IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

In re Entresto (Sacubitril/Valsartan) Patent Litigation	C.A. No. 20-2930-LPS
NOVARTIS PHARMACEUTICALS CORPORATION, Plaintiff, v. ALKEM LABORATORIES LTD., AUROBINDO PHARMA USA INC., AUROBINDO PHARMA LTD., BIOCON PHARMA LIMITED, BIOCON LIMITED, BIOCON PHARMA, INC., CRYSTAL PHARMACEUTICAL (SUZHOU) CO., LTD., LAURUS LABS LIMITED, LAURUS GENERICS INC., LUPIN ATLANTIS HOLDINGS, S.A., LUPIN LIMITED, LUPIN INC., LUPIN PHARMACEUTICALS, INC., NANJING NORATECH PHARMACEUTICAL CO., LIMITED, TEVA PHARMACEUTICALS USA, INC., TORRENT PHARMA INC., TORRENT PHARMACEUTICALS LTD., Defendants.	C.A. No. 19-1979-LPS

NOVARTIS PHARMACEUTICALS CORPORATION, Plaintiff, v. ALEMBIC PHARMACEUTICALS LIMITED, ALEMBIC PHARMACEUTICALS, INC., MACLEODS PHARMACEUTICALS LTD., MACLEODS PHARMA USA, INC., Defendants.	C.A. No. 19-2021-LPS
NOVARTIS PHARMACEUTICALS CORPORATION, Plaintiff, v. DR. REDDY'S LABORATORIES, INC., DR. REDDY'S LABORATORIES, LTD., HETERO USA INC., HETERO LABS LIMITED, HETERO LABS LIMITED UNIT III, MSN PHARMACEUTICALS INC., MSN LABORATORIES PRIVATE LIMITED, MSN LIFE SCIENCES PRIVATE LIMITED, NOVUGEN PHARMA (MALAYSIA) SDN. BHD., ZYDUS PHARMACEUTICALS (USA) INC., CADILA HEALTHCARE LTD., Defendants.	C.A. No. 19-2053-LPS

NOVARTIS PHARMACEUTICALS CORPORATION, Plaintiff, v. ALEMBIC PHARMACEUTICALS LIMITED, ALEMBIC PHARMACEUTICALS, INC., Defendants.	C.A. No. 20-74-LPS
NOVARTIS PHARMACEUTICALS CORPORATION, Plaintiff, v. LUPIN ATLANTIS HOLDINGS, S.A., LUPIN LIMITED, LUPIN INC., LUPIN PHARMACEUTICALS, INC., Defendants.	C.A. No. 20-415-LPS C.A. No. 21-229-LPS
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JOINT CLAIM CONSTRUCTION BRIEF

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'134 Patent	U.S. Patent No. 9,388,134 (Ex. 4)
'331 Patent	U.S. Patent No. 8,796,331 (Ex. 2)
'659 Patent	U.S. Patent No. 8,101,659 (Ex. 1)
'938 Patent	U.S. Patent No. 8,877,938 (Ex. 3)
ARB	angiotensin-receptor blocker (also called AT 1-antagonist or Ang II antagonist)
Butcher Resp. Decl.	Declaration of Raymond Butcher, Ph.D. (Ex. B)
Butcher Sur-Reply Decl.	Sur-Reply Declaration of Raymond Butcher, Ph.D. (Ex. D)
Ex. __	Exhibits attached to the Joint Claim Construction Brief Appendix, submitted herewith.
FH	file history
Kaneniwa 1984	Kaneniwa & Otsuka, "The Interaction between Water and Cephalexin in the Crystalline and Noncrystalline States," *Chem. Pharm. Bull.* 32(11): 4551-4559 (1984) (Ex. 55)
Klibanov Decl.	Declaration of Alexander M. Klibanov, Ph.D. (Ex. A)
Klibanov Reply Decl.	Reply Declaration of Alexander M. Klibanov, Ph.D. (Ex. C)
NEP	neutral endopeptidase
Novartis	Novartis Pharmaceuticals Corporation
PI	Prescribing Information
POSA	person of ordinary skill in the art
PTO	United States Patent and Trademark Office
PTE	patent term extension

sacubitril	N-(3-carboxy-1-oxopropyl)-(4S)-(p-phenylphenylmethyl)-4-amino-2R-methylbutanoic acid ethyl ester
sacubitrilat	(2R,4S)-5-biphenyl-4-yl-4(3-carboxy-propionyl amino)-2-methyl-pentanoic acid
trisodium [sacubitril-valsartan] hemipentahydrate	trisodium [3-((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
valsartan	(S)-3′-methyl-2′-(pentanoyl{2″-(tetrazol-5-ylate)biphenyl-4′-ylmethyl}amino) butyrate
Webb	WO 03/059345

Pursuant to the September 18, 2020 Scheduling Order (C.A. No. 20-2930-LPS, D.I. 102, ¶ 14), Plaintiff Novartis Pharmaceuticals Corporation ("Novartis") and Defendants Alembic Pharmaceuticals Limited and Alembic Pharmaceuticals, Inc. (collectively, "Alembic"); Alkem Laboratories Ltd. ("Alkem"); Aurobindo Pharma USA Inc. and Aurobindo Pharma Ltd. (collectively "Aurobindo"); Biocon Pharma Limited, Biocon Limited, and Biocon Pharma, Inc. (collectively, "Biocon"); Crystal Pharmaceutical (Suzhou) Co., Ltd. ("Crystal Pharma"); Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd. (collectively, "Dr. Reddy's"); Hetero USA Inc., Hetero Labs Limited, and Hetero Labs Limited Unit III (collectively, "Hetero"); Laurus Labs Limited and Laurus Generics Inc. (collectively, "Laurus"); Lupin Atlantis Holdings, S.A., Lupin Limited, Lupin Inc., and Lupin Pharmaceuticals, Inc. (collectively, "Lupin"); Macleods Pharmaceuticals Ltd. and Macleods Pharma USA, Inc. (collectively, "Macleods"); MSN Pharmaceuticals Inc., MSN Laboratories Private Limited, and MSN Life Sciences Private Limited (collectively, "MSN"); Mylan Pharmaceuticals Inc. ("Mylan"); Nanjing Noratech Pharmaceutical Co., Limited ("Noratech"); Novugen Pharma (Malaysia) Sdn. Bhd. ("Novugen"); Teva Pharmaceuticals USA, Inc. ("Teva"); Torrent Pharma Inc. and Torrent Pharmaceuticals Ltd. (collectively, "Torrent"); and Zydus Pharmaceuticals (USA) Inc. and Cadila Healthcare Ltd. (collectively, "Zydus,") (all collectively, "Defendants") hereby submit the following Joint Claim Construction Brief along with a Joint Appendix filed concurrently herewith containing the patents, portions of the intrinsic record, and extrinsic evidence relied upon in support of the parties' proposed constructions.

AGREED-UPON CONSTRUCTIONS

Claim Term (claim in which it appears)	Agreed-Upon Construction
"amounts effective to treat hypertension or heart failure" ('659 patent, claim 2)	amounts of each component sufficient in combination to treat hypertension or heart failure
"therapeutically effective amount" ('331 patent, claim 1)	amount sufficient to treat heart failure or hypertension
"therapeutically effective amount" ('134 patent, claim 1)	amount sufficient to treat heart failure or hypertension
"effective amount" ('938 Patent, claim 11)	amount sufficient to have a therapeutic effect

DISPUTED CONSTRUCTIONS

I. Disputed "combination" Terms:

"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 disputed "combination" terms appear in claim 1 of U.S. Patent No. 8,101,659 (Ex.[1] 1, "the '659 Patent") and claim 1 of U.S. Patent No. 8,796,331 (Ex. 2, "the '331 Patent"), shown below with the "combination" terms emphasized:

'659 Patent:

> **1.** A pharmaceutical composition comprising:
>
> (i) the AT 1-antagonist valsartan or a pharmaceutically acceptable salt thereof;
>
> (ii) the NEP inhibitor [sacubitril[2]] or [sacubitrilat[3]] or a pharmaceutically acceptable salt thereof; and
>
> (iii) a pharmaceutically acceptable carrier;
>
> ***wherein said (i)*** AT 1-antagonist valsartan or a pharmaceutically acceptable salt thereof ***and said (ii)*** NEP inhibitor [sacubitril] or [sacubitrilat] or a pharmaceutically acceptable salt thereof, ***are administered in combination*** in about a 1:1 ratio.

[1] "Ex. __" refers to the exhibits to the Joint Claim Construction Brief Appendix, filed herewith.

[2] The common name for "N-(3-carboxy-1-oxopropyl)-(4S)-(p-phenylphenylmethyl)-4-amino-2R-methylbutanoic acid ethyl ester" recited in the '659 and '331 Patent claims is sacubitril.

[3] Sacubitril is a prodrug that is metabolized after administration into the compound "(2R,4S)-5-biphenyl-4-yl-4(3-carboxy-propionyl amino)-2-methyl-pentanoic acid" recited in the '659 and '331 Patent claims and commonly known as sacubitrilat.

'331 Patent:

1. A method for the treatment of a condition or disease selected from the group consisting of hypertension and heart failure, comprising ***administering*** to a patient in need thereof a therapeutically effective amount of ***the combination of***:

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

(ii) the NEP inhibitor [sacubitril] or a pharmaceutically acceptable salt thereof, or [sacubitrilat] or a pharmaceutically acceptable salt thereof***; and***

wherein said components (i) and (ii) are administered in one unit dose form or in two separate unit dose forms.

The '659 and '331 Patents are in the same family and share substantively the same specification.[4] Ex. 1, '659 Patent at cover; Ex. 2, '331 Patent at cover. The parties have proposed the following constructions for the "combination" terms:

"wherein said (i) … and said (ii) … are administered in combination"
('659 Patent, claim 1)

Novartis's Proposal	Defendants' Proposal
wherein said (i) … and said (ii) …, are administered in combination	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 one unit dose form or in two separate unit dose forms"
('331 Patent, claim 1)

Novartis's Proposal	Defendants' Proposal
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	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

[4] As the '659 and '331 Patents share substantively the same specification, for simplicity, only citations to the '659 Patent specification are provided.

A. Novartis's Opening Position: The "combination" Terms Are Not Limited To Separate Components

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.[5] Defendants' constructions should be rejected as they lack support in the claims themselves, the patent specifications, and the file histories. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1316–17 (Fed. Cir. 2005). The Defendants seek to improperly narrow the claims by importing limitations, but the intrinsic evidence unambiguously shows that Novartis never limited the "combination" terms to two separate components. Accordingly, Novartis's constructions are the same as the claim language for claim 1 of the '659 Patent and claim 1 of the '331 Patent, respectively, which are not limited to separate components.

Defendants seek to limit the claims to valsartan and sacubitril "as two separate components" in an attempt to avoid literal infringement by some of their generic Entresto® (valsartan and sacubitril) ANDA Products. The Entresto® Product is a combination drug product comprising pharmaceutically acceptable salts of valsartan and sacubitril. While some combination drug products contain physically separate active agents, the valsartan and sacubitril salts in the Entresto® Product (and generic copies) are present in a chemical structure associated by non-covalent bonds, rather than as physically separate components.

[5] Defendants insert the phrase "in concert" in their constructions. Novartis is not aware of, and Defendants have not identified, any difference between the meaning of "combination" and "in concert."

A person of ordinary skill in the art[6] ("POSA") as of the priority date on January 17, 2002 would have readily understood the full scope of the "combination" terms, which is not limited to two separate components in view of the intrinsic evidence. *See Phillips*, 415 F.3d at 1312–13. There are two exceptions to the rule that a claim term is accorded its full scope: first, when the patentee acts as his own lexicographer, and second, when the patentee disavows the scope of a claim term either in the specification or during prosecution. *Phillips*, 415 F.3d at 1316–17. Neither exception applies here. Novartis never defined the disputed "combination" terms as separate components in the intrinsic evidence. And Novartis never disclaimed the full scope of the combination terms wherein valsartan and sacubitril were not separate. In fact, the opposite is true. Novartis told the Patent Office in applications for patent term extension that the '659 and '331 Patents claim the Entresto® Product (wherein valsartan and sacubitril are not physically separate), and the Patent Office found those patents eligible for such extension. *Infra* 11-12. Disclaimer of claim scope must be "clear and unmistakable." *See Avid Tech., Inc. v. Harmonic, Inc.*, 812 F.3d 1040, 1045 (Fed. Cir. 2016) (internal quotation marks omitted). This is a demanding standard that Defendants will not meet on the facts here.

1. **The Entresto® Product And Patents-In-Suit**

The Entresto® Product is a combination drug product that comprises two active agents with different mechanisms of action: (1) the angiotensin receptor blocker (AT 1-antagonist) valsartan and (2) the neutral endopeptidase (NEP) inhibitor sacubitril. *See, e.g.*, Ex. 11, '659

[6] A POSA in January 2002 with respect to the '659 and '331 Patents would have had an M.D. or a Ph.D. in medicinal chemistry, biochemistry, chemistry, pharmacology, biology, or a related field with two years of specific training, research, or experience studying and/or treating heart failure and/or hypertension, and/or pharmacotherapies therefor. Alternatively, a POSA would have had a master's degree in pharmacology, biology, or a related field with six years of the above-described training, research, or experience. A POSA would have collaborated with others having ordinary skills and experience in areas pertinent to the subject matter of the claims.

Patent File History ("FH"), 2015/09/01 PTE Application at 2. Valsartan and sacubitril are present as their pharmaceutically acceptable sodium "salts."[7] Klibanov Decl. ¶ 24.[8] In the Entresto® Product, the valsartan and sacubitril salts are present in a single chemical structure called a "compound" or "complex," where the components are associated by non-covalent bonds, and are thus distinct from a mixture of valsartan and sacubitril as physically separate components. Klibanov Decl. ¶ 24.

The four patents at issue in this litigation 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, wherein the disputed "combination" terms appear, claim priority to that 2002 application.[9]

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. Novartis filed priority patent applications for that invention on April 4 and August 11, 2006. Novartis's U.S. Patent Nos. 8,877,938 and 9,388,134 ("the '938 and '134 Patents") claim priority to those later 2006 applications.[10] The parties dispute constructions of '938 and '134 Patent claim terms, addressed in Section II.

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[7] For convenience, "valsartan" and "sacubitril" are used with respect to the "combination" terms to encompass valsartan and pharmaceutically acceptable salts thereof, and sacubitril and pharmaceutically acceptable salts thereof, respectively, unless otherwise specified.

[8] "Klibanov Decl. ¶ __" refers to the Declaration of Alexander M. Klibanov, Ph.D. in support of Novartis's Opening Claim Construction Brief, submitted concurrently herewith (Ex. A).

[9] Ex. 1, '659 Patent at cover (claiming priority to "provisional application No. 60/349,660, filed on Jan. 17, 2002"); Ex. 2, '331 Patent at cover (claiming priority to "provisional application No. 60/349,660, filed on Jan. 17, 2002").

