sacubitril between

7. Sacubitrilat is the claimed active metabolite of sacubitril into which sacubitril converts *in vivo*. (Tr. at 90:2–11 (Dr. Fintel); D.I. 521-1, Ex. 1 at 6).

1997 and 2002. (Tr. at 300:12–18 (Dr. Spinale)). As of 2002, sacubitril had never been administered to humans or tested in an animal model of hypertension and heart failure. (Tr. at 125:22–126:6 (Dr. Fintel)). Other NEPis, however, had been clinically tested in hypertension and heart failure patients, and the results were discouraging. For example, Cleland (JTX-56) reported that the NEPi ecadotril failed to improve heart failure symptoms, and Asher (JTX-38) discussed similarly disappointing results with respect to NEPis' effectiveness as a monotherapy for hypertension. (*See id.* at 387; Tr. 299:25–300:11 (Dr. Spinale)). By 2002, a POSA would have understood that NEPis had not performed well in clinical trials with respect to hypertension and heart failure treatment. (Tr. at 92:13–21, 94:2–16 (Dr. Fintel); JTX-352 at 1689).

The parties dispute a POSA's interpretation of these disappointing results. Defendants say that a POSA would have understood that the beneficial effects of NEPis might have been masked by their negative effect of increasing angiotensin II levels. (D.I. 600 at 10). Defendants rely on Cleland (JTX-56), which disclosed a clinical study in which the NEPi ecadotril failed to improve symptoms for heart failure patients who were also receiving ACEis and conventional diuretic therapy. (*Id.* at 1657–58). Defendants' theory is that, because ACEis have no effect on already-existing angiotensin II, the negative activity of ecadotril (that is, increased angiotensin II) obscured ecadotril's positive activity. (*See* D.I. 600 at 9–10; D.I. 620 at 7–8). I do not think that a POSA would have understood this from Cleland. I credit Dr. Spinale's testimony that compelling prior art suggested that NEPis reduce,

rather than increase, angiotensin II levels, and that theories to the contrary were purely theoretical. (Tr. at 308:21–309:12 (citing JTX-91; JTX-92)). Cleland does not suggest otherwise; indeed, Defendants admit that Cleland reported that angiotensin levels did not increase after patients were administered the NEPi. (D.I. 600 at 10; JTX-56 at 1658). I am therefore unmoved by Defendants' argument that Cleland would motivate a POSA to unmask the benefits of NEPis by combining a NEPi with an ARB, which blocks the action of already-existing angiotensin II. (D.I. 600 at 10).

e. Combination Strategies

NEP inhibition, although largely ineffective as a standalone treatment for heart failure and hypertension, showed more promise when combined with other mechanisms of action. I discuss these combinations below.

i. ARB plus NEPi

Defendants rely on a single ARB-NEPi combination disclosed in the prior art: that of the ARB irbesartan and the NEPi SQ 28,603. This combination was disclosed in Bristol-Myers Squibb's ("BMS's") European Patent Application No. 726,072 ("EP '072") (JTX-368), which reports data in a heart failure animal model (the cardiomyopathic hamster in Example 1) and a hypertension animal model (the 1K1C dog in Example 2). (D.I. 600 at 27; D.I. 619 at 6). Trippodo (JTX-369) discloses the same experiment as Example 1. (D.I. 619 at 6). The parties agree that, in the hypertensive dog experiment disclosed in EP

'072 Example 2, the ARB-NEPi combination did not result in a statistically significant effect on the main response variable—mean arterial pressure, i.e., the average blood pressure in the arteries (Tr. at 118:6–8 (Dr. Fintel))—as compared to vehicle alone. (D.I. 619 at 8; D.I. 600 at 18; Tr. at 119:12–16 (Dr. Fintel)). The focus of the parties' disagreement is the cardiomyopathic hamster experiment disclosed by EP '072 Example 1/Trippodo. Both parties agree that EP '072 Example 1/Trippodo disclosed that an ARB-NEPi combination caused decreases in left ventricular end diastolic pressure ("LVEDP") and left ventricular systolic pressure ("LVSP") that were "synergistic"—i.e., greater than the sum of the decreases produced by each drug alone. (D.I. 619 at 7–8; D.I. 600 at 8). What the parties dispute is whether a POSA would view these findings as favorable with respect to the treatment of hypertension and heart failure.

I begin with hypertension. As mentioned above, Defendants acknowledge that EP '072 Example 2 reported a "lack of a statistically significant difference in the hypertensive dogs" with respect to lowering blood pressure.[8] (D.I. 600 at 18). Defendants argue, however, that a POSA would nevertheless have concluded that ARB-NEPi combination is promising for hypertension, given the success of the cardiomyopathic hamster experiment disclosed in EP '072 Example 1/Trippodo. (D.I. 599 at 7 (citing Dr. Fintel's testimony that "the demonstration [of success] in at least one model, in this case the hamster

8. The parties do not dispute that a POSA would have known that lowering blood pressure treats hypertension. (D.I. 600 at 15; *see* D.I. 619 at 8).

heart failure model . . . would be very encouraging." Tr. at 134:13–19)).

Plaintiff disagrees. First, Plaintiff challenges the idea that the reported reductions in LVEDP and LVSP are sufficient to demonstrate that the ARB-NEPi combination had antihypertensive effects. (D.I. 618 at 4–5). Plaintiff's primary argument is that a POSA would have understood that the LVSP measure reported in EP '072 Example 1/Trippodo—i.e., peak LVSP—has no bearing on blood pressure. (*Id*. at 5). According to Dr. Spinale, peak LVSP reflects the heart's "ejection performance, or how much blood has been propelled out into the body," which is different from blood pressure. (Tr. at 293:12–25). Dr. Spinale also stated that LVEDP measurements are irrelevant to blood pressure. (*Id*. at 294:3–10). I am more convinced by Defendants' evidence that a POSA would have considered reductions in LVEDP and LVSP to be antihypertensive. Dr. Fintel explained that reducing LVSP reduces aortic pressure, thereby reducing systolic blood pressure (*id*. at 83:4–8), and that reducing LVEDP treats hypertension for "preload dependent" patents by lowering ventricular output. (*Id*. at 82:7–9). I find Dr. Fintel's testimony persuasive.

Second, Plaintiff disputes the extent to which a POSA would be able to draw conclusions about hypertension treatment from EP '072 Example 1/Trippodo, given the nature of the animal model used in that experiment. (D.I. 618 at 4–6). Plaintiff notes that "the cardiomyopathic hamster model is not a model of hypertension" (*id*. at 4)—a fact that Defendants do not dispute. (D.I. 600 at 18). Plaintiff argues that, consequently, the EP '072 Example

1/Trippodo findings are irrelevant to hypertension, as "to answer the question of whether a combination treats hypertension, a POSA would need to test it in a hypertension model." (D.I. 618 at 6). Plaintiff emphasizes the distinctions between heart failure and hypertension and argues that, because of these differences, "a POSA would not have considered heart failure data relevant to treating hypertension." (*Id.*).

Dr. Fintel acknowledged that the combination in EP '072 Example 1/Trippodo was "not treating the clinical problem of hypertension because [cardiomyopathic hamsters] were not hypertensive animals." (Tr. at 120:14–16). Dr. Fintel also admitted that, to answer the question of whether a combination treats hypertension, a POSA would need to test the combination in a hypertensive animal. (*Id.* at 120:20–21). But Dr. Fintel explained that, even so, a POSA would have understood that a combination that lowers blood pressure in non-hypertensive individuals is likely to do so in hypertensive individuals as well. (*Id.* at 120:20–21, 134:10–19). Dr. Fintel called into question Plaintiffs sharp differentiation between heart disease and hypertension by, for example, highlighting drugs that were utilized to treat both conditions. (*Id.* at 52:5–24; *see supra* Section III.B.2.a.i).

Dr. Fintel's testimony is convincing. Notably, Dr. Fintel's testimony is consistent with the conclusion of EP '072, which found that the reported reductions in LVSP and LVEDP are encouraging with respect to hypertension

treatment. (JTX 368 at 1,2).[9] I therefore conclude that a POSA would view the reductions in LVEDP and LVSP reported in EP '072 Example 1/Trippodo as favorable for hypertension.

Plaintiff contends that certain real-world facts suggest that the EP '072 and Trippodo data were problematic. (D.I. 618 at 6–7). Plaintiff says, "Prior to 2002, BMS abandoned EP '072, and neither BMS nor anyone else clinically developed an ARB/NEP inhibitor combination." (*Id.* at 7). Indeed, BMS withdrew EP '072 in late 2000. (Tr. at 294:20–25 (Dr. Spinale)). It is not clear why, exactly, BMS opted not to pursue the EP '072 application to issuance. Plaintiff does not present evidence on BMS's rationale, and as Defendants note (D.I. 620 at 9), numerous factors other than EP '072 and Trippodo may have impacted its decision. (D.I. 600 at 27 (e.g., another company's ownership of the rights to irbesartan)). It is similarly unclear why no one else picked up BMS's findings and advanced any studies regarding ARB-NEPi combinations for hypertension

9. Thus, I disagree with Plaintiff's argument that Defendants improperly focus on the results that support their position (i.e., the cardiomyopathic hamster data) and ignore the results that don't (i.e., the hypertensive dog data). (D.I. 618 at 5 (citing *In re Wesslau*, 353 F.2d 238, 241, 53 C.C.P.A. 746 (CCPA 1965)). Although a party cannot "pick and choose from any one reference only as much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art," 353 F.2d at 241, I do not think that this is what Defendants have done here. As discussed, Defendants have sufficiently shown that EP '072, considered in its entirety, suggests to a POSA that the disclosed ARB-NEPi combination is encouraging for hypertension.

and heart failure. Thus, I do not afford great weight to Plaintiff's conclusion that the EP '072 and Trippodo data were the cause.

ii. ACEi plus NEPi

Whatever the reason for BMS's decision not to progress with EP '072, BMS turned to an alternative strategy for heart failure and hypertension: omapatrilat, a single molecule that acts as both an ACE and a NEPi. (Tr. at 295:3–7 (Dr. Spinale); *id.* at 63:4–13 (Dr. Fintel)). Omapatrilat looked promising in early clinical trials; for instance, Cases (JTX-49), which was published in 2000, described vasopeptidase inhibitors (the class to which omapatrilat belongs) as "a promising strategy for the treatment of hypertension and cardiac diseases." (*Id.* at 817 (also stating that omapatrilat "reduces blood pressure to a greater extent than existing agents" and "not only improves [heart failure] symptoms but also reduces the risk of and [sic] hospitalization and death when compared with ACE inhibitors alone.")). Cases also noted that "the incidence of angioedema with omapatrilat seems to be greater than with ACE inhibitors." (*Id.* at 822).