[10] Ex. 3, '938 Patent at cover (claiming priority to "provisional application No. 60/789,332, filed on Apr. 4, 2006" and "provisional application No. 60/822,086, filed on Aug. 11, 2006"); Ex. 4,

2. Nothing In The Intrinsic Record Limits The "combination" Terms To Separate Components

The disputed "combination" terms appear in two independent claims: claim 1 of the '659 Patent and claim 1 of the '331 Patent, neither of which is limited by the claim language to separate components in one pharmaceutical composition or one unit dose form. *See Phillips*, 415 F.3d at 1314 ("[T]he claims themselves provide substantial guidance as to the meaning of particular claim terms."). All remaining claims of the '659 and '331 Patents depend directly or indirectly from these two independent claims.

Claim 1 of the '659 Patent (Ex. 1 at 16:17-33 (emphasis added)) is reproduced below:

> **1.** A pharmaceutical composition comprising:
>
> **(i)** the AT 1-antagonist **valsartan** or a pharmaceutically acceptable salt thereof;
>
> **(ii)** the NEP inhibitor [**sacubitril**] or [sacubitrilat] or a pharmaceutically acceptable salt thereof; and
>
> (iii) a pharmaceutically acceptable carrier;
>
> ***wherein said (i)*** AT 1-antagonist **valsartan** or a pharmaceutically acceptable salt thereof ***and said (ii)*** NEP inhibitor [**sacubitril**] or [sacubitrilat] or a pharmaceutically acceptable salt thereof, ***are administered in combination*** in about a 1:1 ratio.

'134 Patent at cover (claiming priority to "provisional application No. 60/789,332, filed on Apr. 4, 2006" and "[p]rovisional application No. 60/822,086, filed on Aug. 11, 2006").

Claim 1 of the '331 Patent (Ex. 2 at 16:15-28 (emphasis added)) follows a similar structure, and is reproduced below:

> **1.** A method for the treatment of a condition or disease selected from the group consisting of hypertension and heart failure, comprising ***administering*** to a patient in need thereof a therapeutically effective amount of ***the combination of***:
>
> ***(i)*** the AT 1-antagonist **valsartan** or a pharmaceutically acceptable salt thereof***;***
>
> ***(ii)*** the NEP inhibitor [**sacubitril**] or a pharmaceutically acceptable salt thereof, or [sacubitrilat] or a pharmaceutically acceptable salt thereof***; and***
>
> ***wherein said components (i) and (ii) are administered in one unit dose form or in two separate unit dose forms***.

As shown above, claim 1 of the '659 Patent claims pharmaceutical compositions comprising three components: (i) valsartan, (ii) sacubitril, and (iii) a pharmaceutically acceptable carrier, "wherein said ***(i)*** . . . and said ***(ii)*** . . . , are administered ***in combination*** . . . ." The phrase "in combination" refers back to the claim elements identified with "(i)" and "(ii)" (valsartan and sacubitril, respectively). Likewise, claim 1 of the '331 Patent is directed to "the combination of" two components identified with "(i)" and "(ii)": valsartan and sacubitril, respectively, which may be in "one unit dose form ***or*** in two separate unit dose forms." While the valsartan and sacubitril components will necessarily be physically separate when administered in "two separate" unit dose forms, '331 Patent claim 1 does not limit the valsartan and sacubitril to separate components when they are administered in "one" dosage form as in '331 Patent claim 1 or in a "pharmaceutical composition" as in '659 Patent claim 1. Thus, nothing in these claims as a whole limits valsartan and sacubitril to separate components when they are in a single unit dose form or pharmaceutical composition.

That valsartan and sacubitril are listed separately and identified with "(i)" and "(ii)" in the claims does not limit them to physically separate components. *See Applied Med. Res. Corp. v. U.S. Surgical Corp.*, 448 F.3d 1324, 1333 n.3 (Fed. Cir. 2006) ("[T]he use of two terms in a claim requires that they connote different *meanings*, not that they necessarily refer to two different *structures*." (emphasis in original)). Considering claims to a pharmaceutical composition comprising (a) an active ingredient, (b) an excipient, and (c) a buffer, the court in *Merck Sharp & Dohme Corp. v. Fresenius Kabi USA, LLC* rejected the argument that the buffer must be "separate and distinct" from the active ingredient. No. 14-4989 (SRC), 2015 U.S. Dist. LEXIS 148064, at *4–10 (D.N.J. Oct. 30, 2015). As the *Merck* Court explained, "[t]he elements of a claim . . . do not need to be physically distinct things." *Id.* at *7. Romanettes (*e.g.*, "(i)," "(ii)," or "(iii)") are used to identify elements in a list that must be present, not to require the listed elements to be physically separate.

Nothing in the specification of the '659 and '331 Patents limits the claims to valsartan and sacubitril as separate components either. The '659 and '331 Patent 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). *Supra* 6-7. However, the Federal Circuit has repeatedly and "expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment." *See Phillips*, 415 F.3d at 1323. Claims are only read restrictively where the patentee demonstrates a "clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction" (*Meda Pharm., Inc. v. Apotex Inc.*, No. 14-1453-LPS, 2016 WL 2760336, at *2 (D. Del. May 12, 2016) (internal citation and quotation omitted)), which Novartis never did. Novartis neither acted as its

own lexicographer to limit the disputed "combination" terms to separate components, nor disclaimed single unit dose combinations wherein valsartan and sacubitril were not separate. Indeed, none of the intrinsic evidence that Defendants cited in the Joint Claim Construction Chart (D.I. 199) disclosed any such definition or disclaimer. Instead, the '659 and '331 Patent specification explains that the examples are "not intended to restrict the scope of the invention in any manner." Ex. 1, '659 Patent, 12:15-17.

In fact, in the file histories of both of the '659 and '331 Patents, Novartis explicitly characterized the claimed "combination" as not limited to separate components. In applications for patent term extension[11] ("PTE") filed for the '659 and '331 Patents, Novartis told the Patent Office that the claims of the '659 and '331 Patents covered Novartis's Entresto® Product and a method of using that Product, respectively, which as explained above (*supra* 6-7) comprises a chemical structure (complex) wherein the components are associated by non-covalent bonds and does not include sacubitril and valsartan as separate components:

> The approved product of ENTRESTO™ (sacubitril and valsartan), which is a ***combination of*** sacubitril, a [NEP] inhibitor, and valsartan, an [AT 1-antagonist], in the form of a complex . . . .

Ex. 11, '659 Patent FH, 2015/09/01 PTE Application at 1 (emphasis added), *see also* 5 ("Claim 1 reads on the approved product as follows: As mentioned above, the approved product, ENTRESTO™, is a ***combination of*** sacubitril and valsartan." (emphasis added)); Ex. 16, '331 Patent FH, 2015/09/01 PTE Application at 2, 5. The Patent Office thereafter reported to the Food and Drug Administration that each of the '659 and '331 Patents "claims a product

[11] PTE is an extension of patent term provided by Congress to restore the term of a patent which claims an approved product (in this case, Novartis's Entresto® Product) or method of using an approved product that was subject to regulatory review during the patent's term. *See* 35 U.S.C. § 156.

[ENTRESTO® (valsartan and sacubitril)] which has been subject to [regulatory] review" and was "eligible for patent term extension" subject to final review of the regulatory review period. Ex. 12, '659 Patent FH, 2017/02/14 Letter; Ex. 17, '331 Patent FH, 2017/02/14 Letter. In sum, Novartis told the Patent Office that it understood the '659 and '331 Patent claims were not limited to valsartan and sacubitril as separate components, and the Patent Office agreed.

3. Defendants' Constructions Are Inconsistent With The Claim Language

While Novartis's constructions are entirely consistent with the claim language, Defendants' proposals are not.

Defendants ignore that where Novartis intended to specify "separate" in the claims, as with "separate unit dose forms" in '331 Patent claim 1, it did so expressly. That Novartis did not also expressly limit the rest of claim 1 of the '331 Patent and claim 1 of the '659 Patent to "separate components" shows that Novartis did not intend for these claims to be limited. As shown in the table below, the '331 Patent claims administering the combination of valsartan and sacubitril "in one unit dose form or in two ***separate*** unit dose forms." *See* Ex. 2, '331 Patent, claim 1 (emphasis added). When Novartis wanted to indicate separateness it clearly knew how, and the claims at issue include no similar language limiting the "combination" terms to valsartan and sacubitril as "separate components." As illustrated below by inserting Defendants' construction into '331 Patent claim 1 and '659 Patent claim 1 (additions shown with underlining and deletions shown with strikethrough), Defendants' construction improperly adds "separate" to the combination claim terms even though that word is expressly used in a different part of '331 Patent claim 1 and not used at all in '659 Patent, claim 1. *See Photonic Imaging Sols., Inc. v. Lenovo Grp.*, No. 18-636 (MN), 2019 WL 4305335, at *4 (D. Del. Sept. 11, 2019) (finding the fact that patentees included terms in some claims and not others showed "the patentees knew

how to claim specific aspects of the [terms] when they wanted to," and declining to read such limitations into the claims).

'331 Patent	
claim 1	**Defendants' construction of claim 1**
1. A method . . . comprising administering . . . a therapeutically effective amount of the combination of: (i) [valsartan]; (ii) [sacubitril or sacubitrilat]; and wherein said components (i) and (ii) are administered in one unit dose form or in two separate unit dose forms.	**1.** A method . . . comprising administering . . . a therapeutically effective amount of the combination of: (i) [valsartan]; (ii) [sacubitril or sacubitrilat]; 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**.

'659 Patent	
claim 1	**Defendants' construction of claim 1**
1. A pharmaceutical composition comprising: (i) [valsartan]; (ii) [sacubitril or sacubitrilat]; and (iii) a pharmaceutically acceptable carrier; wherein said (i) [valsartan] and said (ii) [sacubitril or sacubitrilat], are administered in combination-in about a 1:1 ratio.	**1.** A pharmaceutical composition comprising: (i) [valsartan]; (ii) [sacubitril or sacubitrilat]; and (iii) a pharmaceutically acceptable carrier; wherein said (i) [valsartan] and said (ii) [sacubitril or sacubitrilat], are administered ~~**in combination**~~ **in concert as two separate components** in about a 1:1 ratio.

If Novartis intended to limit the combination of valsartan and sacubitril to separate components, Novartis could have easily added the term "separate" to that part of the claims, but Novartis did not. *See Photonic Imaging*, 2019 WL 4305335, at *4. Defendants' constructions should be rejected as they are not consistent with the language of the claims.

4. **Extrinsic Evidence Should Not Be Used To Contradict The Unambiguous Intrinsic Evidence**

The intrinsic evidence alone resolves the dispute here; nothing in the intrinsic evidence limits the "combination" terms to physically separate components. Sections I.A.1–3. Where a

claim construction is clear in view of the intrinsic evidence, this "should [be] the end of the [Court's] analysis." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1584 (Fed. Cir. 1996). "[Extrinsic evidence] may not be used to vary or contradict the claim language" or "contradict the import of other parts of the specification." *Id.* To the extent that Defendants disregard the case law and raise extrinsic evidence, the Court should give it no weight.

* * *

The Court should deny Defendants' proposals to limit the "combination" terms to separate components.

B. Defendants' Responsive Position:

The "combination" terms, which appear in claim 1 of each of the '659 and '331 Patents, recite that certain claimed active ingredients are administered in "combination."[12] In accordance with Defendants' proposed constructions, and by their plain meaning, the "combination" terms require that the two active ingredients, valsartan and sacubitril, are physically separate components administered in concert (i.e., at the same, or approximately the same, time). On the other hand, Novartis's proposed construction merely parrots the claim language in a litigation-inspired attempt to encompass greater scope, including specific solid-state forms, that are neither contemplated by nor described in the specification. Novartis admits that the specifications of the '659 and '331 Patents disclose ***nothing*** about the sacubitril-valsartan complex it now wishes to capture in its claim construction, and further admits that it did not "invent" the sacubitril-valsartan complex until "[s]everal years later." *Supra* 7, 10. Nevertheless, Novartis now attempts to capture this later "invention," for which it sought and obtained additional patent protection, by

[12] Defendants contend that certain terms in the asserted patents are indefinite under 35 U.S.C. § 112. By offering proposed constructions, Defendants are not waiving their right to assert that these claims or terms are indefinite.

improperly broadening the "combination" terms far beyond anything a POSA would understand from reading the '659 and '331 Patents.

1. The Specifications of the '659 and '331 Patents Repeatedly, Consistently, and Exclusively Depict Pharmaceutical Compositions Comprising Separate Valsartan and Sacubitril Components

Although "the claims of a patent define the invention to which the patentee is entitled the right to exclude," claim terms "must be read in view of the specification, of which they are a part." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312, 1315 (Fed. Cir. 2005). "[A] patent's repeated and consistent description of a claim term may inform its construction." *Groove Digital, Inc. v. United Bank*, 825 F. App'x 852, 856 (Fed. Cir. 2020). Indeed, "[e]ven when guidance is not provided in explicit definitional format, the specification may define claim terms by implication such that the meaning may be found in or ascertained by a reading of the patent documents." *Irdeto Access, Inc. v. Echostar Satellite Corp.*, 383 F.3d 1295, 1300 (Fed. Cir. 2004) (internal quotations omitted).

Here, the specifications of the '659 and '331 Patents consistently refer to combination treatments as administering the two active ingredients as physically separate components.[13] In the Background of the Invention, the specification summarizes prior art "combination" treatments where distinct active ingredients were administered. Ex. 1, '659 Patent at 2:46-49 (discussing that EP Appl. No. 498361 discloses "a combination of certain Ang II antagonists or certain renin inhibitors with certain NEP inhibitors"); 2:50-56 (discussing that EP Appl. No. 726072 discloses "a combination of" an Ang II antagonist and a NEP inhibitor). The specification further distinguishes these prior art combination therapies from single molecular

[13] The '659 and '331 Patents are related and share a common specification. Unless otherwise noted, citations herein are to the '659 Patent specification.

entities that have dual activity. *Id.* at 2:55-56 (discussing single molecular entities having both ACE and NEP inhibitory activity). This distinction carries through to the Detailed Description of the invention, where the patentees consistently and exclusively refer to combinations of two distinct active ingredients.

The specification discloses only sacubitril and valsartan combinations where the two active ingredients are administered in concert as separate components either in a single dosage form or in separate dosage forms and not as a chemical complex of the two. *Id.* at 3:30-5:45 (disclosing valsartan as the AT 1-receptor antagonist and separately disclosing various NEP inhibitors); 5:45-46 (disclosing that the compounds to be combined can be present as pharmaceutically acceptable salts); 6:53-55 (discussing the dosage amounts of the individual drugs to be combined); 7:33-10:2 (discussing studies wherein valsartan and sacubitril are administered as separate components); 11:24-31 (discussing "combining separate pharmaceutical compositions in kit form," which is "particularly advantageous when the separate components must be administered in different dosage forms, e.g., parenteral [intravenous] valsartan formulation and oral NEP formulation; or are administered at different dosage intervals."). In particular, the specification notes that "[a] therapeutically effective amount of each of the component [*sic*] of the combination of the present invention may be administered simultaneously or sequentially in any order." *Id.* at 10:57-59. This instruction would make little sense in the context of a sacubitril-valsartan chemical complex, where the components cannot be administered sequentially, nor "in any order."

Moreover, the specification further clarifies that although the components may be administered as a "unit dose form" (e.g., they may be combined in a single tablet), even when so combined, they remain separate components: "In this composition, components (i) and (ii) can

be obtained and administered together, one after the other or ***separately*** in one combined unit dose form or in two separate unit dose forms." *Id.* at 10:27-30.[14] The specification goes on to provide seven Formulation Examples that "illustrate the above-described invention," but notably not one of these examples teaches a claimed combination, let alone a chemical complex, of the two components. Rather, each of these examples describes the manufacture of a dosage form containing the single active ingredient valsartan. *Id.* at 12:20-16:12. The sole prophetic disclosure of the clinical administration of the claimed combination only discusses administering the two as separate active ingredients and not as a complex. *Id.* at 8:46-59; 9:24-52. In short, the specification "repeatedly, consistently, and exclusively depict[s]" pharmaceutical compositions comprising valsartan and sacubitril administered in concert (either "***separately*** in one combined unit dose form or in two separate unit dose forms"), requiring that the claims be construed commensurate in scope with the specification. *See In re Abbott Diabetes Care Inc.*, 696 F.3d 1142, 1148-50 (Fed. Cir. 2012) (no "clear disavowal" or "express disclaimer" of claim scope needed if specification "repeatedly, consistently, and exclusively" describes the invention in a certain way).

The Federal Circuit has repeatedly held that where the specification makes clear what the inventors contemplated as their invention by consistently and exclusively describing the invention in a particular way, the claims should be limited to that invention. For example, in *Abbott Diabetes Care*, the Federal Circuit reversed the district court's construction of "electrochemical sensor" that encompassed sensors with external cables, because the specification "'repeatedly, consistently, and exclusively' depict[s] an electrochemical sensor without external cables or wires." *Abbott Diabetes Care*, 696 F.3d at 1148-50; *see also Groove*

[14] Unless otherwise noted, all emphasis is added.

Digital, 825 F. App'x at 856-57 (defining the term "applet" narrowly, because the specification "'repeatedly, consistently, and exclusively' depicts applets as being geotargeted;" *Profectus Tech. LLC v. Huawei Techs. Co., Ltd.*, 823 F.3d 1375, 1380-81 (Fed. Cir. 2016) (construing "mountable" as requiring "having a feature for mounting," because every embodiment in the specification included a "mounting feature" and the patentee was unable to identify any disclosure that "contemplates a situation where *no* mounting features exist."). Similarly, in *Route1 Inc. v. AirWatch LLC*, 829 F. App'x 957, 960-62 (Fed. Cir. 2020), the Federal Circuit construed claim terms narrowly as limited to host-initiated connections because "[t]he specification discloses host-initiated connections, not remote-initiated connections," and the patentee "d[id] not identify a disclosure in which 'the host establishes the connection by responding to a request from the remote device,'" and admitted that no such disclosure exists; *Poly-America, L.P. v. API Indus., Inc.*, 839 F.3d 1131, 1137 (Fed. Cir. 2016) (construing "short seal" as requiring "inward extension," because "[e]very embodiment described in the specification has inwardly extended short seals.").

As detailed above, the specification consistently and repeatedly refers to the combination of valsartan and sacubitril as separate compounds. Novartis points to ***no disclosure*** in the specification even hinting at the existence of a valsartan-sacubitril chemical complex. Nor could it, as no such disclosure exists in the '659 and '331 Patents. To the contrary, Novartis ***admits*** that "[t]he '659 and '331 Patent 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)." *Supra* 10. In fact, the specification states that the pharmaceutical compositions "according to the invention can be prepared in a manner known per se." Ex. 1, '659 Patent, at 10:63-65. If the complex was

not invented until years later, it could not have been prepared by conventional methods as stated in the specification. Because patent terms are to be construed as a POSA would understand the term in view of the specification and file history at the time of the claimed invention, Novartis essentially concedes that a POSA would not have understood these claims to encompass the later-invented valsartan-sacubitril chemical complex. Indeed, based on these admissions, if the Court were to adopt Novartis's construction for the "combination" terms, the '659 and '331 Patent claims would be invalid for lack of written description and enablement. *Ruckus Wireless, Inc. v. Innovative Wireless Sols., LLC*, 824 F.3d 999, 1004 (Fed. Cir. 2016) (noting that canons of claim construction counsel limiting construction of disputed term to subject matter described in the specification, where a broader construction encompassing subject matter not mentioned in the specification "would likely render the claims invalid for lack of written description").

Novartis nevertheless insists that it can expand the clear meaning of the '659 and '331 Patent claims to capture a complex it developed "[s]everal years later," *supra* 7, because it did not act as its own lexicographer or demonstrate a "clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Id.* at 10-11 (citing *Meda Pharm. Inc. v. Apotex Inc.*, No. 14-1453-LPS, 2016 WL 2760336, at *2 (D. Del. May 12, 2016)). Novartis is incorrect.

The Federal Circuit has expressly rejected Novartis's suggestion that the specification must contain an express definition to inform the meaning of a claim term. To the contrary, "[a]n explicit definition is not required." *Groove Digital*, 825 F. App'x at 856. Rather, as is the case here, the specification "may define claim terms by implication" by "repeatedly, consistently, and exclusively" depicting the invention in a particular way. *Abbott Diabetes Care*, 696 F.3d at 1148-50. Where, as here, "the specification makes clear what the inventors contemplated as their

invention," it is appropriate, and indeed, necessary, to construe the terms as limited to that invention. *Hologic, Inc. v. Senorx, Inc.*, 639 F.3d 1329, 1335 (Fed. Cir. 2011).

Novartis's protestation that it has not expressly disclaimed that which it had not invented likewise makes little sense. "[T]his is not an instance where the specification would necessarily have to disavow an embodiment that would otherwise be covered by the plain language of the claims," because the plain language of the claims is "entirely consistent with and even support[s] the specification's exclusive depiction" of a pharmaceutical composition comprising valsartan and sacubitril in combination where each is a separate component. *Abbott Diabetes Care*, 696 F.3d at 1149-50.

Indeed, Novartis confirmed during the prosecution of the subsequently-filed '938 and '134 Patents—which, as discussed below, are expressly directed to the later-developed sacubitril-valsartan complex—that the '659 and '331 Patent claims ***cannot*** include the valsartan-sacubitril complex that Novartis is now trying to capture. Specifically, the application that led to the '938 Patent was rejected as obvious over WO 03/059345 ("Webb"). Webb claims priority to the same provisional application—US 60/349,660—as the '659 and '331 Patents and has a specification that is nearly identical in all material respects.

To overcome the rejection over Webb, Novartis explicitly argued that "there is no suggestion or motivation in any of the cited references, either alone or in combination, ***that suggests the possibility of a single compound*** which contains [valsartan and sacubitril]" and that the "***references do not disclose or suggest Applicants' claimed compound*** having both [valsartan] and [sacubitril] in the same compound structure." Ex. 22, Sept. 9, 2010 Amendment, at 6. Novartis further argued that "Webb does not teach the specific elected compound ***or identify the elected components together as being a compound***" and that the teachings in Webb

do not "suggest[], let alone teach[] how to make Applicant's claimed compound." *Id.* at 6, 7. In response to the Examiner's argument that the teaching of Webb of sacubitril and valsartan dissolved together in a solution would create the claimed compound, Novartis argued that "[a] solution of [valsartan] and [sacubitril] compounds of Webb would produce ***a solution of two compounds*** in an excess of solvent, ***not Applicants' claimed compound***." *Id.* at 7. Having unequivocally admitted that Webb, which is nearly identical in all material respects to the '659 and '331 Patents, does not "suggest[] the possibility of a single compound which contains [sacubitril and valsartan]," Novartis cannot now argue the opposite. *See Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 979 (Fed. Cir. 1999) ("Arguments made during the prosecution of a patent application are given the same weight as claim amendments.")

2. The File History Further Reinforces Defendants' Proposed Construction

The prosecution history of the '659 Patent, like the specification, only refers to valsartan and sacubitril administered in combination as separate components. The application that issued as the '659 Patent was rejected as obvious because "[t]o employ combinations of specific NEP inhibitor and valsartan would have been obvious because all the components are well known individually for treating hypertension." Ex. 5, Aug. 7, 2009 Office Action, at 5 (emphasis in original). In arguing against this rejection, Novartis asserted that during the prosecution of its parent, U.S. Patent No. 7,468,390 ("the '390 Patent"), "Applicants presented experimental data showing that the combination of valsartan and the specific NEP inhibitor … had a synergistic, unexpected and surprising antihypertensive effect which was not taught or obvious from the cited prior art." Ex. 6, Dec. 23, 2009 Amendment, at 4-5. Based on this argument, the obviousness rejection was withdrawn and the claims were allowed. Importantly, however, the data submitted during the prosecution of the '390 Patent, like the specification, only discusses

administering valsartan and sacubitril separately. *See* Ex. 37, '390 Patent file history, May 11, 2006 Webb Affidavit, at 2-5.

3. Novartis's Reference to Its Patent Term Extension Request Is Unavailing and Irrelevant

Novartis contends that the PTO somehow acquiesced to Novartis's now proposed construction when, in the context of Novartis's request for Patent Term Extension ("PTE") on the '659 and '331 Patents based on the Entresto® product, the PTO forwarded Novartis's application to the FDA for determination of the regulatory review period. Not so. As an initial matter, courts have held that PTE applications and the FDA's subsequent action are considered extrinsic evidence and not, as Novartis asserts, part of the prosecution history of the patents at issue. *See Abbott Labs. v. Dey, L.P.*, 110 F. Supp. 2d 667, 673 (N.D. Ill. June 28, 2000).

Novartis argues that extrinsic evidence should not be considered in this case, yet seeks to rely on its self-serving PTE submissions and related proceedings, all of which contradict the intrinsic record. *See supra* 14 ("'[Extrinsic evidence] may not be used to vary or contradict the claim language' or 'contradict the import of other parts of the specification.'" (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1584 (Fed. Cir. 1996))). But these documents have no bearing on construing the claims. *Vitronics*, 90 F.3d at 1584; *see also Ferring B.V. v. Barr Labs, Inc.*, No. 7:02-CV-9851 CLB MDF, 2005 WL 437981, at *16 (S.D.N.Y. Feb. 7, 2005) (explaining that definitions relating to PTEs are not implicated in the claim construction analysis, "nor do they relieve [the patentee] of the traditional obligation to specify accurately the invention claimed."). Indeed, contrary to Novartis's assertions, "[c]laim construction is a matter of law and, therefore, does not fall within the PTO's technical expertise (assuming that the PTO went through the claim construction exercise in the first instance)." *Genetics Inst., LLC v. Novartis Vaccines and Diagnostics, Inc.*, No. 08-290-SLR, 2010 WL 677745, at *2 (D. Del. Feb. 24,

2010). Here, there is no evidence that the PTO engaged in any claim construction analysis in considering Novartis's PTE applications. And even if the PTO did implicitly acquiesce in Novartis's description of Entresto® in relation to the '659 and '331 Patents—although there is no such evidence of record—that acquiescence "does not fall within the PTO's technical expertise" and is accorded no deference. *Id.*

4. Novartis's Proposed "Construction" Does No More Than Repeat the Claim Language

Finally, Novartis argues that its constructions "are entirely consistent with the claim language." *Supra* 12. This argument also misses the point because Novartis offers no proposed construction at all. Rather, Novartis's "proposed construction" merely repeats the words of the claims without elaboration, elucidation, or explanation. To the extent Novartis suggests that the terms do not need to be construed or argues for some undisclosed and unexplained plain and ordinary meaning, the Court should reject these arguments outright. The parties have presented a fundamental dispute regarding the scope of each of the two claim terms at issue—whether the scope of the claims of the '659 and '331 Patents encompasses a sacubitril-valsartan complex. That dispute cannot be resolved by merely repeating the claim terms. *See, e.g.*, *Hill-Rom Services, Inc. v. Stryker Corp.*, No. 1:11–cv–1120–JMS–DKL, 2013 WL 364568, *6 (S.D. Ind. Jan. 30, 2013) (*rev'd on other grounds*) (rejecting a proposed construction that merely recited the words of the claim without elaboration); *see also Maytag Corp. v. Electrolux Home Prods., Inc.*, 411 F. Supp. 2d 1008, 1037 (N.D. Iowa 2006) ("The court does not agree with Maytag's assertion that terms to be given their 'ordinary meanings' do not require any construction. … Moreover, determining what is the 'ordinary meaning ... as understood by a person of skill in the art' is part of the ***process*** of claim construction." (emphasis in original)). Novartis's "proposed

construction" here is unhelpful in resolving the parties' dispute and should be rejected for that additional reason.

Novartis's contention that the Defendants' proposed construction is inconsistent with the claim language is equally unavailing. Novartis argues that claim 1 of the '331 Patent refers to "separate unit dose forms," and therefore, "[w]hen Novartis wanted to indicate separateness it clearly knew how." *Supra* 12. Novartis ignores the fact that the entire specification, when discussing pharmaceutical compositions of valsartan and sacubitril administered in combination, refers to compositions involving separate components, and by its own admission "does not disclose the later-invented ***compound***." *Id.* at 10 (emphasis in original). It is of no moment that under these circumstances, Novartis did not explicitly include the word "separate" in the claims to describe the components. The specification "repeatedly, consistently, and exclusively" depicts the claimed pharmaceutical compositions as having separate components, and therefore implicitly defines the claimed pharmaceutical composition as such. *Abbott Diabetes Care*, 696 F.3d at 1149-50.

More importantly, the "separate unit dose forms" that Novartis relies upon is different from Defendants' construction of physical separateness. Claim 1 of the '331 Patent is directed to pharmaceutical compositions "in one unit dose form or in two separate unit dose forms." Active pharmaceutical ingredients ("APIs") that are physically separated can be in a single dosage form—for example, in a mixture or in layers or in other forms of combination; or they can be in two separate dose forms, with one API in one unit dose form and the other in a second unit dose form. Accordingly, Defendants' proposed construction is entirely consistent with the language of the claims.

In sum, "because the specification ... consistently and exclusively shows" pharmaceutical compositions comprising valsartan and sacubitril as separate components, and "because that is clearly what the inventors of [the '659 and '331 Patents] conceived of," claim 1 in each of the '659 and '331 Patents is properly construed as directed to pharmaceutical compositions comprising valsartan and sacubitril, wherein the two active ingredients are administered in concert (in one unit dose form or in two separate unit dose forms) as two separate components, and do not include a valsartan-sacubitril complex.