The parties dispute what happened next. They agree that, in 2000, BMS withdrew its new drug application for omapatrilat due to angioedema issues. (D.I. 619 at 18–19; D.I. 600 at 16–17). The parties disagree on the extent to which a POSA would associate omapatrilat with angioedema. Plaintiff, relying primarily on Dr. Spinale's testimony, suggests that, as of the priority date, angioedema was not perceived to be a significant issue with

omapatrilat. (*See, e.g.*, D.I. 619 at 19). I am not convinced. Although Dr. Spinale testified that angioedema was only identified as a problem with omapatrilat after 2002 (Tr. at 312:1–3), BMS's withdrawal suggests otherwise. Furthermore, Dr. Spinale admitted on cross that it was known in the art prior to 2002 that omapatrilat caused angioedema. (*Id*. at 381:10–15).

Nevertheless, I agree with Plaintiff that a POSA in 2002 would consider omapatrilat to be a promising strategy for treating heart failure and hypertension. (*See* D.I. 619 at 18–19 (citing Tr. at 311:12–25 (Dr. Spinale)). Plaintiff says, "While angioedema eventually led to the discontinuation of the development of the dual ACE inhibitor plus NEP inhibitor omapatrilat, that did not occur until after the 2002 priority date." (D.I. 619 at 18). Plaintiff points to evidence suggesting that, shortly before January 2002, clinical development of omapatrilat was, indeed, ongoing. For example, in 2000, Coats (JTX-57) referred to the voluntary withdrawal as "a minor setback" and disclosed that BMS planned to refile with additional data. (*Id*. at 2). And Weber (JTX-197)—which was published a year after BMS's voluntary withdrawal—discussed hypertension and heart failure studies that had been initiated and were ongoing with omapatrilat. (*See id.* at 1528–30). I find Plaintiff's evidence convincing.

3. Comparison of the Prior Art and the Claimed Subject Matter

Defendants offer two theories in asserting the '659 Patent claims are obvious over EP '072, the '996 Patent/

Ksander, and the '578 Patent/Diovan® Label. (D.I. 599 at 12–13; D.I. 600 at 21–22). Defendants' first theory starts with the EP '072 ARB-NEPi combination, replaces the NEPi with sacubitril from the '996 patent/Ksander, and replaces the ARB with valsartan from the '578 patent/Diovan® Label. (*Id.*). Defendants' second, alternative theory starts with sacubitril from the '996 patent/Ksander and valsartan from the '578 patent/Diovan® Label and combines them based on EP '072. (D.I. 599 at 13; D.I. 600 at 22–23). Neither theory passes muster.

Central to both theories is the notion that a POSA would have been motivated to pursue ARB-NEPi combinations to treat heart failure and hypertension. (*E.g.*, D.I. 600 at 17). Defendants' primary argument—that a POSA would have understood from EP '072 that the combination of an ARB (irbesartan) and a NEPi (SQ 28,603) achieved synergistic results for the treatment of hypertension and heart failure—is persuasive. *See supra* Section III.B.2.e.i. I am less convinced by Defendants' other arguments. As discussed, I do not think that Cleland would have motivated a POSA to combine a NEPi with an ABB in order to unmask the benefits of the NEPi. *See supra* Section III.B.2.d. And although a POSA would also have understood that ARBs were associated with a reduced risk of angioedema as compared with ACEis, *see supra* Section III.B.2.c, I do not think that this fact helps Defendants. Defendants argue that ARBs' advantage with respect to angioedema would have motivated a POSA to replace the ACEi activity in omapatrilat with ARB activity. (*E.g.*, D.I. 600 at 18). As explained, however, omapatrilat was viewed quite favorably in 2002. *See supra*

Section III.B.2.e.ii. I therefore doubt whether a POSA would have sought to modify omapatrilat in 2002.

Ultimately, my findings of fact on the ARB-NEPi combination issue do not affect the outcome of the analysis, as I conclude that—even if a POSA would have been motivated to pursue such a combination—Defendants fail to provide clear and convincing evidence that a POSA would have been motivated to select the ARB valsartan and the NEPi sacubitril specifically.

First, valsartan. Defendants argue, "a POSA would have replaced irbesartan in EP '072 or Trippodo with valsartan." (D.I. 599 at 9). I don't think so. Valsartan was not clearly preferable to irbesartan in 2002. Defendants fail to show that a POSA would view valsartan as a preferred ARB by virtue of its potency, selectivity, or liver enzyme affinity. *See supra* Section III.B.2.c. Furthermore, Plaintiff offers evidence suggesting that irbesartan outperformed valsartan in a clinical context. *See id.* I therefore conclude that that the prior art would not provide motivation for a POSA to replace irbesartan in EP '072 or Trippodo with valsartan.

Second, sacubitril. Defendants argue, "A POSA would have replaced SQ 28,603 in EP '072 or Trippodo with sacubitril." (D.I. 599 at 10). This argument falls short as well. In 2002, the universe of candidate NEPis was large—the prior art disclosed over 100 known NEPis, half of which had demonstrated preclinical activity. (Tr. at 440:10–441:6 (Dr. Klibanov); PTX-1021 (summary exhibit of NEPis disclosed in the prior art); Tr. at 297:21–298:9

(Dr. Spinale); *id.* at 126:23–127:1 (Dr. Fintel)). The two prior art references upon which Defendants rely do not convincingly demonstrate that, among these NEPis, sacubitril was preferred. The '996 patent did not compare sacubitril to any other known NEPis. (Tr. at 297:21–298:9 (Dr. Spinale)). And although Ksander taught that sacubitrilat was more potent than the other NEPis that Ksander synthesized, Ksander evaluated only 31 NEPis in total and did not compare sacubitril or sacubitrilat with SQ 28,603. (*See supra* Section III.B.2.d; JTX-352). Indeed, Defendants do not assert any reason why a POSA would have wanted to replace SQ 28,603 in the first place. Thus, I conclude that that the prior art would not provide motivation for a POSA to replace SQ 28,603 in EP '072 or Trippodo with sacubitril.

The drug combination cases upon which Defendants rely do not suggest otherwise. Defendants assert that, as "valsartan and sacubitril were known to treat hypertension and heart failure," "it would have been obvious to combine them." (D.I. 599 at 12). Defendants rely upon two cases—*Nalprioprion Pharms., Inc. v. Actavis Lab'ys FL, Inc.*, 934 F.3d 1344 (Fed. Cir. 2019) and *BTG Int'l Ltd. V. Amneal Pharms. LLC*, 923 F.3d 1063 (Fed. Cir. 2019)—for the proposition that "[a] motivation to combine exists where two drugs are disclosed to treat the same condition." (D.I. 599 at 2–3 (citing *Nalpropion*, 934 F.3d at 1353–54)). I agree with Plaintiffs that this characterization oversimplifies the obviousness analysis. Obviousness "is highly fact-specific and not susceptible to per se rules." *Litton Sys., Inc. v. Honeywell, Inc.*, 87 F.3d 1559, 1567 (Fed. Cir. 1996), *vacated on other grounds*,

520 U.S. 1111, 117 S. Ct. 1240, 137 L. Ed. 2d 323 (1997). As Plaintiffs say: "Motivation to combine valsartan and sacubitril to treat hypertension or heart failure and reasonable expectation of success are findings of fact that Defendants must prove by clear and convincing evidence." (D.I. 618 at 11 (citing *In re Cyclobenzaprine*, 676 F.3d 1063, 1068–69 (Fed. Cir. 2012))).

The facts of *Nalpropion* and *BTG* are distinguishable from the facts of this case. In *Nalpropion*, the Federal Circuit held that combining naltrexone and bupropion for treating obesity was obvious because (1) the prior art combined naltrexone and bupropion to minimize weight gain; (2) naltrexone caused weight loss in clinical trials; and (3) bupropion caused weight loss in clinical trials. 934 F.3d at 1351–54. In other words, the prior art demonstrated that the exact drugs claimed showed effects relevant to weight loss both individually and in combination. *BTG* presented similar facts. There, the Federal Circuit held that combining prednisone and the CYP17 inhibitor abiraterone to treat prostate cancer was obvious because (1) prior art combined prednisone and the CYP17 inhibitor ketoconazole to manage prostate cancer; (2) prednisone was already used to treat prostate cancer; and (3) abiraterone was a more selective CYP17 inhibitor than ketoconazole and effectively suppressed testosterone. *BTG*, 923 F.3d 1063, 1074–75. The court's decision rested on its conclusion that abiraterone and prednisone "were both together and individually considered promising prostate cancer treatments at the time." *Id.* at 1074.

Here, no prior art combined valsartan with sacubitril, sacubitril with an ARB, or valsartan with a NEPi. Nor

were valsartan and sacubitril both considered promising treatments for cardiac conditions in 2002; NEPis, in particular, had a history of discouraging results for heart failure and hypertension, and sacubitril had never been administered in humans. *See supra* Section III.B.2.d. Most importantly, in my view, is the fact that a large number of hypertension and heart failure drugs and drug classes were known in 2002—including multiple ARBs and a myriad of NEPis—with no clear hierarchy within the ARB and NEPi classes and no available information pointing directly at the claimed valsartan-sacubitril combination. I agree with Plaintiff that, within this wide universe of potential drug combinations, Defendants "make a beeline to valsartan and sacubitril." (D.I. 618 at 13). Defendants stress that "case law does not require that a particular combination must be the preferred, or the most desirable, combination described in the prior art to provide motivation for the current invention." (D.I. 599 at 10 (quoting *In re Fulton*, 391 F.3d 1195, 1200 (Fed. Cir. 2004))). Defendants also emphasize that "there is no need for a POSA to study every compound in a particular class in order to conclude that a particular drug within the class is interesting for further consideration" (D.I. 599 at 9 (citing Tr. at 373:21–24 (Dr. Spinale))). Those statements are true enough. But Defendants must nevertheless provide some reason, suggestion, or motivation in the prior art that would lead a POSA to combine valsartan and sacubitril in particular, *see Forest Lab'ys, LLC v. Sigmapharm Lab'ys, LLC*, 918 F.3d 928, 934 (Fed. Cir. 2019), in view of the invention and of the prior art "as a whole." *In re Langer*, 465 F.2d 896, 899, 59 C.C.P.A. 1256 (CCPA 1972). Defendants have not done so here.

Defendants' alternative, obvious-to-try theory falls short as well. Defendants say, "At minimum, a POSA would have tried valsartan in place of irbesartan" (D.I. 599 at 9), and "sacubitril in place of SQ 28,603." (*Id.* at 10). I disagree. The Supreme Court has explained that "obvious to try" may apply when "there are a finite number of identified, predictable solutions" to a known problem. *KSR*, 550 U.S. at 421. When the path has been identified and "leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." *Id.* The Federal Circuit has elaborated that the identified path must "present a finite (and small in the context of the art) number of options easily traversed to show obviousness." *Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008). As illustrated in *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988), it would not be "obvious to try" when "the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful."