C. Novartis's Reply Position: The Disputed "combination" Terms Are Not Limited To Separate Components

Defendants do not contest that the intrinsic evidence never ***expressly*** limits the claimed "combination[s]" to separate components. *See supra* 8-12, 19. Instead, Defendants' theory for limiting the "combination" terms is that the intrinsic evidence "repeatedly, consistently, and exclusively" describes sacubitril and valsartan as separate components, and does not describe the later-invented compound trisodium [sacubitril-valsartan] hemipentahydrate. This argument is both factually and legally incorrect. None of the specification statements Defendants cite, which use only permissive language or focus on irrelevant embodiments, limits "combination" to separate components. *See infra* Section I.C.1. And Defendants misapply their own alleged legal support. *See infra* Section I.C.2. Furthermore, Defendants' written description argument ignores settled law that the claims of an earlier patent can cover a later-discovered embodiment of the claimed subject matter even where the specification of the earlier patent does not describe that embodiment. *See infra* Section I.C.3.

1. The Intrinsic Evidence Does Not "Repeatedly, Consistently, [A]nd Exclusively" Describe The Claimed "combination[s]" As Limited To Separate Components

Novartis twice told the PTO and the public that the claimed combinations of sacubitril

and valsartan were not limited to separate components. First, Novartis knew how to use the term "separate," as it did with "separate unit dose forms" in '331 Patent claim 1, and did not limit the claims to sacubitril and valsartan as "separate" components. *Supra* 12-13. Defendants assert that the phrase "separate unit dose forms" in claim 1 of the '331 Patent is "different from Defendants' construction of physical separateness." *Supra* 24. But Defendants themselves rely on the specification's disclosure of "separate unit dose forms" and other "separate" embodiments to argue in support of their constructions. *Supra* 17. Defendants cannot rely on the intrinsic evidence describing "separate" but ignore that Novartis did not limit the claims to "separate" components. Second, Novartis told the PTO in PTE applications that the '659 and '331 Patents claim the Entresto® Product (wherein sacubitril and valsartan are not physically separate), and the PTO found those patents eligible for such extension, which is intrinsic evidence. *Supra* 11-12; *see infra* Section I.C.5.

To support their argument, Defendants take specification phrases out of context and attempt to import selective parts of the specification into the claims, which is prohibited. *Phillips*, 415 F.3d at 1323. Read in context, these passages, discussed below, demonstrate Novartis's intent to capture the combination of sacubitril and valsartan without limiting the relationship between the sacubitril and valsartan components to separate components.

First, the specification's disclosure that sacubitril and valsartan "***can be*** . . . administered together, one after the other or separately in one combined unit dose form or in two separate unit dose forms" is on its face not limited to separate components. *Contra supra* 16-17 *citing* Ex. 1, '659 Patent, 10:27-30 (emphasis added). Defendants incorrectly suggest the specification only discloses administering the combination "***separately*** in one combined unit dose form." *Supra* 16-17 (emphasis in original). Even though sacubitril and valsartan will be physically separate when

administered "one after the other or separately" and/or "in two separate unit dose forms," the specification also discloses administering sacubitril and valsartan "together," which encompasses administering those agents regardless of whether they are physically separate. *Supra* 9; Ex. 1, '659 Patent, 10:27-29. Likewise, the '331 Patent claims administering sacubitril and valsartan either "in one unit dose form" (in claim 2 without any separate limitation) or "separately in two separate unit dose forms" (claim 3). Moreover, the specification uses the permissive phrase "can be," and therefore the passage at Ex. 1, '659 Patent, 10:27-30 does not limit the claims. *See i4i Ltd. P'ship v. Microsoft Corp.*, 598 F.3d 831, 844 (Fed. Cir. 2010).

Second, the specification's statement that "[a] therapeutically effective amount of each of the components of the combination of the present invention ***may be*** administered simultaneously or sequentially and in any order" is also not limited to separate components, and this language does not appear in any claim. *Contra supra* 16 *citing* Ex. 1, '659 Patent, 10:57-59 (emphasis added). Even though sacubitril and valsartan will be physically separate when administered "sequentially," administering each of the components "simultaneously" would encompass administering those agents regardless of whether they were physically separate. Defendants even admit that sacubitril and valsartan may be present in a single unit dose form (for example, as claimed in the '659 Patent), which cannot be administered "sequentially and in any order" but must be administered "simultaneously." *Supra* 16. Moreover, the specification uses a permissive phrase, "may be," indicating that this statement should not limit claim scope. *See i4i*, 598 F.3d at 844.

Third, that compositions of the invention "***can be*** prepared in a manner known per se. . . ." (*supra* 18-19 *citing* Ex. 1, '659 Patent, 10:63-64 (emphasis added)) is likewise not limiting because it too uses a permissive phrase, "can be." *See i4i*, 598 F.3d at 844. In addition,

none of the claims is directed to any preparation method.

Fourth, while the specification describes valsartan and sacubitril for use in the invention, pharmaceutically acceptable salts thereof, and dosages of those components (*supra* 16 *citing* Ex. 1, '659 Patent, 3:30-5:46, 6:53-55), those passages relate to the identities or amounts of the components, not whether those components are physically separate.

Fifth, the specification describes kits of valsartan and NEP inhibitors in separate dosage forms (*supra* 16 *citing* Ex. 1, '659 Patent, 11:24-31), but Defendants do not suggest that the asserted claims are limited to "kits," and they are not. The '659 Patent claims do not cover such "kits" here because valsartan and sacubitril must be present in the same composition.

Sixth, the specification discloses formulation examples comprising valsartan, and formulations of valsartan and sacubitril used in preclinical studies. *See supra* 16-17 *citing* Ex. 1, '659 Patent, 7:33-10:2, 12:20-16:12. These examples do not limit the claims because, as explained below (*infra* Section I.C.2.), the presence of embodiments of an invention having a particular feature does not by itself limit the claims. Moreover, the specification explains that the examples are not intended to restrict the scope of the invention. *Supra* 11.

Seventh, Defendants point to the statement in the specification's background section that a prior art reference discloses "a combination of [an ARB, not valsartan] with a NEP inhibitor [not sacubitril] or a dual acting vasopeptidase inhibitor (single molecular entity with both [angiotensin converting enzyme] and NEP inhibitory activities)." Ex. 1, '659 Patent, 2:50-56. The description of prior art combinations (an ARB with a NEP inhibitor or an ARB with a vasopeptidase inhibitor) does not limit the novel combination of valsartan and sacubitril at issue here.

Defendants also rely on the prosecution of the parent application for the '659 Patent

(which issued as U.S. Patent No. 7,468,390), wherein Novartis submitted evidence of unexpected results including test data for certain combinations of sacubitril and valsartan as separate components. There is no basis for limiting the claims based on unexpected results evidence submitted during prosecution. *See, e.g.*, *McNeil-PPC, Inc. v. Perrigo Co.*, 443 F. Supp. 2d 492, 505 (S.D.N.Y. 2006) (holding "[t]he submission of extraordinary results that are narrower in scope than the claims [during prosecution] does not, by itself, impose a limitation on the construction of the claims"). Defendants cited no reason to believe that a compound of sacubitril and valsartan, *e.g.*, trisodium [sacubitril-valsartan] hemipentahydrate, would not produce similar or better results. *See id.* at 506 (rejecting attempt to limit claim scope based on unexpected results where "Perrigo offer[ed] no evidence demonstrating that the same results would not be achieved" for an invention of broader scope). Moreover, the Examiner did not require Novartis to limit the claims to separate components in view of its test data, and Novartis never did so.

2. Defendants' "Repeatedly, Consistently, [A]nd Exclusively" Argument Also Lacks Legal Support

Claims are only read restrictively where the patentee demonstrates a "clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Supra* 10-11. That did not happen here. *Poly-America*, on which Defendants rely, explains this "clear intention" standard applies both when the claim limitations are express or implied. *See Poly-America*, 839 F.3d at 1136 ("While disavowal must be clear and unequivocal, it need not be explicit."); *see also Idenix Pharm., Inc. v. Gilead Scis., Inc.*, No. 13-1987-LPS *et al.*, 2015 WL 9048010, at *3 (D. Del. Dec. 16, 2015). Defendants have not met this demanding standard.

The mere disclosure of physical mixtures, and absence of the compound trisodium [sacubitril-valsartan] hemipentahydrate specifically (which was invented later), are not legally sufficient to limit the "combination" terms to separate components. *See Idenix*, 2015 WL

9048010, at *3-4 (finding no implicit disclaimer even though the specification did not disclose any embodiments with the relevant feature); *supra* 10-11.

In each of Defendants' cited cases, clear intrinsic evidence narrowed the disputed claims, not the mere absence of an embodiment. The Federal Circuit has repeatedly and "expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment." *See Phillips*, 415 F.3d at 1323; *supra* 10. None of Defendants' cases considered whether to exclude a *later-invented* embodiment from the scope of a claim, as Defendants argue here.

The *Irdeto* Court limited the claim because the applicant expressly argued that the disputed terms had no accepted meaning and "unequivocally directed the patent examiner, as well as the public, to the specification as the complete source of meaning for the disputed terms. . . ." *See Irdeto*, 383 F.3d at 1300-03. Here, Novartis never told the Examiner that the term "combination" was limited to what was specifically described in the specification. *See Chervon (HK) Ltd. v. One World Techs., Inc.*, No. 19-1293-LPS, 2020 WL 6561229, at *4 n. 4 (D. Del. Nov. 9, 2020) (distinguishing *Irdeto* where record did not support narrowing claim scope).

In *Poly-America*, *Route1*, *Profectus,* and *Abbott Diabetes*, claims were limited because the intrinsic evidence distinguished and disparaged certain prior art features and/or the claim language itself suggested limiting the claims. *See Poly-America*, 839 F.3d at 1133-37; *Route1*, 829 F. App'x at 960-63; *Profectus*, 823 F.3d at 1381; *Abbott Diabetes*, 696 F.3d at 1149-50. In fact, Defendants omit a key part of the analysis in *Abbott Diabetes*: "Abbott's patents 'repeatedly, consistently, and exclusively' depict an electrochemical sensor without external cables or wires ***while simultaneously disparaging sensors with external cables or wires***." *Abbott Diabetes*, 696 F.3d at 1150 (emphasis added). Novartis never distinguished the disputed

"combination" terms over or disparaged the later-invented hemipentahydrate compound.[15] Nor does the claim language exclude such a compound. *Supra* 8-10, Section I.C.1.

In *Groove Digital* and *Hologic*, the intrinsic evidence described the disputed limitations as important aspects of the invention. *Groove Digital*, 825 F. App'x at 856-57; *Hologic*, 639 F.3d at 1335. By contrast here, the intrinsic evidence does not describe *physically separate* sacubitril and valsartan as a necessary or important aspect of the claimed invention.

3. The '659 And '331 Patents Need Not Describe Trisodium [Sacubitril-Valsartan] Hemipentahydrate To Cover That Compound

By attempting to limit the claims because the intrinsic evidence does not describe trisodium [sacubitril-valsartan] hemipentahydrate (*supra* 14-16, 20-22), Defendants ignore the law on after-discovered embodiments and its application to the '659/'331 Patents and the '938/'134 Patents. The '659/'331 Patents claim combinations of sacubitril and valsartan, and the later '938/'134 Patents claim an after-discovered embodiment of that invention: trisodium [sacubitril-valsartan] hemipentahydrate, having non-covalent associations between the components. *Supra* 5, 7; *infra* 47. The instant case is analogous to *In re Depomed Patent Litigation*, which involved both an earlier patent, which "relate[d] generally to a class of compounds" including tapentadol hydrochloride, and a later patent, which "relate[d] generally to a crystalline form of tapentadol hydrochloride" called Form A. No. 13-4507 (CCC-MF), 2016 WL 7163647, at *3, *13-16 (D.N.J. Sept. 30, 2016), *aff'd on other grounds*, *Grunenthal GmbH v. Alkem Labs. Ltd.*, 919 F.3d 1333, 1347 (Fed. Cir. 2019). During the earlier patent invention work, the patentee "did not have knowledge" of the later-discovered crystalline Form A (*id.* at

[15] *Poly-America* has been distinguished where the intrinsic evidence did not disparage the feature at issue, and this Court should do so here as well. *See Princeton Digital Image Corp. v. Konami Digital Entm't, Inc.*, No. 12-1461-LPS-CJB *et al.*, 2016 WL 7042066, *6 n. 12, *8 (D. Del. Dec. 2, 2016).

*14-16), and the earlier patent undisputedly did not "disclose" that crystalline Form A (*id.* at *46, *51). Yet the earlier-patented claims undisputedly covered the later-patented crystalline Form A. *Id.* at *1-2, *19-20.

Construing the "combination" terms as Novartis proposes will not render the claims invalid for lack of written description under *Ruckus*, 824 F.3d at 1004. *See Oyster Optics, LLC v. Infinera Corp.*, No. 2:18-CV-00206-JRG, 2019 WL 6843483, at *6 (E.D. Tex. May 3, 2019) (distinguishing *Ruckus* where "no ambiguity was apparent" and the defendant "failed to identify any intrinsic evidence compelling that [the claim limitation] must be [limited]"); *contra supra* 19. Written description is only required for the invention specifically claimed; "[t]he applicant is not required to include in his application support for matters not set forth in the claim." *See Phillips Petroleum Co. v. U.S. Steel Corp.*, 673 F. Supp. 1278, 1290-91 (D. Del. 1987) (finding claims to crystalline polypropylene, which were not limited to any specific intrinsic viscosity, would not be invalid for lack of written description even if they did not describe crystalline polypropylene having a high intrinsic viscosity), *aff'd*, *U.S. Steel Corp. v. Phillips Petroleum Co.*, 865 F.2d 1247, 1254 (Fed. Cir. 1989). In any event, only "***[i]f***, after applying all other available tools of claim construction, ***a claim is ambiguous***, it should be construed to preserve its validity." *Ruckus*, 824 F.3d at 1004 (emphases added) *citing Phillips*, 415 F.3d at 1327 (A validity analysis should not be "a regular component of claim construction."). And "[t]hat the product claimed in the [later-invented] patent may be patentable does not mean that a person making, using, or selling that product cannot be guilty of infringing the [earlier-invented] patent. 'Dominating' patents are not uncommon." *U.S. Steel*, 865 F.2d at 1253 n.11 (citation omitted).

Defendants also misstate Novartis's statements to the Examiner regarding WO 03/059345 ("Webb," a published application related to the '659 and '331 Patents) from the '938 and '134

Patent file histories (*supra* 20-21) by confusing disclosure with claim scope. Defendants assert "Novartis confirmed during the prosecution of the subsequently-filed '938 and '134 patents . . . that the '659 and '331 patent claims ***cannot*** include the valsartan-sacubitril complex that Novartis is now trying to capture." *Supra* 20 (emphasis in original). To the contrary, Novartis only told the Examiner that Webb did not ***disclose*** or ***suggest*** trisodium [sacubitril-valsartan] hemipentahydrate to overcome a prior art rejection. Ex. 22, 2010/9/9 Amendment at 6-7. Novartis never said the '659 and '331 Patents did not ***claim*** that compound; Novartis has said only that those patents do not disclose or suggest it. *Supra* 10.

4. The '659 And '331 Patents Need Not Enable Trisodium [Sacubitril-Valsartan] Hemipentahydrate

While trisodium [sacubitril-valsartan] hemipentahydrate is covered by the '659 and '331 Patent claims, "that does not mean that the patent specification must enable the [that compound] as opposed to merely the claimed [combination]." *Inline Connection Corp. v. AOL Time Warner, Inc.*, No. 02-272-MPT *et al.*, 2007 WL 275928, at *4 n.16 (D. Del. Jan. 29, 2007). "[P]ost-filing developments in the art [like trisodium [sacubitril-valsartan] hemipentahydrate] are irrelevant to the enablement inquiry." *Phillips Petroleum*, 673 F. Supp. at 1291-92. Moreover, enablement should not be "a regular component of claim construction" and is premature at this stage. *See Phillips*, 415 F.3d at 1327; *Idenix*, 2015 WL 9048010, at *4.

5. Novartis's PTE Applications Are Relevant For Claim Construction

There is no reason why PTE applications should not be considered during claim construction. *See Phillips*, 415 F.3d at 1317 ("The prosecution history . . . consists of the complete record of the proceedings before the PTO. . . ."). The Federal Circuit and this Court have also held that patentee statements after issuance are relevant for claim construction. *See, e.g.*, *Howmedica Osteonics Corp. v. Tranquil Prospects, Ltd.*, 401 F.3d 1367, 1372-73 (Fed. Cir.

2005) (concerning reexamination statements); *Forest Labs. Inc. v. Cobalt Labs. Inc.*, No. 08-21-GMS-LPS, 2009 WL 1916935, at *8 (D. Del. July 2, 2009) ("[T]he patentee's [reexamination] statement [was] important because it show[ed] the patentee telling the PTO exactly what Plaintiffs . . . advocat[ed] in Court"), *adopted in relevant part*, 2009 WL 3010837, at *2 (D. Del. Sept. 21, 2009). Defendants cite one decision from the Northern District of Illinois which states without support that PTE applications are not intrinsic evidence. *Supra* 22 *citing Abbott*, 110 F. Supp. 2d at 673. This Court should follow *Phillips*, *Howmedica*, and *Forest*, not *Abbott*.

Defendants do not dispute that Novartis told the PTO and the public that the "combination" terms cover the Entresto® Product (wherein valsartan and sacubitril are not physically separate). *Supra* 7; Ex. 53, 2021 Entresto® Prescribing Information ("PI") at 8-9; Ex. 54, 2021 Entresto® PI at 8-9. Defendants instead focus on the PTO's determination that the patents were eligible for extension, asserting that because claim construction is a matter of law and "does not fall within the PTO's technical expertise," it should not be considered. *Supra* 22-23. But the PTO makes claim construction determinations all the time, for example, when determining whether a prior art species falls within the scope of (anticipates) a claimed invention. Defendants' *Ferring* and *Genetics* cases do not support their argument. *Ferring* considered a completely different issue, *i.e.*, whether regulatory definitions of "drug product" and "pharmaceutical equivalents" related to PTE eligibility were relevant to claim construction, not whether a patentee's PTE statement was relevant. *See Ferring*, 2005 WL 437981, at *16. *Genetics* simply determined that other intrinsic evidence outweighed the PTO's determination of PTE eligibility. *See Genetics*, 2010 WL 677745, at *2. By contrast, here, that the PTO found the '659 and '331 Patents eligible for extension is consistent with the rest of the intrinsic evidence and should be considered.

6. Changing Words Of The Claims Does Not Address The Parties' Dispute

Defendants admit that there is one disputed issue: whether the "combination" terms are limited to the active agents sacubitril and valsartan "as two separate components" or not. *Supra* 23-25. While Defendants fault Novartis for repeating the words of the claim, changing the words of the claims as Defendants propose, for example, by adding "in concert" does not resolve that issue. The claims and other intrinsic evidence undisputedly do not limit sacubitril and valsartan to separate components, so there is no reason to modify the claims to resolve this issue. *Hill-Rom* and *Maytag* are inapposite because repeating the claim language there did not resolve the disputes. *See Hill-Rom*, 2013 WL 364568, at *5-6; *Maytag*, 411 F. Supp. 2d at 1043-78.

In summary, when Novartis wanted to add "separate," as it did in modifying the term "unit dose forms," it knew how. Novartis did not use the word "separate" to modify the active ingredient components when they are in one "pharmaceutical composition" or "one unit dose form." *Supra* 25-26. Thus, it is Defendants that must change the words of the claims to limit them.

D. Defendants' Sur-reply Position:

1. The Specifications of the '659 and '331 Patents Repeatedly, Consistently, and Exclusively Depict Pharmaceutical Compositions Comprising Separate Valsartan and Sacubitril Components

Phillips makes clear that "[t]he claims … do not stand alone. Rather, they are part of a 'fully integrated written instrument,' consisting principally of a specification that concludes with the claims." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1315 (Fed. Cir. 2005) (internal citation omitted). It is undisputed that the '659 and '331 Patents' inventors did not invent or describe a sacubitril-valsartan complex. *Supra* 25. Novartis nevertheless argues that the claimed

"combination" extends to such complexes. None of the specification excerpts that Novartis cites would have told a POSA that the inventors possessed a "combination" of this type.

Novartis relies on purportedly "permissive" specification language (*supra* 26-27), but does not dispute that the specifications exclusively refer to combinations of two distinct active ingredients. *See Irdeto Access, Inc. v. Echostar Satellite Corp.*, 383 F.3d 1295, 1301 (Fed. Cir. 2004)[16] (rejecting similar argument that examples in the specification "are permissive rather than mandatory," and finding that the plaintiff "cannot explain every example in the specification, all of which consistently point to an implicit definition" with a limited meaning). Novartis cites *i4i Ltd. Partnership v. Microsoft Corp.*, 598 F.3d 831, 844 (Fed. Cir. 2010), for the proposition that allegedly "permissive" language "should not limit claim scope." *Supra* 27. But *i4i Ltd.* is inapposite. There, the court refused to limit a claim term to a preferred embodiment with a limiting feature because the specification disclosed an embodiment without it. *i4i Ltd.*, 598 F.3d at 843–44. Here, unlike *i4i Ltd*., the '659 and '331 Patents disclose only one type of "combination"—where the two active ingredients, valsartan and sacubitril, are physically separate components.

Novartis tries to explain away various specification passages (*supra* 26-28), but cannot point to a single sentence that would inform a POSA that the claimed "combination" could include a complex. As the Federal Circuit has explained, the "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." *Trs. of Columbia Univ. in City of N.Y. v. Symantec Corp.*, 811

[16] *Irdeto's* holding is not limited to where "disputed terms had no accepted meaning," as Novartis suggests. *Supra* 30; *see also In re Abbott Diabetes Care Inc*., 696 F.3d 1142, 1149–50 (Fed. Cir. 2012) (applying *Irdeto* in finding "Abbott's patents 'repeatedly, consistently, and exclusively' depict an electrochemical sensor without external cables or wires," where the "claims themselves suggest connectivity without the inclusion of cables or wires").

F.3d 1359, 1366 (Fed. Cir. 2016). That "Novartis never distinguished the disputed 'combination' terms over or disparaged the later-invented hemipentahydrate compound" (*supra* 30-31) is of no moment, as the Federal Circuit has held that "a patent applicant need not expressly state 'my invention does not include X' to indicate his exclusion of X from the scope of his patent because 'the patentee's choice of preferred embodiments can shed light on the intended scope of the claims.'" *Id.* at 1364; *Irdeto*, 383 F.3d at 1300; *Abbott Diabetes*, 696 F.3d at 1149–50.[17]

Likewise, during prosecution of the '659 Patent's parent, Novartis admits that it yet again characterized its invention as "combinations of sacubitril and valsartan as separate components," consistent with the breadth of disclosures of the specification. *Supra* 28-29; *cf. McNeil-PPC, Inc. v. Perrigo Co.*, 443 F. Supp. 2d 492, 504–07 (S.D.N.Y. 2006) (rejecting defendants' construction that would have excluded embodiments disclosed in the specification; finding that the examiner was persuaded that the unexpected results applied to all embodiments disclosed in the specification). The specification of the '659 and '331 Patents, after discussing studies wherein valsartan and sacubitril are administered as separate components, similarly limits the "unexpected results" by stating that "available results indicate an unexpected therapeutic effect of a combination ***according to the invention***."[18] Ex. 1, '659 Patent, at 10:1–2; *see Poly-Am., L.P. v. API Indus., Inc.*, 839 F.3d 1131, 1136 (Fed. Cir. 2016) ("an inventor may disavow claims

[17] *Idenix Pharm.* is distinguishable. There, the court rejected Gilead's attempt to import a "negative limitation," where it was otherwise "undisputed that the plain and ordinary meaning of this term include[d]" the excluded feature. *Idenix Pharm. Inc. v. Gilead Scis., Inc.*, No. CV 14-846-LPS, 2015 WL 9048010, at *4 (D. Del. Dec. 16, 2015). Here, the plain meaning given to "combination" in the specification requires that the two active ingredients, valsartan and sacubitril, are physically separate components. *See supra* 15-16. Novartis fails to mention that this Court later found the *Idenix* claims non-enabled, partly due to the breadth of the claims as construed. *Idenix Pharm. LLC v. Gilead Scis., Inc.*, No. CV 14-846-LPS, 2018 WL 922125, at *11 (D. Del. Feb. 16, 2018).

[18] All emphasis added unless noted otherwise.

lacking a particular feature when the specification describes 'the present invention' as having that feature"). Thus, the specification as a whole confirms that the claimed "combinations" require that the two active ingredients, valsartan and sacubitril, are physically separate components administered in concert.

2. Novartis's Statements Confirm the "Combination" of the '659 and '331 Patents Requires Separate Components, and That a Complex Is Not Sufficiently Disclosed or Enabled

Novartis's statements to the Patent Office are unambiguous that the later-invented "single compound" was distinct from—not a species of—the "***combinations*** of … two compounds" earlier taught and claimed in Webb (a related publication of the '659 and '331 Patents):

> Rejections under 35 U.S.C 103
>
> Claims 86-104 were rejected as allegedly being obvious as set forth in Paragraph No. 18 of the Office Action. Applicants first note, that there is no suggestion or motivation in any of the cited references, either alone or in combination, that suggests the possibility of a single compound which contains an ARB, a NEPi and a cation component as set forth in the claims. Rather the cited references teach pharmaceutical compositions containing only combinations of at least two compounds. In view of the lack of suggestion or motivation in the cited references, Applicants submit that the Examiner has not established a *prima facie case* of obviousness.
>
> The Examiner notes that Webb does not teach the specific elected compound or identify the elected components together as being a compound as set forth in the claims (see Office Action at page 10). Applicants submit that none of the secondary references cited by the Examiner remedies the deficiencies of Webb.

Ex. 22, Sept. 9, 2010 Amendment, at 6 (annotations added). By comparison, *In re Depomed Patent Litig.* (*supra* 31-32) concerned an earlier genus claim to a chemical compound and a later species claim to a crystalline form of that same compound. No. 13-4507 (CCC-MF), 2016 WL 7163647, at *13–14 (D.N.J. Sept. 30, 2016). Here, Novartis claims to have developed a complex that is distinct from the "combination" of two compounds disclosed and claimed in the '659 and

'331 Patents. Ex. 22, Sept. 9, 2010 Amendment, at 6[19], 8.[20] Notably, the specification of the later '938 Patent describes dual-acting compounds that have "distinct properties different to the above physical combination." *See* Ex. 3, '938 Patent, at 5:39–44 (emphasis added). This description of the later-invented complex makes clear that it is not a species of combination claimed in the '659 and '331 Patents, but an inherently different product.

Because Novartis's later-invented complex is not a species of the earlier-claimed genus,[21] Novartis's admissions that the '659 and '331 Patents lack written description of the later-invented complex warrant adoption of Defendants' constructions to preserve the claims' validity. *Supra* 19 (citing *Ruckus*); *supra* 33 ("Novartis never said the '659 and '331 Patents did not ***claim*** that compound; Novartis has said only that those patents do not disclose or suggest it."); *Ansell Healthcare Prods. LLC v. Reckitt Benckiser LLC*, No. 15-cv-915-RGA, 2018 WL 620968, at *3 (D. Del. Jan. 30, 2018) (applying *Ruckus* where "claim language is subject to more than one interpretation, including the interpretations of the parties"). And although Novartis asserts that it is "premature" to assess enablement (*supra* 33), Novartis has already admitted to the Patent Office that "undue experimentation would be required by a POSA attempting to prepare, purify

[19] Tellingly, Novartis only paraphrases its statements to the Examiner. *Supra* 32-33.

[20] Continuing a theme, Novartis's citation to *Phillips Petroleum Co. v. U.S. Steel Corp.* is inapposite. There, the court merely found that a patent need only provide written description for limitations expressly included in the claim. 673 F. Supp. 1278, 1291 (D. Del. Oct. 28, 1987) (rejecting argument that patent needed to disclose materials of a certain viscosity or molecular weight, as "there is no limitation in the '851 claim regarding the intrinsic viscosity or molecular weight of the polymer"). Here, the "combination" is expressly claimed, and, under Novartis's construction, includes the later-invented complex, which must be described and enabled.

[21] Even if the later-invented complex were a species of a claimed genus, the claims would still be invalid for lack of written description, because "a sufficient description of a genus … requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus." *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1350 (Fed. Cir. 2010).

and characterize the claimed compound [of the later '938/'134 Patents] in view of" Webb. Ex. 22, Sept. 9, 2010 Amendment, at 7–8 (relying on inventor declaration describing "more than one thousand separate experiments");[22] *see also MagSil Corp. v. Hitachi Glob. Storage Techs., Inc.*, 687 F.3d 1377, 1381 (Fed. Cir. 2012) (holding that the enablement "doctrine prevents both inadequate disclosure of an invention and overbroad claiming that might otherwise attempt to cover more than was actually invented. Thus, a patentee chooses broad claim language at the peril of losing any claim that cannot be enabled across its full scope of coverage.").

3. Novartis's Reference to Its PTE Request Is Unavailing and Irrelevant

The patent term extension proceedings are not relevant to claim construction because they do not constitute "[the] understanding of the patentee, expressed by him, or on his half [sic], ***when his application for the original patent was pending***." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995).[23] Novartis's PTE Applications were filed in September 2015, years after the '659 Patent issued, rendering Novartis's self-serving statements unreliable. *See Buyerleverage Email Sols., LLC v. SBC Internet Servs., Inc.*, No. 11-645-RGA, 2013 WL 5730426, at *3 (D. Del. Oct. 22, 2013) (rejecting patentee's reliance on its own pre-litigation statement in an Examiner interview during prosecution that its claims were not limited to a particular type of method as "unreliab[le]" and "litigation inspired").