The surfeit of potentialities with respect to drug combinations for heart failure and hypertension treatment weighs heavily against Defendants here. Defendants assert in their reply brief that the number of classes of drugs for heart failure and hypertension was finite and easily traversed. (D.I. 620 at 6 (citing Tr. at 52:5–24)). But Defendants do not adduce any evidence to that effect; the testimony they cite, in which Dr. Fintel describes the variety of drug classes available to treat heart failure and hypertension in 2002 (*see* Tr. at 52:5–24), seems to undermine Defendants' point. Defendants disregard those

other drugs and drug classes, instead opting to use the invention—an ARB-NEPi combination, or worse, in the case of their second theory, valsartan and sacubitril—as their starting point. "In other words, [Defendants] simply retraced the path of the inventor with hindsight, discounted the number and complexity of the alternatives, and concluded that the invention . . . was obvious." *Ortho-McNeil Pharm., Inc.*, 520 F.3d at 1364.

Thus, I find that Defendants have not proven by clear and convincing evidence that claims 1–4 of the '659 Patent are invalid as obvious.

C. Conclusions of Law

Defendants assert that the asserted claims would have been obvious over EP '072 in view of the '578 Patent/Diovan® Label and the '996 Patent. (D.I. 599 at 12). Based on my factual findings, a POSA would not have found it obvious to combine valsartan and sacubitril for the treatment of hypertension and heart failure. I therefore conclude that Defendants have not presenting clear and convincing evidence of obviousness.

The parties also dispute whether secondary considerations would offer support that the asserted claims are not obvious. I do not need to address the secondary considerations. Generally, when secondary considerations are proven, that helps the patentee in an obviousness analysis. When they are unproven, the secondary considerations are neutral, and they do not

impact the analysis. Since, even if I were to agree with Defendants that they were entirely unproven, I would still, and do, find that Defendants have not proved obviousness by clear and convincing evidence.

I therefore find that Defendants have not shown by clear and convincing evidence that any of the asserted claims of the '659 Patent are invalid as obvious.

IV. 35 U.S.C. § 112

A. Findings of Fact

1. Background

The active ingredient in Entresto® is LCZ696. (Tr. at 408:11–13 (Dr. Klibanov)). LCZ696 is a non-covalently bound complex ("complex") of valsartan and sacubitril. (*Id*. at 415:8–11 (Dr. Klibanov)). A complex is a single-component material in which multiple types of molecule are linked together in a non-covalent manner, such as by ionic or hydrogen bonding. (*Id*. at 186:14–19 (Dr. Steed)). Co-crystals and co-salts are types of complexes. (*Id*. at 186:13–24, 190:7–9, 192:10–23 (Dr. Steed)). In contrast to a complex, in a physical mixture of valsartan and sacubitril, those non-covalent associations do not exist. (*Id.* at 403:17–22 (Dr. Klibanov)). LCZ696 was the first complex of valsartan and sacubitril. (*Id*. at 252:23–253:6 (Dr. Steed)). LCZ696 was first synthesized in January 2006. (*Id*. at 205:13–23 (Dr. Steed)).

Appendix B

The priority date of the '659 Patent is January 2002 (D.I. 521-1, Ex. 1 at 11)—that is, four years before the discovery of LCZ696. The parties agree that the '659 Patent does not disclose or suggest complexes of valsartan and sacubitril, and that, as of 2002, a POSA would not have contemplated, foreseen, or envisioned such complexes. (D.I. 599 at 15; D.I. 619 at 33; Tr. at 223:1-17 (Dr. Steed); Tr. at 408:1–7, 457:6–458:24 (Dr. Klibanov)).

A *Markman* hearing involving the '659 Patent was held on June 8, 2021. (*In re Entresto*, D.I. 275). The Court concluded that the claims of the '659 Patent are not limited to physical mixtures of valsartan and sacubitril, and do not exclude combinations of valsartan and sacubitril in the form of a complex. *(In re Entresto*, D.I. 294 at 5–7 (recognizing that "[n]othing in the specification of the '659 [Patent] limits the claims," and "the patentee did not define or disclaim the 'combination' of [valsartan and sacubitril]")). This was Plaintiff's preferred construction. (*Id.*). The parties do not dispute that "the claims at issue are directed to a genus of 'combinations' of sacubitril and valsartan," which includes complexes of sacubitril and valsartan. (D.I. 599 at 29; D.I. 618 at 43).

In its *Markman* opinion, the Court noted Plaintiff's statement that "its two patents 'do not disclose or suggest' a [complexed] embodiment." (D.I. 294 at 7 (citing *In re Entresto*, D.I. 253 at 39)). The Court said, "This [statement] seems to be an admission by [Plaintiff] that, at the very least, there will be a non-frivolous issue of written description and/or lack of enablement as this case proceeds on [Plaintiff's] preferred construction." (*Id.*).

The Court's predictions have borne out. Those written description and lack of enablement issues are before me now. I address them in detail below.

2. Level of Ordinary Skill in the Art

As an initial matter, the parties dispute the identity of a POSA with respect to the '659 Patent. The heart of their disagreement concerns a POSA's familiarity with solid-state chemistry, which is the area of chemistry involved in making complexes. (Tr. at 202:14–19 (Dr. Steed)).

The Federal Circuit has enumerated "a non-exhaustive list of factors that may guide the fact finder in finding the appropriate level of skill in the art. These factors include: (1) the educational level of the inventor; (2) type of problems encountered in the art; (3) prior art solutions to those problems; (4) rapidity with which innovations are made; (5) sophistication of the technology; and (6) educational level of active workers in the field." *Best Medical Int'l, Inc. v. Elekta Inc.*, 46 F.4th 1346, 1353 (Fed. Cir. 2022) (cleaned up). The patent's purpose can also be a relevant factor. *Id.*

Here, a POSA is "a medical doctor or Ph.D. in medicinal chemistry or a related field who is interested in developing new drugs for heart failure and hypertension. . . ." (D.I. 619 at 30–31; Tr. at 47:17–23 (Dr. Fintel); *Id.* at 279:24–280:8 (Dr. Spinale); *Id.* at 399:8–21 (Dr. Klibanov)).[10]

10. The parties appear to agree that this aspect of the POSA definition does not affect the outcome of the invalidity analyses.

Defendants contend that a POSA would have had experience and knowledge in solid-state chemistry. (*See* D.I. 599 at 5; D.I. 600 at 2–3; D.I. 620 at 11). Defendants present little evidence relating to the factors listed above. Rather, Defendants hinge their argument on the Court's *Markman* opinion. Defendants argue, "Because the scope of the claims has been construed to include crystalline co-crystals, co-salts, and other non-covalently bound complexes, such complexes are part of the relevant art, and a POSA should have experience in, or access to one with experience in, solid-state chemistry, including supramolecular complexes and knowledge of that relevant art." (D.I. 600 at 2; *see also* D.I. 599 at 5 (citing *Best Medical*, 46 F.4th at 1354)). A conclusion to the contrary, Defendants say, would "fly in the face of the Court's claim construction and the positions that [Plaintiff] took to obtain that construction." (D.I. 620 at 11).

Plaintiff disagrees. (D.I. 618 at 35–38; D.I. 619 at 30–31). So do I. First, I do not think that the Court's claim construction decision is dispositive here. As Plaintiff puts it: "That the claims do not exclude complexes does not suggest that the pertinent art is solid-state chemistry or that a POSA would have known about complexes." (*Id*. at 37). I do not think that *Best Medical* helps Defendants. There, the Federal Circuit determined that defining the POSA as having "formal computer programming

(*See, e.g.*, D.I. 618 at 35–36 (explaining that the "key aspect" in dispute is to what extent a POSA would have had experience, familiarity, or interest in solid-state chemistry)). Therefore, I adopt Plaintiff's version, noting that adopting Defendants' version instead would not change my conclusions.

experience" was not unreasonable where the claims expressly required using a computer and the specification was "replete with references to the invention being on the computer." *See Best Medical*, 46 F.4th at 1353–54. The "claimed invention" was therefore relevant to defining the appropriate level of skill in the art. *See id.* at 1354. Here, by contrast, the claims and specification of the '659 Patent do not reference complexes at all. The facts of this case are therefore distinguishable from those of *Best Medical*.

Second, considering the trial record as a whole, I agree with Plaintiff that "[a] POSA would not have had experience, familiarity, or interest in solid-state chemistry . . . and such art would not be part of the 'pertinent art' of which a POSA is aware." (D.I. 618 at 36). Defendants' only argument for including solid-state chemistry experience in the POSA definition, and for complexes being a part of the pertinent art, relies on hindsight knowledge—i.e., the knowledge that the asserted claims were later construed to cover complexes of valsartan and sacubitril. Defendants do not point to anything in the '659 Patent (or the remainder of the intrinsic record) directed to making a complex of two active pharmaceutical ingredients that would lead a POSA to search for or consider such art, or that would require solid state chemistry experience.

Plaintiff offers compelling evidence to the contrary. (*See* D.I. 618 at 35–37). The undisputed field of art for the '659 Patent is the treatment of hypertension and heart failure. (Tr. at 125:14–18 (Dr. Fintel); *id.* at 202:25–203:5 (Dr. Steed); *id.* at 411:22–25 (Dr. Klibanov)). The purpose of the '659 Patent is to address a need for an improved

treatment for those conditions. *See* '659 Patent at 2:61–64, 2:66–3:5. The specification of the '659 Patent relates to pharmaceutical compositions and methods of using such compositions for treating hypertension or heart failure (Tr. at 45:17–25 (Dr. Fintel)) and is completely silent on complexes of valsartan and sacubitril. (*Id.* at 408:1–3, 452:4–14 (Dr. Klibanov)). Likewise, the claims of the '659 Patent do not disclose or even suggest complexes of valsartan and sacubitril. (Tr. at 259:14–21 (Dr. Steed)).

I therefore conclude that pertinent art does not include solid-state chemistry, and that a POSA would not be familiar with solid-state chemistry.

3. State of the Prior Art

Having adopted Plaintiffs definition of a POSA, I now turn to the issue of that POSA's understanding of complexes in 2002.

As discussed, the parties agree that, as of the 2002 priority date, a POSA with the '659 Patent in hand would not have known of or contemplated complexes of valsartan and sacubitril or foreseen that a complex of valsartan and sacubitril would exist. (D.I. 619 at 33; D.I. 599 at 29 (admitting "a POSA reviewing the specification as [of] the priority date would not have contemplated, foreseen, or envisioned such complexes")). The parties disagree as to whether a POSA would have been aware of complexes, generally.