[22] *Inline Connection Corp. v. AOL Time Warner Inc.* (*supra* 33), is not to the contrary, as there, the court found the patent need not enable the ***accused*** system, which was "particularly important … because the accused system contains features that are not part of the claimed system." No. 02-272, 2007 WL 275928, at *4 (D. Del. Jan. 29, 2007).

[23] Novartis asks this Court to disregard *Abbott* and follow *Howmedica* and *Forest* (*supra* 33-34), but each of those cases involved statements made while re-examination of the claims at issue was pending. *Howmedica Osteonics Corp. v. Tranquil Prospects, Ltd.*, 401 F.3d 1367, 1372–73 (Fed. Cir. 2005); *Forest Labs. Inc. v. Cobalt Labs. Inc.*, No. 08-21-GMS-LPS, 2009 WL 1916935, at *8 (D. Del. July 2, 2009).

4. Novartis's Proposed "Construction" Does Not Resolve the Parties' Dispute

Novartis agrees that the parties' dispute regarding the "combination" terms boils down to a difference in claim scope (namely, whether claims of the '659 and '331 Patents encompass a sacubitril-valsartan complex). Rather than address the parties' dispute over claim scope, Novartis argues that "there is no reason to modify the claims to resolve this issue." *Supra* 35. However, the Federal Circuit has made clear that reliance on "'plain and ordinary meaning' may be inadequate," where, as here, "reliance on a term's 'ordinary' meaning does not resolve the parties' dispute." *O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co., Ltd.*, 521 F.3d 1351, 1361–62 (Fed. Cir. 2008) ("[w]hen the parties present a fundamental dispute regarding the scope of a claim term, it is the court's duty to resolve it"). The Court should reject Novartis's attempt to side-step this issue, and adopt Defendants' proposed constructions, which interpret, not "modify," the claims.

II. "trisodium [3-((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-2′-(pentanoyl{2″-(tetrazol-5-ylate)biphenyl-4′-ylmethyl}amino) butyrate] hemipentahydrate"

The disputed terms appear in claim 1 of the '938 Patent (Ex. 3) and claims 1, 4–11, and 13–15 of the '134 patent (Ex. 4). Claim 1 of the '938 Patent and claims 1 and 5 of the '134 patent, which are representative, are shown below with these terms emphasized:

'938 Patent:

> **1.** ***Trisodium [3-((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***.

'134 Patent:

> **1.** A method for treatment of a cardiovascular condition or disease, wherein the cardiovascular condition or disease is heart failure or hypertension, in a patient in need thereof comprising administering to the patient a therapeutically effective amount of ***trisodium[3-((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***.
>
> **5.** The method according to claim **1**, wherein the compound ***trisodium[3-((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*** is in the crystalline form.

The '938 and '134 Patents are in the same family and share substantively the same specification.[24] Ex. 3, '938 Patent at cover; Ex. 4, '134 Patent at cover. The parties have proposed the following constructions for the disputed terms:

[24] As the '938 and '134 Patents share substantively the same specification, for simplicity, only citations to the '134 Patent specification are provided.

"trisodium [3-((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" ('938 Patent, claim 1)

Novartis's Proposal	Defendants' Proposal
substantially pure trisodium [3-((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	a substantially pure crystalline supramolecular complex having formula units of trisodium [3-((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, wherein each formula unit in a unit cell of the crystalline complex has 2.5 water molecules and 3 sodium ions
in crystalline form	

"trisodium [3-((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" ('134 Patent, claims 1, 4-11, 13-15)

Novartis's Proposal	Defendants' Proposal
Trisodium [3-((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	a substantially pure crystalline supramolecular complex having formula units of trisodium [3-((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, wherein each formula unit in a unit cell of the crystalline complex has 2.5 water molecules and 3 sodium ions

The '938 and '134 Patent claims recite the chemical name "trisodium [3-((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," referred to herein for convenience as "trisodium [sacubitril-valsartan] hemipentahydrate."

A. Novartis's Opening Position: The Court Should Not Add Defendants' Unsupported Limitations Into "trisodium [sacubitril-valsartan] hemipentahydrate" And "in crystalline form"

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? (Section II.A.1);

(2) Are the claim terms "trisodium [sacubitril-valsartan] 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"? (Section II.A.2); and

(3) Are the '134 Patent claims limited to "substantially pure" trisodium [sacubitril-valsartan] hemipentahydrate? (Section II.A.3)

The answer to each of these questions is no. Defendants repeatedly and improperly try to narrow the claims by adding limitations that are not supported by the claims themselves, the patent specifications, or the file histories. *See Phillips*, 415 F.3d at 1316–17. Defendants assert that the claim term "trisodium [sacubitril-valsartan] hemipentahydrate" by itself is limited to crystalline form, which would violate the doctrine of claim differentiation, render the separate express "crystalline form" limitations of certain claims superfluous, and contradict the specification and prosecution history. Defendants also try to limit the claims to a "supramolecular complex" having "formula units" and "unit cell[s]" in another attempt to restrict "trisodium [sacubitril-valsartan] hemipentahydrate" to crystalline form. Finally, Defendants assert that the '134 Patent claims are limited to "substantially pure" trisodium [sacubitril-valsartan] hemipentahydrate, even though Novartis never suggested that the '134 Patent claims

were so limited. The Court should reject the Defendants' constructions that improperly add limitations into the claims.

Because the claimed compound and its form are distinct concepts as explained in Section II.A.1.a below, "trisodium [sacubitril-valsartan] hemipentahydrate" and "in crystalline form" are distinct claim elements and should be construed separately, to the extent the Court finds that either of these terms requires construction. Defendants' construction of claim 1 of the '938 Patent, which groups "trisodium [sacubitril-valsartan] hemipentahydrate" and "in crystalline form" together into a single term, ignores the distinction between the claimed compound and the form of that compound.

1. "trisodium [sacubitril-valsartan] hemipentahydrate" By Itself Is Not Limited To Crystalline Form

The parties dispute whether the claimed "trisodium [sacubitril-valsartan] hemipentahydrate" alone is limited to "crystalline" form as Defendants assert, or not so limited, as Novartis contends.

Nothing in the intrinsic evidence limits "trisodium [sacubitril-valsartan] hemipentahydrate" to "crystalline form." Specifically, neither of the two exceptions to the rule that a claim term is accorded its full scope applies here: (1) when the patentee acts as his own lexicographer, and (2) when the patentee disavows the full scope of a claim term either in the specification or during prosecution. *Phillips*, 415 F.3d at 1316–17.

Novartis consistently used a separate "crystalline form" limitation (in '134 Patent claim 5 and '938 Patent claim 1) to claim a crystalline form of trisodium [sacubitril-valsartan] hemipentahydrate. In contrast to those claims, claim 1 of the '134 Patent does not include a crystalline form limitation. Defendants' construction of "trisodium [sacubitril-valsartan] hemipentahydrate" as crystalline therefore violates the doctrine of claim differentiation and

renders superfluous the separate "crystalline form" limitations of '938 Patent claim 1 and '134 Patent claim 5. Moreover, the '938 and '134 Patent specification explains that crystalline trisodium [sacubitril-valsartan] hemipentahydrate was a preferred, but not exclusive, embodiment of the invention. And the file histories of both patents show that Novartis and the Examiner understood that "trisodium [sacubitril-valsartan] hemipentahydrate" was not limited to crystalline form.[25]

In sum, there is no reason to limit the full scope of "trisodium [sacubitril-valsartan] hemipentahydrate" to only a crystalline form of that compound.

a) A Compound And Its Form Are Distinct Concepts

By way of background, a POSA[26] as of the April or August 2006 Complex Patent priority date[27] would understand a "compound" and the "form" of that compound are distinct concepts in the intrinsic evidence. Klibanov Decl. ¶¶ 25-31.

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[25] For the avoidance of doubt, an examiner's unilateral statement does not constitute a clear disavowal of claim scope where the rest of the prosecution history and intrinsic evidence shows that the patentee clearly did not intend to limit the claims. *See Sorensen v. Int'l Trade Comm'n*, 427 F.3d 1375, 1378–79 (Fed. Cir. 2005); *Cree, Inc. v. SemiLEDs Corp.*, No. 10-866-RGA, 2012 WL 975697, *15–*17 (D. Del. Mar. 21, 2012).

[26] A POSA with respect to the '938 and '134 Patents would have had an advanced degree (a Ph.D. or master's degree) in chemistry or a related field with two or more years of pharmaceutical chemistry experience, or a bachelor's degree in chemistry or a related field with four or more years of such experience, or an M.D. with two years of specific training, research, or experience studying and/or treating heart failure and/or hypertension, and/or pharmacotherapies therefor. Klibanov Decl. ¶ 23. A POSA could have collaborated with others of ordinary skill having experience in medicine, pharmacology, biology, biochemistry, medicinal chemistry, or a related field with specific training, research or experience studying and/or treating heart failure and/or hypertension, and/or pharmacotherapies therefor. Klibanov Decl. ¶ 23.

[27] Novartis's '938 and '134 Patents claim priority to applications filed on April 4 and August 11, 2006. *Supra* 7. For the purposes of these *Markman* proceedings, Novartis uses these dates as the priority date. A POSA's understanding of the "trisodium [sacubitril-valsartan] hemipentahydrate" and "in crystalline form" terms at issue would be the same as of either April 4 or August 11, 2006. Klibanov Decl. ¶ 22.

The ’938 and ’134 Patents describe trisodium [sacubitril-valsartan] hemipentahydrate as a “compound,” meaning a chemical substance comprising pharmaceutically active agents, cations, and other entities such as water molecules, which interact via non-covalent chemical bonding. Klibanov Decl. ¶¶ 26–27 (Ex. 3, ’938 Patent, title, abstract, claims 2–11; Ex. 4, ’134 Patent, title, 6:22-43, 7:3-26, 10:42-47, 13:11-14, 16:1-13, claims 4–11, 13–15). The claimed compound’s chemical name identifies the pharmaceutically active agents and other entities present and their relative amounts. Klibanov Decl. ¶ 28. Specifically, “***tri***sodium” and “***hemipenta***hydrate” refer to the ratios of sodium cations (3) and water molecules (half of five, *i.e.*, 2.5), respectively, for each molecule of valsartan and sacubitril. Klibanov Decl. ¶ 28. The chemical names “3-((1S,3R)-1-biphenyl-4-ylmethyl-3-ethoxycarbonyl-1-butylcarbamoyl)propionate” and “(S)-3'-methyl-2'-(pentanoyl{2"-(tetrazol-5-ylate)biphenyl-4'-ylmethyl}amino)butyrate” describe a sacubitril anion (a negatively charged ion) and a valsartan anion, respectively. Klibanov Decl. ¶ 28. In sum, the chemical name for trisodium [sacubitril-valsartan] hemipentahydrate tells a POSA that the compound comprises a sacubitril anion, a valsartan anion, sodium cations, and water molecules in a 1:1:3:2.5 molar ratio. Klibanov Decl. ¶ 28 (Ex. 4, ’134 Patent, 15:1-50).

By contrast, the “form” of a compound refers to the three-dimensional arrangement of the components described above, not the components themselves. The ’938 and ’134 Patent specification teaches that the disclosed compound could be in crystalline form, meaning the components are organized in regular arrangements that are repeated in three dimensions, or in amorphous form, meaning the compound lacks this repeated, regular three-dimensional arrangement. Klibanov Decl. ¶ 29 (Ex. 4, ’134 Patent, 15:63-67).

b) Defendants' Construction Violates The Doctrine Of Claim Differentiation And Renders "Crystalline Form" Superfluous

Defendants' construction adding "crystalline" to claim 1 of the '134 Patent by construing the "trisodium [sacubitril-valsartan] hemipentahydrate" as "crystalline" in this claim (which unlike certain other claims does not include a "crystalline" limitation) is at odds with the claims of both the '134 and '938 Patents.

'134 Patent: Claim 1 of the '134 Patent claims a method of administering trisodium [sacubitril-valsartan] hemipentahydrate, and dependent claim 5 further limits the method of claim 1 to trisodium [sacubitril-valsartan] hemipentahydrate in "crystalline form" (Ex. 4, '134 Patent, 30:56-63, 31:7-11 (emphases added)):

> **1.** A method for treatment of a cardiovascular condition or disease, wherein the cardiovascular condition or disease is heart failure or hypertension, in a patient in need thereof comprising administering to the patient a therapeutically effective amount of trisodium [sacubitril-valsartan] hemipentahydrate.
>
> **5.** The method according to claim **1**, ***wherein the compound*** trisodium [sacubitril-valsartan] hemipentahydrate ***is in the crystalline form***.

Because the only difference between claim 5 and claim 1, on which claim 5 depends, is the limitation "wherein the compound . . . is in the crystalline form," a POSA would understand that "trisodium [sacubitril-valsartan] hemipentahydrate" by itself is not limited to crystalline form. Klibanov Decl. ¶¶ 32–33; *see Abbott Labs. v. Andrx. Pharm. Inc.*, 473 F.3d 1196, 1209 (Fed. Cir. 2007). Defendants' proposal violates the doctrine of claim differentiation, which is "at its strongest" in situations like those here, involving reading a limitation into an independent claim that already appears in a dependent claim and is the only meaningful difference between the claims. *See Meda*, 2016 WL 2760336, at *1.

'938 Patent: Because "trisodium [sacubitril-valsartan] hemipentahydrate" is not by itself limited to crystalline form, a POSA would understand that a separate crystalline form limitation is required to denote a crystalline form of that compound. Klibanov Decl. ¶ 34. Claim 1 of the '938 Patent adds such a separate limitation requiring trisodium [sacubitril-valsartan] hemipentahydrate to be "in crystalline form" (Ex. 3, '938 Patent, 31:41-45 (emphasis added)):

> **1**. Trisodium [sacubitril-valsartan] hemipentahydrate ***in crystalline form***.

Defendants' construction effectively reads "crystalline form" into the chemical name "trisodium [sacubitril-valsartan] hemipentahydrate." This renders "crystalline form" in claim 1 of the '938 Patent (and "crystalline form" of claim 5 of the '134 Patent, above) superfluous (Klibanov Decl. ¶¶ 35–36), contrary to the principle that claims should be construed to give effect to each claim term. *See Phillips*, 415 F.3d at 1314 ("[T]he claim in this case refers to 'steel baffles,' which strongly implies that the term 'baffles' does not inherently mean objects made of steel.").

In sum, as shown in the chart below, only claim 1 of the '938 patent and claim 5 of the '134 patent (and claims that depend from these claims) are limited to crystalline form. Claim 1 of the '134 patent does not contain a crystalline limitation.

'134 Patent	**'938 Patent**
No Crystalline Limitation	
1. A method for treatment of a cardiovascular condition or disease … comprising administering to the patient a therapeutically effective amount of **trisodium [sacubitril-valsartan] hemipentahydrate**.	
Crystalline Limitation	
5. The method according to **claim 1**, wherein the compound trisodium [sacubitril-valsartan] hemipentahydrate is ***in the crystalline form***.	**1.** Trisodium [sacubitril-valsartan] hemipentahydrate ***in crystalline form***.