Defendants argue, "[C]omplexes generally were known" in 2002. (D.I. 599 at 30). Indeed, generally

speaking, complexes were known to exist long before 2002; the earliest known co-crystals were discovered in the late 1700s. (Tr. at 187:19–21 (Dr. Steed)). Whether complexes were known to a POSA in 2002, however, is less clear. Defendants argue in the affirmative. (D.I. 600 at 32). Dr. Steed testified to this effect. (*See, e.g.*, Tr. at 186:20–188:22, 215:23–216:10, 245:11–18). I am not convinced by his testimony. In describing a POSA's awareness of complexes, Dr. Steed cited Ngilirabanga (JTX-240), a review article published in 2021. (*See* Tr. at 186:20–188:22). Dr. Steed explained that Ngilirabanga "summarizes the state of the field . . . going back all the way through to the time of the filing of the patents in question." (Tr. at 187:14–17).[11] But neither Defendants nor Dr. Steed have explained how, exactly, Ngilirabanga demonstrates that a POSA was aware of complexes in 2002. Dr. Steed cited two additional references published after 2002: Morissette (JTX-252) and Almarsson (JTX-234), both of which were published in 2004. (Tr. at 218:13–222:25). Dr. Steed testified that Morissette and Almarsson taught that, by 2004, co-crystals of drug and drug candidates "represent[ed] a new type of material for pharmaceutical development" (*Id.* at 220:4–221:10 (citing Morissette (JTX-252))) and were "a new and unexplored class." (*Id.* at 222:4–12 (citing Almarsson (JTX-234))). Dr. Steed's testimony does not clearly and convincingly demonstrate that such co-crystals were known to a POSA in 2002.

11. Defendants have acknowledged that Ngilirabanga is not, and was not admitted as, prior art. (Tr. at 189:10–18).

Appendix B

Defendants rely on a single reference available within the relevant time period: Aakeroy (JTX-254), a 1997 review article published in *Acta Crystallographica* (a journal that publishes results of crystallographic studies). (Tr. at 410:25–411:18 (Dr. Klibanov)). Aakeroy teaches that co-crystal preparation is not routine or easy. (D.I. 600 at 33; JTX-249 at 71–72 (citing JTX-254)). Discussing the application of crystal engineering to the pharmaceutical industry, Aakeroy states, "With several billion dollars at stake (which does tend to make people pay attention), we can expect much more interest in this field over the next few years, not just from the pharmaceutical industry." (JTX-254 at 580). Defendants maintain that Aakeroy shows that complexes were known to a POSA in 2002. (*E.g.*, D.I. 620 at 11–12). Plaintiff counters that a POSA "would not have followed the literature or been aware of solid-state chemistry references such as Aakeroy 1997." (D.I. 618 at 39; D.I. 619 at 33–34). Dr. Klibanov testified to this effect. (Tr. at 410:25–411:18 (opining that a POSA, who is interested in developing new drugs to treat cardiovascular disease, would not follow solid-state chemistry literature)). As I have already found that solid-state chemistry is a different field of art from the '659 Patent and not a subject about which a POSA would be knowledgeable, *see supra* Section IV.A.2, I agree with Dr. Klibanov's testimony.[12]

12. As Defendants point out (D.I. 600 at 32), however, Plaintiff appeared to concede at closing argument that complexes were generally known in the art. (*See* Tr. at 540:13–17 (" . . . Novartis does not dispute that co-crystals generally were known. . . .")). I do not think Plaintiff conceded anything of significance. I think that confusion might arise from the fact that co-crystals were known to

In short, although the parties agree that the existence of complexes, generally, was known quite a bit before 2002, it is not clear that complexes were known in the art for the purposes of the '659 Patent. It is even less clear that a POSA in 2002 would have been aware of the use of complexes comprising one or more active pharmaceutical ingredients ("pharmaceutical complexes"). As Plaintiffs note (D.I. 619 at 34), Defendants have not identified any such complex that was known in 2002. Although Dr. Steed testified that pharmaceutical complexes were known in the 2002 timeframe (*see, e.g.*, Tr. at 215:23–216:10, 187:9–18), I agree with Plaintiff (D.I. 619 at 40–41) that Dr. Steed's testimony is largely unsupported. Dr. Steed primarily relied upon Ngilirabanga—again, an article dated nearly two decades after 2002—without explaining how Ngilirabanga was relevant to 2002 knowledge. (*See* Tr. at 187:9–18). Indeed, Dr. Steed's testimony suggests that pharmaceutical co-crystals were a new and little-explored class even in 2013, when Dr. Steed authored and published a paper on the subject. (*See id.* at 256:17–257:5). At the time of the paper, Dr. Steed was not aware of any pharmaceutical co-crystals approved as drug substances. (*Id.* at 256:25–257:5 (Dr. Steed)). The 2013 paper reported that "the possibility of combining two active ingredients

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some people—just not our POSA. Such confusion underlies another apparent concession that Defendants identify. Defendants say that Dr. Klibanov admitted that a POSA would have been aware of complexes in 2002. (D.I. 600 at 32). Although Dr. Klibanov at one point indicated that, in 2002, a POSA knew that co-crystals existed in the prior art (Tr. at 464:19-465:9), Dr. Klibanov later clarified that he gave that testimony from the perspective of Defendants' definition of a POSA (one with familiarity with solid-state chemistry), not Plaintiff's. (*Id.* at 473:6-12).

in a single co-crystal [was] an interesting one." (*Id.* at 257:6–20 (Dr. Steed)).

4. The Discovery of LCZ696 in 2006

Novartis's scientists first synthesized LCZ696 in January 2006, after conducting over one thousand separate experiments between March 2005 and January 2006. (JTX-355 at 5, 7; JTX-802 at 33:3–7, 33:22–34:5, 40:23–24, 41:2–5, 8–11, 46:14–16, 46:18, 48:18–20, 48:22–49:5, 49:14–18, 49:20 (Dr. Karpinski); Tr. at 205:13–23 (Dr. Steed); *id.* at 408:14–16, 409:2–11 (Dr. Klibanov)). Even in 2005, Novartis's scientists did not know whether it was possible to make a complex of valsartan and sacubitril. (JTX-802 at 114:16–17, 20 (Dr. Karpinski); Tr. at 206:14–207:5, 209:13–17, 242:20–243:5 (Dr. Steed); *id.* at 408:23–409:1 (Dr. Klibanov)). Dr. Karpinski, a Novartis scientist involved in the efforts to create such a complex, described the project as a "loooong shot" in April 2005 (DTX-643 at NPC-VS-016880042), reported "diminishing hope" for the project's success in August that same year (DTX-645 at NPC-VS-016680066), and, by October, stated that they "ha[d] not yet proven" that such complexes were "feasible." (DTX-646 at NPC-VS-016650514). Another Novartis scientist suggested, also in October 2005, that they "try[] as many and as wild [approaches] as we can" to try to form a complex of valsartan and sacubitril. (DTX-647). According to Dr. Karpinski, they ultimately succeeded in creating LCZ696 using an "Out-of-the-box (Irrational?) Approach." (DTX-359 at NPC-VS-016626522; JTX-802 at 116:22–23, 121:18–23, 122:1 (Dr. Karpinski)).

B. Enablement

1. Legal Standard

The Supreme Court recently reaffirmed that a patent's "specification must enable the full scope of the invention as defined by its claims." *Amgen Inc. v. Sanofi*, 598 U.S. 594, 143 S. Ct. 1243, 1254, 215 L. Ed. 2d 537 (2023). For a patent claim to be enabled, the patent specification must "contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same[.]" 35 U.S.C. § 112(a). "The enablement requirement is met where one skilled in the art, having read the specification, could practice the invention without 'undue experimentation.'" *Streck, Inc. v. Rsch. & Diagnostic Sys., Inc.*, 665 F.3d 1269, 1288 (Fed. Cir. 2012) (citation omitted); *see also Amgen*, 143 S. Ct. at 1255 ("[A] specification may call for a reasonable amount of experimentation to make and use a patented invention. What is reasonable in any case will depend on the nature of the invention and the underlying art."). Factors for assessing whether a disclosure would require undue experimentation include:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the

> art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

"Enablement is a question of law based on underlying facts." *Wyeth & Cordis Corp. v. Abbott Lab'ys*, 720 F.3d 1380, 1384 (Fed. Cir. 2013). The party challenging validity must prove lack of enablement by clear and convincing evidence. *Cephalon, Inc. v. Watson Pharms., Inc.*, 707 F.3d 1330, 1336 (Fed. Cir. 2013).

The Federal Circuit has consistently held, "Enablement is determined as of the effective filing date of the patent." *Plant Genetic Sys., NV. v. DeKalb Genetics Corp.*, 315 F.3d 1335, 1339 (Fed. Cir. 2003) (citing *In re Hogan*, 559 F.2d 595, 604 (CCPA 1977)). A patent need not enable later-existing state of the art (i.e., art that comes into existence after the priority date). *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247, 1254 (Fed. Cir. 2004); *U.S. Steel Corp. v. Phillips Petroleum Co.*, 865 F.2d 1247, 1249–52 (Fed. Cir. 1989); *Hogan*, 559 F.2d at 605.[13] "Nascent technology, however, must be enabled with a 'specific and useful teaching.'" *Chiron Corp.*, 363 F.3d at 1254 (quoting *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1368 (Fed. Cir. 1997); *see Plant Genetic*, 315

13. Defendants argue that this portion of *Hogan* is dicta. (*In re Entresto*, D.I. 599 at 23). I disagree. The Federal Circuit has treated this part of *Hogan* as the holding. *See Plant Genetic*, 315 F.3d at 1340 (Fed. Cir. 2003) ("*Hogan* simply held that one could not use a later-existing state of the art to invalidate a patent that was enabled for what it claimed at the time of filing.").

F.3d at 1340 (finding transformed monocot cells needed to be enabled because they were not an unknown concept as of the priority date). Nascent technology is "unpredictable technology in the early stages of development," *Genentech*, 108 F.3d at 1367–68, in which a POSA has "little or no knowledge independent from the patentee's instruction." *Chiron*, 363 F.3d at 1254.

2. Conclusions of Law

The parties dispute whether the specification is required to enable the full scope of the claims. As discussed, this Court has construed the asserted claims to cover valsartan and sacubitril as a physical combination and as a complex. (*See In re Entresto*, D.I. 294 at 5–7). It is not disputed that the specification neither discloses nor suggests a complex of valsartan and sacubitril. (D.I. 599 at 15; D.I. 619 at 33; Tr. at 223:1–17 (Dr. Steed); Tr. at 408:1–7, 457:6–458:24 (Dr. Klibanov)). Accordingly, Defendants argue that the claims are invalid for lack of enablement for not enabling the complex. (*See, e.g.*, D.I. 599 at 16–29). Plaintiff argues that the complex is an after-arising invention that the patent need not enable. (*See* D.I. 618 at 27–43).