Defendants' construction of the claim term "trisodium [sacubitril-valsartan] hemipentahydrate" by itself as crystalline violates the doctrine of claim differentiation and renders superfluous the separate "crystalline form" limitations of '938 Patent claim 1 and '134 Patent claim 5 (illustrated below by adding "crystalline" in brackets).

'134 Patent	**'938 Patent**
No Crystalline Limitation	
1. A method for treatment of a cardiovascular condition or disease … comprising administering to the patient a therapeutically effective amount of [**crystalline**] **trisodium [sacubitril-valsartan] hemipentahydrate** ….	
Crystalline Limitation	
5. The method according to **claim 1**, wherein the compound [**crystalline**] trisodium [sacubitril-valsartan] hemipentahydrate is ***in the crystalline form***.	**1.** [**crystalline**] Trisodium [sacubitril-valsartan] hemipentahydrate ***in crystalline form***.

Indeed, Defendants propose identical constructions of the terms "trisodium [sacubitril-valsartan] hemipentahydrate" ('134 Patent) and "trisodium [sacubitril-valsartan] hemipentahydrate ***in crystalline form***" ('938 Patent, emphasis added), further evidencing that Defendants' constructions improperly render the claim element "crystalline form" superfluous.

c) Nothing In The Specification Limits The Claimed "trisodium [sacubitril-valsartan] hemipentahydrate" To Crystalline Form

The specification describes the inventors' discovery of a novel compound and identifies trisodium [sacubitril-valsartan] hemipentahydrate as an example. *Supra* Section I.A.1. The specification expressly defines the term "compound" as a chemical substance comprising active agents and other entities, not as any particular form of the compound, much less crystalline form. Klibanov Decl. ¶¶ 26–27, 37; Ex. 4, '134 Patent, 6:22-43, 7:3-6, 16:1-13. With respect to the form of the compound, the specification explains that it "can be in the crystalline, partially

crystalline, amorphous, or polymorphous form, preferably [*i.e.*, not exclusively] in the crystalline form." Klibanov Decl. ¶¶ 29, 37; Ex. 4, '134 Patent, 15:63-67.

The Court should not limit the compound trisodium [sacubitril-valsartan] hemipentahydrate to the "preferred embodiment" of the form of that compound (crystalline form) absent a "clear intention" in the intrinsic evidence as a whole that the patentee intended for the "trisodium [sacubitril-valsartan] hemipentahydrate" to be so limited. *See Meda*, 2016 WL 2760336, at *2. There is no such "clear intention" here. *See* Klibanov Decl. ¶ 38; Ex. 4, '134 Patent, 26:63-67 ("It should be understood that [the examples disclosed in the specification] . . . should not be taken in any way to limit the scope of the present invention."), 30:50-54.

Defendants, as Torrent did in its Rule 12(c) motion (D.I. 47 at 2), will point to the specification language that "[t]he invention relates to trisodium [sacubitril-valsartan] hemipentahydrate, a crystalline solid which is characterized by the data and parameters obtained from" certain characterization techniques, but that language does not limit the claimed compound to crystalline form in view of the specification as a whole. Klibanov Decl. ¶¶ 39–42; Ex. 4, '134 Patent, 17:42-48. By contrast with this "relates to trisodium [sacubitril-valsartan] hemipentahydrate" language, when the inventors wanted to define a term, they used clear definitional language: the phrases "as used herein" or "[f]or the purpose of the present invention," and with the defined term in quotation marks followed by "refers to" or "is intended to describe." '134 Patent, 6:8-10 ("*as used herein*, 'substantially pure' *refers to* . . ."), 6:15-27 ("*For the purpose of the present invention*, the term 'dual-acting compound' *is intended to describe*. . . . *For the purpose of the present invention*, the term 'compound' *is intended to describe*. . . ."), 6:52-57 ("*For the purpose of the present invention*, the term 'supramolecular complex' *is intended to describe*. . . .") (emphases added). A POSA would understand that the

language in column 17 does not define the scope of "trisodium [sacubitril-valsartan] hemipentahydrate" as limited to crystalline form because that language does not follow the format that the inventors used to define other terms in the specification. Klibanov Decl. ¶ 41; *see Abbott*, 473 F.3d at 1209–10 (finding specification language "is" was not definitional where, *inter alia*, the patentee "unambiguously provide[d] definitions of other claim terms . . . by stating the term ha[d] particular meaning within the patent" using the phrase "as used herein, means").

As the scope of the claim term "trisodium [sacubitril-valsartan] hemipentahydrate" (not limited to crystalline) is clear from the claims themselves, and the specification never disclaims that broad scope, a POSA would understand that "relates to" describes a non-limiting embodiment of trisodium [sacubitril-valsartan] hemipentahydrate and thus does not limit this term to only crystalline form. Klibanov Decl. ¶¶ 41–42; *see Meda*, 2016 WL 2760336, at *3–*5 (finding "the present invention relates [to treatments for] allergic reactions" was "insufficient . . . to limit the scope of the claim term 'condition'" where such a construction was not supported by the specification and was inconsistent with dependent claims).

Defendants, as Torrent did in its Rule 12(c) motion, will also assert that "'hydrate form' is a subset of 'crystalline form,' but not 'amorphous' form" based on the specification's description of valsartan salts. D.I. 47 at 3. The specification's disclosure of valsartan salts "in amorphous form," "in amorphous or crystalline form, especially in hydrate form" and "in crystalline, especially in hydrate form" (Ex. 4, '134 Patent, 8:61-9:14) is inapposite. This disclosure only mentions valsartan salts as separate compounds, not valsartan salts present in compounds with sacubitril. Klibanov Decl. ¶ 43. That the specification discloses crystalline valsartan salts, especially in hydrate form, does not teach or suggest anything about whether trisodium [sacubitril-valsartan] hemipentahydrate (which is not valsartan alone) must be limited

to crystalline form. Klibanov Decl. ¶ 43. Even if the specification teaches a POSA that *valsartan* hydrates are crystalline, a POSA would understand the specification teaches that the "trisodium [sacubitril-valsartan] hemipentahydrate" compound of the invention can be non-crystalline. *Supra* 50-52.

d) The Prosecution History Shows That The Examiner And Novartis Understood "trisodium [sacubitril-valsartan] hemipentahydrate" Is Not Limited To Crystalline Form

The prosecution history of the '938 and '134 Patents reveals that both the Examiner and Novartis understood that the compound "trisodium [sacubitril-valsartan] hemipentahydrate" is not limited to crystalline form.[28] Klibanov Decl. ¶ 44.

'938 Patent: During the '938 Patent prosecution, the Examiner considered several claims to trisodium [sacubitril-valsartan] hemipentahydrate that did not specify "crystalline form," including the following application claims (Klibanov Decl. ¶ 45; Ex. 22, '938 FH, 2010/9/9 Amendment at 4):

> **99.** Trisodium [sacubitril-valsartan] hemipentahydrate.
>
> **102.** Substantially pure trisodium [sacubitril-valsartan] hemipentahydrate.

With respect to these application claims, the Examiner recognized, "*none* of the instant claims *recite any crystal*," and "[t]he instant claims (even claim 102), do not require isolated compound; *they do not require* solid or *crystalline forms*," revealing that the Examiner understood that the claim element "trisodium [sacubitril-valsartan] hemipentahydrate" was not

[28] An examiner's unilateral statement does not constitute a clear disavowal of claim scope where the rest of the prosecution history and intrinsic evidence shows that the patentee clearly did not intend to limit the claims. *See Sorensen*, 427 F.3d at 1378–79; *Cree*, 2012 WL 975697, *15–*17.

by itself limited to crystalline form. Klibanov Decl. ¶ 46; Ex. 24, '938 FH, 2010/11/3 Office Action at 12–13 (emphases added).

Later during prosecution, Novartis added application claims 105 and 106 claiming trisodium [sacubitril-valsartan] hemipentahydrate "in the solid form" and "[t]he compound of claim 105 in crystalline form," respectively. Ex. 26, '938 FH, 2013/12/17 Amendment at 3, 6. Because the only difference between application claims 106 and 105, on which application claim 106 depended, was the "crystalline form" limitation, a POSA would understand that "trisodium [sacubitril-valsartan] hemipentahydrate" by itself is not limited to crystalline form. Klibanov Decl. ¶ 47. In addition, application claim 106 was later cancelled and application claim 105 was amended to replace "the solid" with "crystalline," shown below, which change would have been superfluous if "trisodium [sacubitril-valsartan] hemipentahydrate" was already limited to crystalline form (Klibanov Decl. ¶ 47; Ex. 27, '938 FH, 2014/03/4 Interview, Ex. 28, '938 FH, 2014/03/14 Notice of Allowance at 3):

> **105.** Trisodium [sacubitril-valsartan] hemipentahydrate in ~~the solid~~ **crystalline** form. (Application claim 105 issued as '938 Patent, claim 1.)

'134 Patent: During the '134 Patent prosecution before the same Examiner, Novartis filed application claim 1 reciting "trisodium [sacubitril-valsartan] hemipentahydrate," which did not contain a crystalline limitation, and later added application claim 18, which expressly required crystalline form, shown below (Klibanov Decl. ¶ 48; Ex. 35, '134 FH, 2015/07/28 Amendment at 2, 4):

> **1.** A method . . . comprising administering to the patient a therapeutically effective amount of trisodium [sacubitril-valsartan] hemipentahydrate. (Application claim 1 issued as '134 Patent, claim 1.)

> **18.** The method according to claim 1, wherein the compound trisodium [sacubitril-valsartan] hemipentahydrate is in the **crystalline form**. (Application claim 18 issued as '134 Patent, claim 5 (emphasis added).)

The Examiner allowed the claims, showing again that the Examiner, like Novartis, understood that application claim 1 (which issued as '134 Patent, claim 1) was not limited to "crystalline form" as recited in dependent application claim 18 (which issued as '134 Patent, claim 5). Klibanov Decl. ¶ 49; Ex. 36, '134 FH, 2016/03/21 Notice of Allowance.

In sum, if Novartis and the Examiner understood that the claimed "trisodium [sacubitril-valsartan] hemipentahydrate" was necessarily crystalline, there would have been no reason for Novartis to propose claims limiting trisodium [sacubitril-valsartan] hemipentahydrate to "crystalline form," or for the Examiner to have allowed claims with that limitation.

e) Extrinsic Evidence Should Not Be Used To Contradict The Unambiguous Intrinsic Evidence

As the intrinsic evidence shows unambiguously that the claimed "trisodium [sacubitril-valsartan] hemipentahydrate" is not limited to crystalline form; the claim construction analysis should end there. Sections II.A.1.a-d. Where a claim construction is clear in view of the intrinsic evidence, this "should [be] the end of the [Court's] analysis." *Vitronics*, 90 F.3d at 1584. "[Extrinsic evidence] may not be used to vary or contradict the claim language" or "contradict the import of other parts of the specification." *Id.* To the extent that Defendants disregard the case law and raise extrinsic evidence, the Court should give it no weight.

* * *

The Court should not limit the claimed "trisodium [sacubitril-valsartan] hemipentahydrate" to crystalline form.

2. The Claims Should Not Be Limited To A "Supramolecular Complex Having Formula Units" And "Unit Cell[s]"

The Court should not limit the claims to a "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," as proposed by Defendants.

First, Defendants told Novartis during the claim construction meet-and-confer that their proposed "formula units" and "unit cell" limitations require the compound trisodium [sacubitril-valsartan] hemipentahydrate to be in crystalline form.[29] This is yet another improper attempt to import a crystallinity requirement into the "trisodium [sacubitril-valsartan] hemipentahydrate" term, which fails for the same reasons as above. Section II.A.1; Klibanov Decl. ¶ 51.

Second, several claims of the '938 and '134 Patents, which depend from '938 Patent claim 1 and '134 Patent claim 5, respectively (which require crystalline form), are further limited to certain "unit cells" and "formula units." Klibanov Decl. ¶ 52; Ex. 3, '938 Patent, claims 2, 7–10; Ex. 4, '134 Patent, claims 10–14. Clearly, Novartis knew how to limit the claims to "formula units" and "unit cells" if that was Novartis's intention. But Novartis did not do so. *See Photonic Imaging*, 2019 WL 4305335, at *4.

Finally, the meaning of the chemical name "trisodium [sacubitril-valsartan] hemipentahydrate" is clear in the intrinsic evidence. Section II.A.1.a. There is no need to

[29] Defendants also told Novartis during the claim construction meet-and-confer that "supramolecular complex" has the meaning disclosed in the '938 and '134 Patent specification, which is not limited to crystalline form. *See* Ex. 4, '134 Patent, 6:53-7:2. Novartis requested confirmation by email but did not receive any response from Defendants.

incorporate Defendants' unnecessary "formula units" and "unit cell" language into the claims. Klibanov Decl. ¶ 50.

3. The '134 Patent Claims Are Not Limited To "Substantially Pure"

While the parties agree that claim 1 of the '938 Patent is limited to "substantially pure" trisodium [sacubitril-valsartan] hemipentahydrate, the parties dispute whether the claims of the '134 Patent are limited to "substantially pure" trisodium [sacubitril-valsartan] hemipentahydrate. The intrinsic evidence shows the '134 Patent claims are not so limited.

During the prosecution of the '938 Patent, the Examiner and Novartis explicitly agreed during an interview that the application claim that issued as '938 Patent claim 1 "should be amended to require a substantially pure compound." Ex. 27, '938 FH, 2014/03/14 Interview Summary at 2.

By contrast with the '938 Patent prosecution, there is no similar agreement in the '134 Patent file history. The words "substantially pure" only appear once during the '134 Patent prosecution: where the Examiner quotes the reasons of allowance from the '938 Patent (which claims were limited to "substantially pure" compound). Ex. 36, '134 FH, 2016/03/21 Notice of Allowance at 4; Ex. 27, '938 FH, 2014/03/14 Interview Summary, Ex. 28, '938 FH, 2014/03/14 Notice of Allowance at 4. The Examiner's statement in the Notice of Allowance does not constitute a clear disavowal of the '134 Patent claim scope where, as here, Novartis never suggested that the '134 Patent claims were limited to a "substantially pure" compound. *See Sorensen*, 427 F.3d at 1378–79; *Cree*, 2012 WL 975697, *15–*17. Thus, Defendants' proposal to add this limitation should be rejected.

B. <u>Defendants' Responsive Position</u>:

Novartis is correct that there are three questions for the Court to decide with respect to the "trisodium … hemipentahydrate" claim term:

1) Whether the claimed "trisodium … hemipentahydrate" is crystalline;

2) Whether "trisodium … hemipentahydrate" is a supramolecular complex; and

3) With regard to the '134 Patent, whether "trisodium … hemipentahydrate" is "substantially pure." *Supra* 44-45.

The answer to each of these questions is yes because Novartis claimed a single, specific species that is a crystalline, supramolecular complex. And, during prosecution, Novartis limited this single, claimed species to "substantially pure" crystalline material. While Novartis accurately states the questions for the Court to decide, it inaccurately frames the issue. Here, the Court is not faced with a case where a party seeks to import limitations from the specification. Instead, the Court is greeted with the familiar situation where a patentee deliberately limits its claims to a specific species disclosed in the specification.