The principal cases are *Hogan, Plant Genetic*, and *Chiron*. I discuss each case in turn.

First, *Hogan*. There, the CCPA—the predecessor Court to the Federal Circuit—reviewed an appeal for a rejection of a patent application filed in 1953 with claims covering ways to make and use "a solid polymer." 559

F.2d at 606. The specification enabled preparation of a crystalline form of that polymer, which was the sole form of the polymer known as of the patent's filing date. *Id.* at 604–06. The PTO rejected the claims as non-enabled. *Id.* at 605. The PTO did so because it found that the claims also encompassed a non-crystalline (amorphous) form of the polymer, yet the patent failed to enable that non-crystalline form. *Id.* The non-crystalline form, however, did not exist until 1962—nearly a decade after the patent was filed. *Id.* The CCPA reversed and remanded the case to the PTO. *Id.* at 609. The CCPA held that the PTO had improperly based the enablement rejection on a later-existing state of the art. *Id.* at 604–05. The CCPA explained that the specification should have been tested for compliance with the enablement requirement as of the priority date, and that a later-existing state of the art cannot be used to invalidate a patent for lack of enablement. *Id.* at 604–07. The Federal Circuit endorsed the CCPA's position in *U.S. Steel*. *See* 865 F.2d at 1249–52 (holding that evidence "directed solely to a later state of the art" was insufficient to prove lack of enablement.).

Second, *Plant Genetic*. The patent in *Plant Genetic* taught a plant cell genetically engineered to produce a protein that prevents certain herbicides from blocking the function of glutamine synthetase. 315 F.3d at 1337. Although flowering plants can be broadly categorized as either monocots or dicots, the working examples disclosed in the patent pertained solely to dicots. *Id.* The issue was whether the claims, which the parties agreed covered all plant cells, were required to enable monocot cells. *Id.* at 1338, 1339. The Federal Circuit found that,

unlike the amorphous polymer in *Hogan*, "monocots and stably transformed monocot cells were not an unknown concept that came into existence only after" the patent's priority date. *Id.* at 1340; *see also Chiron*, 363 F.3d at 1257 (describing the stably-transformed monocots in *Plant Genetic* as "nascent technology"). Accordingly, the patent was required to enable monocots. *Plant Genetic*, 315 F.3d at 1340–41. The Federal Circuit concluded that the patent had not done so, and its plant cell claims were therefore invalid for lack of enablement. *Id.* at 1344.

Third, *Chiron*. In *Chiron*, the Federal Circuit analyzed whether a patent could claim priority to three earlier patent applications, which were filed in 1984, 1985, and 1986. 363 F.3d at 1249, 1251. The patent claimed monoclonal antibodies that bound to a specified antigen. *Id.* at 1250. The district court broadly construed the claims to cover murine, humanized, and chimeric antibodies. *Id.* at 1252. The 1984 patent application disclosed murine antibodies, but not chimeric antibodies—which was not surprising, as the first publication to disclose chimeric antibody technology did not appear until May 1984, four months after the 1984 patent application was filed. *Id.* at 1251, 1254. The Federal Circuit held, "Because the first publication documenting the successful creation of chimeric antibodies arose after the filing date of the 1984 application, . . . this new technology arose after the filing date and thus was, by definition, outside the bounds of the enablement requirement." *Id.* at 1254 (citing *Hogan*, 559 F.2d at 605–06).[14] The Federal Circuit explained that

14. The Federal Circuit went on to determine the patent could not claim priority to the 1984 application due to inadequate written description. *Id.* at 1255.

"a patent document cannot enable technology that arises after the date of application. The law does not expect an applicant to disclose knowledge invented or developed after the filing date. Such disclosure would be impossible." *Id.*

The Federal Circuit came to the opposite conclusion with respect to the 1985 and 1986 patent applications. Those applications, like the 1984 application, did not specifically disclose chimeric antibodies; indeed, the later applications "provide[d] no disclosure of either how to make and use chimeric antibodies or working examples of chimeric antibodies" within the scope of patent's claims. *Id.* at 1256. Unlike the 1984 application, however, the 1985 and 1986 applications were filed after the first disclosure of chimeric antibodies. *Id.* The Federal Circuit found that substantial evidence supported the jury's finding that, at the time of these applications, chimeric antibodies were nascent—as opposed to unknown—technology. *Id.* at 1256–57. As chimeric antibodies constituted nascent technology with respect to the 1985 and 1986 applications, they were required to be enabled with "a 'specific and useful teaching.' *Id.* at 1255 (quoting *Genentech*, 108 F.3d at 1368). The Federal Circuit held that the applications fell short of this requirement. *Id.* at 1256.

Hogan, Plant Genetic, and *Chiron* stand for the same proposition: Enablement is judged as of the priority date, and later-existing state of the art may not be properly considered in the enablement analysis. Defendants cite numerous other authorities to support their argument that, "because the law requires that a patent provide an

enabling disclosure for the full claim scope of the claims, the '659 patent is invalid." (D.I. 599 at 16–20 (citing, *e.g.*, *Trustees of Boston Univ. v. Everlight Elecs. Co.*, 896 F.3d 1357 (Fed. Cir. 2018); *Alza Corp. v. Andrx Pharms., LLC*, 603 F.3d 935 (Fed. Cir. 2010); *Liebel-Flarsheim Co. v. Medrad, Inc.*, 481 F.3d 1371 (Fed. Cir. 2007))). None of these cases contradict *Hogan* and its progeny. As Plaintiff notes, "Each [of these cases] found the claim(s) at issue lacked enablement based on the state of the art that existed as of the relevant filing date, not a later state of the art as prohibited by *Hogan*." (D.I. 618 at 33).

The key question is whether the same is true here. Plaintiff argues, "The facts in this case are analogous to those of *Hogan*, the earliest application in *Chiron*, and *U.S. Steel*, and like in those cases, the claims here are enabled." (D.I. 618 at 27). Specifically, Plaintiff argues that Defendants have failed to prove that the relevant technology here is nascent technology that existed in the art in 2002, rather than unknown, after-arising technology.[15] (*Id.* at 40–43).

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15. Plaintiff has not cited any cases holding that a patentee may claim as-yet-undeveloped technology that the patentee did not enable. Such a scenario would present an uneasy discrepancy between the scope of infringement and the scope of enablement. Although the Federal Circuit and the CCPA acknowledged this potential issue in *Hogan* and *Chiron*, both of those cases were decided on other grounds. *See Chiron*, 363 F.3d at 1258; *Hogan*, 559 F.2d at 606–607.

Both opinions contain dicta suggesting that a patentee may indeed claim technology without enabling it. *See Chiron*, 363 F.3d

Before I proceed to that issue, however, I address a threshold question: What, exactly, is the relevant technology? The parties disagree on its proper scope. Defendants characterize the relevant technology broadly; they focus on a POSA's awareness of complexes, generally. (*See, e.g.*, D.I. 599 at 15). Plaintiff, by contrast, characterizes the relevant technology narrowly; it focuses on a POSA's awareness of complexes of valsartan and sacubitril. (*See* D.I. 618 at 40–43).

I think that the correct answer lies somewhere in-between. *Plant Genetic* and *Chiron* are instructive. In both cases, the Federal Circuit characterized the relevant technology as a category somewhat broader than the

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at 1258 (noting that a potential option for construing the claims was to construe the Willi "broader than the disclosure of the earliest application"); *Hogan*, 559 F.2d at 606–607. In *Plant Genetics*, however, the Federal Circuit explicitly cautioned against reading *Hogan* to "expand the coverage of claims, yet create a new, lower standard of enablement." 315 F.3d at 1341; *see also Chiron*, 363 F.3d at 1262–63 (Bryson, J., concurring).

I am inclined to agree. I think the better approach is to "address cases of new technology by construing claims, where possible, as they would have been understood by one of skill in the art at the time of the invention, and not construing them to reach the as-yet-undeveloped technology that the applicant did not enable." *Chiron*, 363 F.3d at 1263 (Bryson, J., concurring). I did not do the claim construction of the patent in this case, and no one has asked me to revisit it. I have not independently examined it. Thus, I cannot say that I would have construed the claims differently. But I note that had the claims been construed more narrowly, they would have been enabled and have adequate written description.

claimed invention itself. In *Plant Genetic*—where the claims recited plant cells genetically transformed to make the cells invulnerable to a certain herbicide, 315 F.3d at 1337–38—the Federal Circuit characterized the relevant technology as "stably-transformed monocot cells." *See id.* at 1340. In *Chiron*—where the claims recited monoclonal antibodies that bind to a specified antigen, 363 F.3d at 1250—the Federal Circuit characterized the relevant technology as "chimeric antibodies" and "chimeric antibody technology." *See id.* at 1254–55, 1256. Considering these cases, I think that the characterization that Plaintiff urges me to adopt—that is, complexes of valsartan and sacubitril—is too narrow. And I agree with Plaintiff that Defendants' characterization—complexes, generally—is too broad. (*See* D.I. 618 at 40; Tr. at 540:13–541:9). My sense is that an intermediate category, one which bears more directly on a POSA's knowledge of the claimed invention, is appropriate here. One such category is pharmaceutical complexes, which Plaintiff identifies and discusses in its answering brief. (*See* D.I. 618 at 40–41).

For the purposes of this opinion, however, the definition I choose does not affect the outcome of the analysis, as I conclude that, under any of these definitions of the relevant technology, Plaintiff prevails.

First, complexes of valsartan and sacubitril were unknown in the art in 2002. The parties agree on this point. (D.I. 619 at 33; D.I. 599 at 29). The record reinforces it. As Dr. Steed recognized (Tr. at 206:14–207:5, 209:13–17, 242:20–243:5), a team of scientists at Novartis conducted over one thousand experiments to produce a complex

of valsartan and sacubitril, and the team did not know whether the project was feasible during the lead-up to the first preparation of LCZ696. *See supra* Section IV.A.4. Thus, complexes of valsartan and sacubitril are later-existing technology that need not be enabled. *See Hogan*, 559 F.2d at 604–07.

Second, I do not think that Defendants offer clear and convincing evidence that pharmaceutical complexes were known in the art in 2002. *See supra* Section IV.A.3. Although Dr. Steed testified that pharmaceutical complexes were nascent technology at that time (*see, e.g.*, Tr. at 187:9–18, 215:23–216:10), Dr. Steed relied on post-2002 references that Defendants do not clearly link to a POSA's knowledge in 2002. The rest of the record does not help Defendants; indeed, Defendants have not identified any pharmaceutical complex known in 2002. This is insufficient. In *Chiron*, "substantial evidence support[ed] a finding" that, when the 1985 and 1986 applications were filed, the relevant technology (chimeric antibodies) was nascent in the field. 363 F.3d at 1256–57 (citing evidence that, for example, only a few laboratories had the capacity and expertise necessary to create genetically engineered antibodies; the techniques facilitating chimeric antibodies' manufacture were not widespread; and pioneers in the field considered chimeric antibodies a new, rather than routine, technology). Similarly, *Plant Genetic* relied upon specific evidence that stably-transformed monocots were nascent technology when the application at issue was filed. *See* 315 F.3d at 1340 (citing evidence that, as of the priority date, monocots existed, stably-transformed monocot cells were highly desirable, and monocot cells were already

being stably transformed). Defendants present no such evidence. Accordingly, I think that pharmaceutical complexes, too, are later-existing technology that need not be enabled. *See Hogan*, 559 F.2d at 604–07.

Finally, I do not think that Defendants offer clear and convincing evidence that complexes, generally, were known in the art in 2002. *See supra* Section IV.A.3. Defendants again rely on post-2002 references without explaining the relevance of those references to 2002. *See id.* And, as explained, I do not think that Defendants' pre-2002 reference (Aakeroy) suggests that complexes were known in the art. *See id.* I therefore agree with Plaintiff that complexes are later-existing technology that need not be enabled. *See Hogan*, 559 F.2d at 604–07.

Accordingly, I find that Defendants have not shown by clear and convincing evidence that any of the asserted claims of the '659 Patent are invalid for lack of enablement.

C. Written Description

1. Legal Standard

The written description requirement contained in 35 U.S.C. § 112 requires that the specification "clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (alteration in original). "In other words, the test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art

that the inventor had possession of the claimed subject matter as of the filing date." *Id.* "When determining whether a specification contains adequate written description, one must make an 'objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art.'" *Bos. Sci. Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1366 (Fed. Cir. 2011) (quoting *Ariad*, 598 F.3d at 1351).

For a genus claim, the written description requirement can be satisfied by the "disclosure of . . . structural features common to the members of the genus so that one of skill in the art can 'visualize or recognize' the members of the genus." *Ariad*, 598 F.3d at 1350. "[A]n adequate written description requires a precise definition, such as by structure, formula, chemical name, physical properties, or other properties, of species falling within the genus sufficient to distinguish the genus from other materials." *Id.* However, "merely drawing a fence around the outer limits of a purported genus is not an adequate substitute for describing a variety of materials constituting the genus and showing that one has invented a genus and not just a species." *Id.*

The written description inquiry is a question of fact. *Id.* at 1351. "A party must prove invalidity for lack of written description by clear and convincing evidence." *Vasudevan Software, Inc. v. MicroStrategy, Inc.*, 782 F.3d 671, 682 (Fed. Cir. 2015).

2. Conclusions of Law

Defendants argue that the '659 Patent is invalid for lack of written description. (D.I. 599 at 29–30; D.I. 620 at 14–15). I agree.

The touchstone of written description is possession as of the priority date. *See Chiron*, 363 F.3d at 1255 (explaining that "'[t]he function of the description requirement is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him.") (quoting *In re Wertheim*, 541 F.2d 257, 262 (CCPA 1976)). Defendants contend that, because complexes were unknown as of the 2002 priority date, Plaintiff did not possess such complexes and therefore could not have described them. (D.I. 599 at 30).

Defendants analogize to *Chiron*. (*Id.*). There, the facts that helped the patentee with respect to enablement proved fatal for written description. As discussed, the Federal Circuit held, "Because the first publication documenting the successful creation of chimeric antibodies occurred after the filing of the 1984 application, . . . this new technology arose after the filing date and thus was, by definition, outside the bounds of the enablement requirement." 363 F.3d at 1254. But the Federal Circuit went on to explain that, because chimeric antibodies did not exist at the time of the 1984 application, "the Chiron scientists, by definition, could not have possession of, and disclose" the subject matter of such antibodies. *Id.* at 1255. Thus, the Court concluded that, "axiomatically, Chiron

cannot satisfy the written description requirement for the new matter appearing in the ['561] patent, namely chimeric antibodies." *Id.*

Such is the case here. It is Plaintiff's position that, in 2002, complexes of valsartan and sacubitril, pharmaceutical complexes, and complexes, generally, were unknown to a POSA. (*See* D.I. 618 at 27, 39–41; D.I. 619 at 33–34). I have found the same. *See supra* Sections IV.A.3, IV.B.2. Thus, I conclude that "the [Novartis] scientists, by definition, could not have possession of, and disclose, the subject matter of [such complexes]" in 2002, and therefore, "axiomatically, [Plaintiff] cannot satisfy the written description requirement" for such complexes. *See Chiron*, 363 F.3d at 1255. The asserted claims are therefore invalid for lack of written description.

Plaintiff's contentions to the contrary (D.I. 618 at 43–44) do not change my mind. Plaintiff argues, "The '659 patent satisfies the written description requirement by disclosing valsartan and sacubitril—the structural features (*i.e.*, chemical names and/or chemical formulas) common to the members of the claimed genus of the pharmaceutical composition containing the valsartan and sacubitril combination." (*Id.* at 43 (citing *Ariad*, 598 F.3d at 1350)). Plaintiff points out that physical mixtures of valsartan and sacubitril, and complexes of valsartan and sacubitril, are mere subsets of the claimed genus. (Tr. at 38:9–40:4). According to Plaintiff, written description does not require disclosure of structural features common to only a subset of the claimed genus, and therefore Plaintiff need not have disclosed complexes. (*Id.* at 39:15–40:4).

Plaintiffs trouble is that written description also requires that common structural features be described "with enough precision that a relevant artisan can visualize or recognize the members of the genus." *Regents of the University of Minnesota v. Gilead Sciences, Inc.*, 61 F.4th 1350, 1356 (Fed. Cir. 2023) (citing *Ariad*, 598 F.3d at 1350–52). "A broad outline of a genus's perimeter is insufficient." *Id.* As the Federal Circuit has explained:

> [A]nalogizing the genus to a plot of land, if the disclosed species only abide in a corner of the genus, one has not described the genus sufficiently to show that the inventor invented, or had possession of, the genus. . . . One describes a plot of land by its furthest coordinates, in effect drawing a perimeter fence around it. That may be akin to the function of patent claims to particularly point out and distinctly circumscribe the outer boundaries of a claimed invention. With the *written description* of a genus, however, merely drawing a fence around a perceived genus is not a description of the genus. One needs to show that one has truly invented the genus, *i.e.*, that one has conceived and described sufficient representative species encompassing the breadth of the genus. Otherwise, one has only a research plan, leaving it to others to explore the unknown contours of the claimed genus.

AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc., 759 F.3d 1285, 1300 (Fed. Cir. 2014). The

common features that Plaintiff identifies—sacubitril and valsartan—draw a fence around a genus that includes both complexes and physical mixtures of valsartan and sacubitril. But the '659 Patent specification describes physical mixtures only. The specification did not, and could not, have allowed a POSA to visualize the members of the entire genus sufficient to show possession of complexes, which, to a POSA's knowledge, had not yet been discovered. *See Chiron*, 363 F.3d at 1255.

Accordingly, I find that Defendants have shown by clear and convincing evidence that the asserted claims of the '659 Patent are invalid for lack of written description.

V. INDEFINITENESS

Defendants argue, "[T]he '659 patent's 'about 1:1 ratio' limitation is indefinite because a POSA could not tell whether the claims cover a molar or weight ratio, which result in different claim scopes." (D.I. 599 at 30 n. 4). Defendants argue this in a footnote on the final page of their opening brief. (*Id.*). I therefore conclude that this argument has been forfeited. *See Higgins v. Bayada Home Health Care Inc.*, 62 F.4th 755, 763 (3d Cir. 2023) ("[T]he District Court was not required to consider [the Plaintiff's argument] because 'arguments raised in passing (such as, in a footnote), but not squarely argued, are considered [forfeited].'") (quoting *John Wyeth & Bro. Ltd. v. CIGNA Int'l Corp.*, 119 F.3d 1070, 1076 n.6 (3d Cir. 1997)).

VI. CONCLUSION

For the foregoing reasons, I find the asserted claims of the '659 Patent invalid for lack of written description. The parties shall submit a final judgment consistent with this memorandum opinion within one week.

APPENDIX C — OPINION OF THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF DELAWARE, FILED JULY 8, 2021

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

No. 20-md-2930-LPS

IN RE ENTRESTO (SACUBITRIL/VALSARTAN)
PATENT LITIGATION

MEMORANDUM OPINION

July 8, 2021
Wilmington, Delaware

/s/ Leonard P. Stark
STARK, U.S. District Judge:

In this multi-district litigation, Novartis Pharmaceuticals Corporation ("Novartis" or "Plaintiff") sued multiple generic drug manufacturers ("Defendants"), specifically: Alembic Pharmaceuticals Limited, Alembic Pharmaceuticals, Inc., Alkem Laboratories Ltd., Aurobindo Pharma USA Inc., Aurobindo Pharma Ltd., Biocon Pharma Limited, Biocon Limited, Biocon Pharma, Inc., Cadila Healthcare Ltd., Crystal Pharmaceutical (Suzhou) Co., Ltd., Dr. Reddy's Laboratories, Inc., Dr. Reddy's Laboratories, Ltd., Hetero USA Inc., Hetero Labs Limited, Hetero Labs Limited Unit III, Laurus Labs Limited, Laurus Generics Inc., Lupin Atlantis Holdings, S.A., Lupin Limited, Lupin Inc., Lupin Pharmaceuticals, Inc., Macleods Pharmaceuticals Ltd.,

Macleods Pharma USA, Inc., MSN Pharmaceuticals Inc., MSN Laboratories Private Limited, MSN Life Sciences Private Limited, Mylan Pharmaceuticals Inc., Nanjing Noratech Pharmaceutical Co., Limited, Novugen Pharma (Malaysia) Sdn. Bhd., Teva Pharmaceuticals USA, Inc., Torrent Pharma Inc., Torrent Pharmaceuticals Ltd., and Zydus Pharmaceuticals (USA) Inc. Novartis asserts that one or more of these Defendants would, if permitted to market their proposed generic drug products, infringe claims of one or more of the following U.S. Patents: 8,101,659 (the "'659 patent"); 8,796,331 (the "'331 patent"); 8,877,938 (the "'938 patent"); and 9,388,134 (the "'134 patent").

As Novartis explains, the asserted patents fall into two families and "cover two distinct inventions. Novartis initially developed the novel combination of valsartan and sacubitril, and methods of administering that combination to treat hypertension and heart failure, and filed a priority patent application to its invention on January 17, 2002. Novartis's '659 and '331 Patents . . . claim priority to that 2002 application." (D.I. 253 at 7)[1] These two patents share "substantively the same specification." (*Id.* at 4 n.4) "Several years later, Novartis developed a novel compound comprising non-covalently bound valsartan and sacubitril salts, and methods of administering that compound to treat hypertension and heart failure," which are covered by the '938 and '134 patents. (*Id.* at 7) The '938 and '134 patents also share a specification. (*Id.* at 42 n.24)

1. Citations to the docket index refer to Case No. 20-md-2930.

Appendix C

The parties submitted a joint claim construction brief (D.I. 253), technology tutorials (D.I. 240, 241), and extensive appendices, including expert reports (DI 254, 255). The Court held a claim construction hearing on June 8, 2021. (D.I. 275) ("Tr.")

I. LEGAL STANDARDS

The ultimate question of the proper construction of a patent is a question of law. *See Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 321, 135 S. Ct. 831, 190 L. Ed. 2d 719 (2015) (citing *Markman v. Westview Instruments, Inc.* ("*Markman II*"), 517 U.S. 370, 388-91, 116 S. Ct. 1384, 134 L. Ed. 2d 577 (1996)). "It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) (internal quotation marks omitted). "[There is no magic formula or catechism for conducting claim construction." *Id.* at 1324. The Court is free to attach the appropriate weight to appropriate sources "in light of the statutes and policies that inform patent law." *Id.*

"[T]he words of a claim are generally given their ordinary and customary meaning," which is "the meaning that the term would have to a person of ordinary skill in the art [POSA] in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Id.* at 1312-13 (internal quotation marks omitted). "[T]he ordinary meaning of a claim term is its meaning to the ordinary artisan after reading the entire patent." *Id.* at 1321 (internal quotation marks omitted). The patent

"specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996).

While "the claims themselves provide substantial guidance as to the meaning of particular claim terms," the context of the surrounding words of the claim also must be considered. *Phillips*, 415 F.3d at 1314. Furthermore, [o]ther claims of the patent in question, both asserted and unasserted, can also be valuable sources of enlightenment" because "claim terms are normally used consistently throughout the patent." *Id.*

It is likewise true that "[d]ifferences among claims can also be a useful guide." *Id.* at 1314. "For example, the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *Id.* at 1314-15. This "presumption is especially strong when the limitation in dispute is the only meaningful difference between an independent and dependent claim, and one party is urging that the limitation in the dependent claim should be read into the independent claim." *SunRace Roots Enter. Co. v. SRAM Corp.*, 336 F.3d 1298, 1303 (Fed. Cir. 2003).

It is also possible that "the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs."

Phillips, 415 F.3d at 1316. It bears emphasis that "[e]ven when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1372 (Fed. Cir. 2014) (internal quotation marks omitted).

In addition to the specification, a court "should also consider the patent's prosecution history, if it is in evidence." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370, 116 S. Ct. 1384, 134 L. Ed. 2d 577 (1996). The prosecution history, which is "intrinsic evidence," "consists of the complete record of the proceedings before the [U.S. Patent and Trademark Office] and includes the prior art cited during the examination of the patent." *Phillips*, 415 F.3d at 1317. "[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Id.*

Sometimes, "the district court will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period." *Teva*, 574 U.S. at 331. "Extrinsic evidence consists of all evidence external to the patent and prosecution history,

including expert and inventor testimony, dictionaries, and learned treatises." *Markman II*, 52 F.3d at 980. For instance, technical dictionaries can assist the court in determining the ordinary and customary meaning of a term because such dictionaries "endeavor to collect the accepted meanings of terms used in various fields of science and technology." *Phillips*, 415 F.3d at 1318. In addition, expert testimony can be useful "to ensure that the court's understanding of the technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Id.* Nonetheless, courts must not lose sight of the fact that "expert reports and testimony [are] generated at the time of and for the purpose of litigation and thus can suffer from bias that is not present in intrinsic evidence." *Id.* Overall, while extrinsic evidence "may be useful to the court," it is "less reliable" than intrinsic evidence, and its consideration "is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." *Id.* at 1318-19. Where the intrinsic record unambiguously describes the scope of the patented invention, reliance on any extrinsic evidence is improper. *See Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1308 (Fed. Cir. 1999) (citing *Vitronics*, 90 F.3d at 1583).

Finally, "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Renishaw PLC v. Marposs SpA*, 158 F.3d 1243, 1250 (Fed. Cir. 1998). It follows that "a claim

interpretation that would exclude the inventor's device is rarely the correct interpretation." *Osram GmbH v. Int'l Trade Comm'n*, 505 F.3d 1351, 1358 (Fed. Cir. 2007) (internal quotation marks omitted).

II. CONSTRUCTION OF DISPUTED TERMS

A. "wherein said (i) . . . and said (ii) . . . are administered in combination" / "administering . . . the combination of: (i) . . . ; . . . ; and wherein said components (i) and (ii) are administered in one unit dose form or in two separate unit dose forms"[2]

Novartis wherein said (i) . . . and said (ii) . . . , are administered in combination / administering . . . the combination of: (i) . . . ; (ii) . . . ; and wherein said components (i) and (ii) are administered in one unit dose form or in two separate unit dose forms
Defendants wherein said (i) . . . and said (ii) . . . are administered in concert as two separate components / administering . . . the combination of (i) . . . ; (ii) . . . ; and wherein said components (i) and (ii) are administered in concert in either one unit-dose form or in two separate unit-dose forms, as two separate components

2. These terms appear in claim 1 of the '659 patent and claim 1 of the '331 patent.

Appendix C

Court
wherein said (i) . . . and said (ii) . . . , are administered in combination / administering . . . the combination of (i) . . . ; (ii) . . . ; and wherein said components (i) and (ii) are administered in one unit dose form or in two separate unit dose forms

"The sole dispute between the parties regarding the 'combination' terms is whether these terms, and thus the '659 and '331 Patent claims, are limited to the active agents valsartan and sacubitril 'as two separate components' as Defendants propose, or not so limited as Novartis proposes." (D.I. 253 at 5) The Court concludes that they are not.

The intrinsic record is silent on whether sacubitril and valsartan must be separate (and not complexed). As Novartis points out, "[n]othing in the specification of the '659 and '331 Patents limits the claims." (D.I. 253 at 10) Indeed, the specification "discloses combinations of physically separate valsartan and sacubitril and does not disclose the later-invented ***compound*** of valsartan and sacubitril (wherein valsartan and sacubitril salts are associated with non-covalent bonds)." (*Id.*) As Novartis also points out, the patentee did not define or disclaim the "combination" of those two ingredients. (*Id.* at 10-11) In the Court's view, the absence of any indication in the written description that the patentee limited its invention solely to separate compounds means, in context, that a person of ordinary skill in the art ("POSA") would not read the claims as so limited.

That the patent is not limited to separate compounds is bolstered by a patent term extension granted on the '659 and '331 patents. (*See generally* D.I. 255 Exs. 11, 16) In seeking and obtaining the patent term extension, Novartis represented to the Patent Office that the '659 and '331 patents cover Entresto, a drug consisting solely of non-separate, complexed valsartan and sacubitril. (*See id.*) The parties devote much of their briefing to argument about whether this evidence is intrinsic or extrinsic (*see, e.g.*, D.I. 253 at 22-23, 33-34), an issue on which there is little helpful authority. *See, e.g., Abbott Labs. v. Dey, L.P.*, 110 F. Supp. 2d 667, 673 (N.D. Ill. 2000) (determining that application for patent term extension was "extrinsic" and "should not be considered"). Here, the patent term extension evidence, whether viewed as intrinsic or extrinsic, does not contradict an unambiguous construction otherwise apparent from the indisputably intrinsic evidence. The Court believes that a POSA would give this evidence some weight in understanding how the patentee is using the claim term in the context of the patent and would find it to support Plaintiff's construction.[3] *See generally Festo*

3. The Court recognizes that "[t]he determination as to whether a patent is eligible for an extension will normally be made solely from the representations contained in the application for patent term extension." Manual of Patent Examining Procedure ("MPEP") § 2755 (9th ed. Rev. 10.2019 June 2020); *see also* 37 C.F.R. § 1.750; *Abbott*, 110 F. Supp. 2d at 673 ("[T]he granting of the extension appears to have had nothing to do with determining what the claims of the patent mean . . . "). While this may mean, as Defendants contend, that Novartis' representations to the PTO in seeking the patent term extension were "litigation-inspired" (*see* D.I. 253 at 14), all statements made by a patentee to the PTO are subject to a "duty of candor and good faith," 37 C.F.R. § 1.765,

Corp. v. Shoketsu Kinzoku Koko Kabushiki Co., 535 U.S. 722, 730-31, 122 S. Ct. 1831, 152 L. Ed. 2d 944 (2002) ("A patent holder should know what he owns, and the public should know what he does not.").

Defendants further contend that Plaintiffs construction will render the claims invalid. (*See* D.I. 253 at 20-21, 39-40) Novartis admits that its two patents "do not disclose or suggest" a one-unit-dose-form embodiment. (*See id.* at 39) This seems to be an admission by Novartis that, at the very least, there will be a non-frivolous issue of written description and/or lack of enablement as this case proceeds on Novartis's preferred construction. *See generally Ruckus Wireless, Inc. v. Innovative Wireless Sols., LLC*, 824 F.3d 999, 1004 (Fed. Cir. 2016). At this point, the Court has no basis to believe that the construction it is adopting is necessarily consigning the asserted claims to a judgment of invalidity. Since this construction is otherwise supported, the Court will adopt it. *See, e.g., Phillips*, 415 F.3d at 1327 ("While we have acknowledged the maxim that claims should be construed to preserve their validity, we have not applied that principle broadly, and we have certainly not endorsed a regime in which validity analysis is a regular component of claim construction.").

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and the patentee may always be asked by the PTO for further information, *see id.* § 1.750; *see also* MPEP § 2755; Tr. at 60-61 (discussing possibility that patent could be rendered unenforceable due to inequitable conduct). Again, understanding all of this, the Court believes that a POSA would nonetheless give consideration to the patent term extension evidence and, correspondingly, the Court has as well.

B. "trisodium [34(1S,3R)-1-biphenyl-4-ylmethyl-3-ethoxycarbonyl-1-butylcarbamoyl) propionate-(S)-3'-methyl-2'-(pentanoyl{2"-(tetrazol-5-ylate)biphenyl-4'-ylmethyl}amino) butyrate] hemipentahydrate in crystalline form" / "trisodium [3-((1S,3R)-1-biphenyl-4-ylmethyl-3-ethoxycarbonyl-1-butylcarbamoyl) propionate-(S)-3'-methyl-21-(pentanoyl{2"-(tetrazol-5-ylate)biphenyl-4'-ylmethyl}amino) butyrate] hemipentahydrate"[4]

Novartis
substantially pure trisodium [sacubitril-valsartan] hemipentahydrate in crystalline form / trisodium [sacubitril-valsartan] hemipentahydrate

4. These terms appear in claim 1 of the '938 patent and claims 1, 4-11, and 13-15 of the '134 patent. In the briefing, the chemical name "trisodium [3-((1S,3R)-1-bipheny1-4-ylmethyl-3-ethoxycarbonyl-1-butylcarbamoyl)propionate-(S)-3'-methyl-2'-(pentanoyl{2"-(tetrazol-5-ylate)biphenyl-4'-ylmethyl}arnino) butyrate] hemipentahydrate" is more conveniently referred to as "trisodium [sacubitril-valsartan] hemipentahydrate." (D.I. 253 at 43) The Court adopts the same convention.

Appendix C

Defendants a substantially pure crystalline supramolecular complex having formula units of trisodium [sacubitril-valsartan] hemipentahydrate, wherein each formula unit in a unit cell of the crystalline complex has 2.5 water molecules and 3 sodium ions / a substantially pure crystalline supramolecular complex having formula units of trisodium [sacubitril-valsartan] hemipentahydrate, wherein each formula unit in a unit cell of the crystalline complex has 2.5 water molecules and 3 sodium ions
Court substantially pure trisodium [sacubitril-valsartan] hemipentahydrate in crystalline form / trisodium [sacubitril-valsartan] hemipentahydrate (claims 1-4); substantially pure trisodium [sacubitril-valsartan] hemipentahydrate in crystalline form (claims 5-15)

There are three issues for the Court to decide with respect to the "trisodium [sacubitril-valsartan] hemipentahydrate" and "in crystalline form" limitations:

(1) Is "trisodium [sacubitril-valsartan] hemipentahydrate" by itself limited to crystalline form?;

(2) Are the claim terms "trisodium [sacubitrilvalsartan] hemipentahydrate" and "crystalline form" limited to "a . . . supramolecular complex having formula units . . . ,

> wherein each formula unit in a unit cell . . . has 2.5 water molecules and 3 sodium ions"?; and
>
> (3) Are the '134 Patent claims limited to "substantially pure" trisodium [sacubitrilvalsartan] hemipentahydrate?

(D.I. 253 at 44 (internal citations omitted); *see also id.* at 57-58)

On the first issue, the Court agrees with Novartis that only certain claims (all of the claims of the '938 patent and dependent claims 5-15 of the '134 patent) are limited to crystalline embodiments. While claim 1 of the '938 patent explicitly requires trisodium [sacubitrilvalsartan] hemipentahydrate in crystalline form, claim 1 of the '134 patent does not; instead, only dependent claims 5-15 of the '134 patent are limited to crystalline forms. The specification of the '134 patent teaches that the compound of the claims "can be in the crystalline, partially crystalline, amorphous, or polymorphous form, preferably in the crystalline form" ('134 patent at 15:63-67), all of which suggests that the claimed compound is not always and necessarily in crystalline form. Moreover, the Examiner never required Novartis to specifically elect the crystalline form during prosecution of the '134 patent. (*See* D.I. 255 Ex. 38)

Defendants are correct that, during prosecution of the '938 patent, the Examiner issued a restriction

requirement, in response to which Novartis elected trisodium [sacubitril-valsartan] in crystalline form with hydrates. (D.I. 255 Ex. 20 at 11) In doing so, Novartis gave up the opportunity to prosecute other, non-crystalline forms claimed in the application that resulted in the '938 patent. The restriction requirement was accepted and understood: the Examiner made an amendment to replace solid forms with "crystalline" forms and noted that the Karpinski declaration was persuasive as to the "undue technical hurdles" to "prepare the ***claimed crystalline compound***." (D.I. 255 Ex. 28 at 3 (emphasis added); *see also id.* Ex. 20 at 11 (restriction response election)) Post-allowance, Novartis stated that "initial experiments to prepare ***the claimed crystalline*** trisodium hemipentahydrate involved screening" wherein "much work was required to prepare the ***claimed crystalline*** trisodium hemipentahydrate." (D.I. 255 Ex. 29 at 1) (emphasis added)

This same restriction requirement and election to prosecute only crystalline claims is not part of the prosecution of the '134 patent. While the specification of the '134 patent states that the patent relates to "trisodium [sacubitril-valsartan], ***a crystalline solid***" ('134 patent at 17:41-48) (emphasis added), this is not a definition of trisodium [sacubitril-valsartan]. Nor is it, in the Court's view (and the view of a POSA, looking at the claim term in the context of the patent), a disclaimer.

On the second issue, the Court agrees with Novartis that the claims are not limited to embodiments in which the trisodium [sacubitril-valsartan] exists as a crystalline,

"supramolecular complex." The Examiner recognized that the complex could exist in crystalline, solid, amorphous, and other forms. (*See* D.I. 253 at 63-65; D.I. 255 Ex. 20 at 11; D.I. 255 Ex. 38) (requiring restriction between these forms) The specification states expressly that trisodium [sacubitril-valsartan] hemipentahydrate "***may*** be considered a sodium supramolecular complex" ('134 patent at 19:10-15) (emphasis added) and ***preferably*** "has a network of noncovalent bonds" (*id.* at 7:7-9), but these are not requirements. (*See also id.* at 6:50-51) ("In a preferred embodiment, the dual-acting compound is a complex, in particular a supramolecular complex.")

On the third issue, however, the Court agrees with Defendants that all of the crystalline claims of both the '938 and '134 patents do contain the substantial purity limitation. The parties agree that the '938 patent requires a substantially pure, crystalline compound. (D.I. 253 at 57) A child patent (such as the '134 patent) that uses the same claim language as the parent patent (such as the '938 patent) imports the same disclaimed meaning as the parent patent. *See Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 980 (Fed. Cir. 1999). Moreover, the '134 patent, as a divisional, incorporates the reasons for allowance of the '938 patent, which is explicitly confirmed in an office action in the '134 patent's prosecution history. (D.I. 206-3 Ex. 34 at 25 ¶ 19) ("Incorporation by reference is made to the reasons for allowance in the parent application. . . .") Even though Novartis never expressly agreed with the Examiner's reasoning and never otherwise disclaimed non-substantially pure forms (*see* D.I. 253 at 57, 90-91), for the reasons just given the disclaimer carries over to

the crystalline claims of the '134 patent (i.e., claims 5-15). The other claims of the '134 patent, not being limited to the crystalline form, do not carry the substantially pure limitation. *See Ventana Med. Sys., Inc. v. Biogenex Labs., Inc.*, 473 F.3d 1173, 1182 (Fed. Cir. 2006) ("[T]he doctrine of prosecution disclaimer generally does not apply when the claim term in the descendant patent uses different language."); *Broadridge Fin. Solutions, Inc. v. Inveshare, Inc.*, 2012 U.S. Dist. LEXIS 51246, 2012 WL 1245723, at *4 (D. Del. Apr. 11, 2012) ("[E]ven if the [parent] patent disclaimer relates to the same subject matter at issue in the [child] patent claims, it may not necessarily affect the [child patent's] claim construction if the claim language is materially different.")

III. CONCLUSION

The Court will construe the disputed terms as explained above. The Court will also adopt the parties' agreed-upon constructions. An appropriate Order follows.

APPENDIX D — ORDER OF THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT, FILED MARCH 25, 2025

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

2023-2218, 2023-2220, 2023-2221

IN RE: ENTRESTO (SACUBITRIL/VALSARTAN)

NOVARTIS PHARMACEUTICALS CORPORATION,

Plaintiff-Appellant,

v.

TORRENT PHARMA INC., TORRENT PHARMACEUTICALS LTD.

Defendants.

NOVARTIS PHARMACEUTICALS CORPORATION,

Plaintiff-Appellant,

v.

ALEMBIC PHARMACEUTICALS LIMITED, ALEMBIC PHARMACEUTICALS INC.,

Defendants.

Appendix D

NOVARTIS PHARMACEUTICALS CORPORATION,

Plaintiff-Appellant,

v.

MSN PHARMACEUTICALS, INC.,
MSN LABORATORIES PRIVATE LTD.,
MSN LIFE SCIENCES PRIVATE LTD.,

Defendants-Appellees,

HETERO USA, INC., HETERO LABS LIMITED,
HETERO LABS LIMITED UNIT-III,

Defendants.

Appeals from the United States District Court for the District of Delaware in Nos. 1:19-cv-01979-RGA, 1:19-cv-02021-RGA, 1:19-cv-02053-RGA, 1:19-cv-02053-RGA, 1:20-md-02930-RGA, Judge Richard G. Andrews.

ON MOTION AND ON PETITION FOR PANEL REHEARING AND REHEARING EN BANC

Before Moore, *Chief Judge*, Lourie, Dyk, Prost, Reyna, Taranto, Chen, Hughes, and Stoll, *Circuit Judges.*[1]

Per Curiam.

1. Circuit Judge Newman, Circuit Judge Cunningham, and Circuit Judge Stark did not participate.

Appendix D

ORDER

MSN Laboratories Private Ltd., MSN Life Sciences Private Ltd. and MSN Pharmaceuticals, Inc. move for re- consideration en banc of the court's January 21, 2025, order. Novartis Pharmaceuticals Corporation responds in opposition and MSN moves for leave to file a reply.

MSN subsequently filed a combined petition for panel rehearing and rehearing en banc. A response to the petition was invited by the court and filed by Novartis. Association for Accessible Medicines requested leave to file a brief as amicus curiae, which the court granted.

The motion for reconsideration and the petition were first referred to the panel that heard the appeal, and thereafter the motion and the petition were referred to the circuit judges who are in regular active service.

Upon consideration thereof,

It Is Ordered That:

(1) The motion for leave to file a reply is denied.

(2) The motion for reconsideration is denied.

(3) The petition for panel rehearing is denied.

(4) The petition for rehearing en banc is denied.

March 25, 2025
Date

APPENDIX E — RELEVANT STATUTORY PROVISION INVOLVED

§ 112. Specification

(a) In General.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

(b) Conclusion.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

(c) Form.—A claim may be written in independent or, if the nature of the case admits, in dependent or multiple dependent form.

(d) Reference in Dependent Forms.—Subject to subsection (e), a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

(e) Reference in Multiple Dependent Form.—A claim in multiple dependent form shall contain a reference, in the alternative only, to more than one claim previously set forth and then specify a further limitation of the

subject matter claimed. A multiple dependent claim shall not serve as a basis for any other multiple dependent claim. A multiple dependent claim shall be construed to incorporate by reference all the limitations of the particular claim in relation to which it is being considered.

(f) ELEMENT IN CLAIM FOR A COMBINATION.—An element in a claim for a combination may be expressed as a means or step for performing a specified function without the recital of structure, material, or acts in support thereof, and such claim shall be construed to cover the corresponding structure, material, or acts described in the specification and equivalents thereof.