The '938 and '134 Patents are generally directed to "dual-acting compounds" containing two active agents: (1) an angiotensin receptor blocker ("ARB"); and (2) a neutral endopeptidase inhibitor ("NEPi"). Ex. 4, '134 Patent, at 1:11-16; 5:16-24.[30] According to the specification, various ARBs and NEPis are suitable for use in the genus of dual-acting compounds. *Id*. at 7:29-8:39; 10:51-12:16.

Against this backdrop, Novartis did not claim the genus. Rather, it ultimately claimed only a single species, "trisodium … hemipentahydrate." That species is a crystalline, supramolecular complex. Because the claimed species is a crystalline supramolecular complex, it has both "formula units" and "a unit cell."

[30] The '938 and '134 Patents are derived from the same patent family and, apart from the abstracts, the specifications are essentially identical. Accordingly, only citations to the '134 Patent specification are provided.

In an effort to broaden its claims, Novartis focuses on generic statements in the specification that refer to the unclaimed genus. But Novartis ignores specific statements in the specification and file history that characterize the sole species that it actually claimed. The claims of a patent define the invention and are not required to capture every disclosed embodiment. The Federal Circuit's cases are "replete with examples of subject matter that is included in the specification, but is not claimed." *TIP Sys., LLC v. Phillips & Brooks/Gladwin, Inc.,* 529 F.3d 1364, 1373 (Fed. Cir. 2008) (citing *Schoenhaus v. Genesco, Inc.*, 440 F.3d 1354, 1359 (Fed. Cir. 2006)); *Maxwell v. J. Baker, Inc.*, 86 F.3d 1098, 1108 (Fed. Cir. 1996); *Unique Concepts, Inc. v. Brown*, 939 F.2d 1558, 1562–63 (Fed. Cir. 1991).

1. The Single Claimed Species, "Trisodium … Hemipentahydrate," in Both the '938 and '134 Patents Can Only Describe a Crystalline Supramolecular Complex

In view of the intrinsic evidence, and as understood by a POSA, the claimed "trisodium … hemipentahydrate," in both the '938 and '134 Patents, is properly construed as a crystalline supramolecular complex having formula units of "trisodium … hemipentahydrate," wherein each formula unit in a unit cell of the crystalline complex has 2.5 water molecules and 3 sodium ions.

a) The specification describes "trisodium … hemipentahydrate" as a crystalline supramolecular complex, having formula units wherein each formula unit in a unit cell of the crystalline complex has 2.5 water molecules and 3 sodium ions

The specification identifies the claimed "trisodium … hemipentahydrate" as a ***crystalline*** form. For example, the specification states: "The invention relates to trisodium … hemipentahydrate, ***a crystalline solid*** which is characterized by the data and parameters obtained from single crystal X-ray analysis and X-ray powder patterns." Ex. 4, '134 Patent, at 17:41-48. By plain English grammar, the emphasized language is definitional and a clear statement that a

POSA would understand "trisodium … hemipentahydrate" as "a crystalline solid."[31] Indeed, the discussion of the term "trisodium … hemipentahydrate" throughout the specification confirms this conclusion, describing the claimed "trisodium … hemipentahydrate" in terms of crystallographic properties. *See, e.g., id.* at 5:7-12 ("FIG. 1 shows a pictorial representation of the ***unit cell*** of the supramolecular complex of trisodium … hemipentahydrate comprising two asymmetric units).

All of the examples disclosed in the specification directed to preparing the "trisodium … hemipentahydrate" describe the production of "crystalline solids" as characterized by various methods.[32] *See id.* at 27:1-30:6. These methods include X-ray powder diffraction ("XRPD"), Raman Spectroscopy, High Resolution CP-MAS ^{13}C NMR Spectroscopy, and others. *Id.* at 27:1-28:62. The "trisodium … hemipentahydrate" exhibited "[s]ignificant spectral peaks" in the XRPD, IR, and Raman spectroscopy tests, confirming that it is crystalline. *Id.*; *see also* Butcher Resp. Decl. ¶¶ 51-52, 65 (only crystalline materials produce X-ray diffraction patterns with defined peaks).[33] The "trisodium … hemipentahydrate" complexes disclosed in the examples were also tested by DSC and TGA, which confirmed that the water molecules were incorporated into the crystal lattice (and were not located on the surface). Ex. 4, '134 Patent, at 27:1-28:62;

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[31] This conclusion arises ***not*** from the "[t]he invention relates" language, but from the "trisodium … hemipentahydrate, a crystalline solid" language. This phrase unambiguously confirms the POSA's understanding that the "trisodium … hemipentahydrate" species is, always, by definition, a crystalline solid. *See supra* 50-53.

[32] Examples 1-3 disclose the preparation of a crystalline complex of "trisodium … hemipentahydrate." Example 4 discloses the production of a separate species, referred to as a "linked pro-drug," which is a distinct species of the "compounds" described in the specification. Indeed, there is no description in the specification which would enable a person of skill in the art to prepare anything other than a crystalline form of the "trisodium … hemipentahydrate."

[33] Citations to "Butcher Resp. Decl." refer to the Declaration of Raymond Butcher, Ph.D., submitted herewith (Ex. B).

see also Butcher Resp. Decl. ¶ 65. Moreover, both examples 2 and 3 describe preparing the "trisodium … hemipentahydrate" by crystallization of the solid followed by drying under reduced pressure, which would remove excess water that is not integrated into the crystal lattice. Ex. 4, '134 Patent, at 27:30-28:47.

Moreover, the specification further describes the "trisodium … hemipentahydrate" with reference to its "unit cell." *Id*. at Fig. 1; 5:7-14; 17:40-19:19. The presence of a "unit cell" is characteristic of crystalline solids and, in fact, ***only*** present in crystalline materials. Butcher Resp. Decl. ¶¶ 31-36, 60. Specifically, the specification states that "[t]he details for trisodium … hemipentahydrate from the ***single crystal measurements***, especially the atom coordinates, the isotropic thermal parameters, the coordinates of the hydrogen atoms as well as the corresponding isotropic thermal parameters, show that ***a monoclinic unit cell exists***, its cell content of ***twelve formula units*** of $C_{48}H_{55}N_6O_8Na3 \bullet 2.5\ H_2O$ occurring as a result of ***two asymmetric units*** on two-fold positions." Ex. 4, '134 Patent, at 18:44-19:19; *see also id.* at 5:7-14; 17:42-18:19. In fact, the sole figure included in both the '938 and '134 Patents is a pictorial representation of the "unit cell of the supramolecular complex of trisodium … hemipentahydrate comprising two asymmetric units." *Id.* at Fig. 1.

In addition, for the purposes of claim construction, there is no dispute between the parties that the claimed "trisodium … hemipentahydrate" requires sacubitril anions, valsartan anions, sodium cations,[34] and water molecules in a ratio of 1:1:3:2.5. *See supra* 47.[35] This ratio is

[34] Anions are negatively-charged molecules, and cations are positively-charged molecules.

[35] Novartis originally ***proposed*** that "trisodium … hemipentahydrate" should be construed as: "a compound of sacubitril in anionic form, valsartan in anionic form, sodium cations, and water molecules in a 1:1:3:2.5 molar ratio." Ex. 52, Novartis Initial Constructions, at 6. Novartis does not dispute this ratio or that this means that the water content of the "hemipentahydrate" must be approximately 4.7 % of water by weight. D.I. 83 at 12-13; *see also*, 19-1979, D.I. 212-1 at 57:12-17. However, recognizing that a discrete chemical "compound" cannot have a fractional

referred to by the specification as a "formula unit." Ex. 4, '134 Patent, at 18:48-64; *see also* Butcher Resp. Decl. ¶¶ 61-64. And these formula units of "trisodium … hemipentahydrate" give rise to (1) an asymmetric unit; and (2) a defined unit cell, which necessarily requires it to be a crystalline material. *See* Butcher Resp. Decl. ¶¶ 60-65. Thus, the "formula unit" and "unit cell" referenced in Defendants' proposed construction flows from the specification and the crystalline nature of "trisodium … hemipentahydrate."

Accordingly, the claimed "trisodium … hemipentahydrate" is crystalline, and the unit cell of the crystalline complex has 2.5 water molecules and 3 sodium ions.

b) Novartis wrongly asserts that the claimed "trisodium … hemipentahydrate" is anything other than crystalline

Novartis and its expert, Dr. Klibanov, argue that the specification explains that the claimed "trisodium … hemipentahydrate" can be crystalline, partially crystalline, amorphous, or polymorphous, based in part on their belief that the '938 and '134 patents describe and claim a "compound." *Supra* 50-51; Klibanov Decl. ¶¶ 29, 37. This ignores that the specification discloses many different ARB and NEPi moieties, cations, and solvents, while Novartis claimed only a single species.

The portion of the specification cited by Novartis as supporting many different "forms" refers not to the claimed "trisodium … hemipentahydrate" but to the broad genus of ARB/NEPi dual-acting compounds. Ex. 4, '134 Patent, at 15:63-67. Referring generally to this genus, the specification states that the "combination or dual-acting compound … can be in the crystalline, partially crystalline, amorphous, or polymorphous form, preferably in the crystalline form." *Id.*

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water content, and that, accordingly, the fractional water content must relate to the number of water molecules in a unit cell of a crystal lattice, Novartis withdrew its proposed construction and elected not to construe the claim term.

Novartis argues this means that the claimed "trisodium … hemipentahydrate" can occur in any form. Its argument is incorrect, as Novartis's cited "support" does not describe the claimed "trisodium … hemipentahydrate." Instead, the citation refers generally to the genus of dual-acting compounds, which may be selected from various combinations of ARBs and NEPis, linked by various different moieties, and in various solid forms. This genus is not claimed. Instead, Novartis limited its claims to a single species, namely "trisodium … hemipentahydrate," which is crystalline, as detailed above. *See* Butcher Resp. Decl. ¶¶ 55-58, 80-84. While Defendants do not dispute that the specification may disclose a range of solid forms for the broader genus, in view of the specification, the "trisodium … hemipentahydrate"—the only ***claimed*** subject matter—is, by definition, crystalline.

c) The file histories of the '938 and '134 Patents describe the "trisodium … hemipentahydrate" as a crystalline form

It is no accident that Novartis limited its claims to a single, crystalline species. As explained further below, this action was necessary for Novartis to obtain allowance of the claims, which were rejected numerous times as obvious. To overcome the rejections, Novartis argued undue experimentation was required to isolate, purify, and characterize "substantially pure trisodium … hemipentahydrate." In so arguing, Novartis limited its claims to this single, crystalline species. *See* Butcher Resp. Decl. ¶¶ 70-79.

i) The '938 Patent

After the application for the '938 Patent was filed, the Examiner issued a Requirement for Restriction/Election, requiring Novartis to choose between sets of claims to a dual-acting compound (Group I), a linked prodrug (Group II), a combination (Group III), pharmaceutical compositions (Groups IV and V), or methods of treatment and preparation (Groups VI-VIII). Ex. 38, Dec. 7, 2009 Requirement for Restriction/Election. If Group I was elected, the Examiner also

required Novartis to (1) "select a single disclosed dual-acting compound"; (2) specify whether the elected compound was present or administered in a form recited by claim 12, which read "[t]he compound of any of claims 1 to 11 in the crystalline, partially crystalline, amorphous, or polymorphous form, preferably in the crystalline form"; and, if so, (3) elect a single species from claim 12 and specify whether the compound is "a solvate," "a hydrate," or "neither." In response, Novartis elected Group I and further elected (1) "trisodium … hemipentahydrate," (2) "crystalline form," and (3) "hydrate form." Ex. 20, Jan. 28, 2010 Amendment and Response to Restriction Requirement, at 11.

Thus, Novartis explicitly informed the Examiner that the species to be examined was a crystalline "trisodium … hemipentahydrate." The Examiner confirmed this choice in a subsequent non-final rejection, noting that the species elected was a crystalline "trisodium … hemipentahydrate." Ex. 21, Apr. 7, 2010 Non-Final Rejection, at 2. Accordingly, from the beginning, both Novartis and the Examiner understood that the claimed species was a crystalline form.

Prosecution proceeded with the understanding that the "trisodium … hemipentahydrate" was crystalline. For example, original claim 99 read "trisodium … hemipentahydrate," without the "in crystalline form" language. In a non-final rejection, the Examiner focused on art teaching the preparation of co-crystals:

> It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare co-crystals of N-(3-carboxy-1-oxyopropyl)… ester, having one sodium equivalent with disodium valsartan, giving an ARB NEP Na_3 "compound" recited in claim 86. ***It would further been obvious to characterize the hydrate forms of this co-crystal, including the crystal in the range of 2.5 H_2O molecule equivalents, giving the elected hemipentahydrate "compound" of claim 99*** and the "compound" of claims 86-96.

Id. at 13.

In response to the Examiner's non-final rejection, Novartis attempted to distinguish the prior art, arguing that it did not disclose the complicated network of interactions depicted in Figure 1 of the specification. Ex. 22, Sept. 9, 2010 Amendment and Response, at 5-9. As explained above, Figure 1 is a pictorial representation of the "unit cell of the supramolecular complex of trisodium … hemipentahydrate comprising two asymmetric units." This discussion of crystalline forms proceeded throughout prosecution, with the Examiner and Novartis focused on prior art methods for forming co-crystals and crystallization techniques. *See, e.g.*, Ex. 24, Nov. 3, 2010 Final Rejection, at 11-12 ("This teaching, taken with Morissette, provides a strong motivation to prepare the elected compound as a co-crystal… A reasonable expectation of preparing the co-crystal of the elected compound is provided … These specific known solid forms lead to a reasonable expectation of combining the component molecules to form ***the co-crystal supramolecular complex, i.e., the elected compound***").

Novartis also submitted a declaration by named inventor Dr. Karpinski arguing that it required over 1000 experiments to successfully isolate, purify, and characterize "trisodium … hemipentahydrate." Ex. 23, Sept. 9, 2010 Declaration. In view of Dr. Karpinski's work, Novartis argued that undue experimentation was required to prepare the claimed "trisodium … hemipentahydrate." Ex. 22, Sept. 9, 2010 Amendment and Response, at 7-8.

All pending claims were cancelled on December 17, 2013, and new claims were presented for examination. Ex. 26, Dec. 17, 2013 Amendment. Notably, these new claims recited the "trisodium … hemipentahydrate" in the "solid form" and in the "crystalline form." *See id.* at 3 (pending claims 105, 106). Novartis stated that "support for the amended claims is found on pages 23, 25-26 and 27 of the [filed] specification, which describe the ***crystal structure*** of the

claimed compound." *Id.* at 6. This statement applied to all the "trisodium … hemipentahydrate" claims.

During an Examiner Interview, Novartis authorized the Examiner to amend the claims to recite a substantially pure, crystalline material because otherwise the claims were not commensurate in scope with the declaration of Dr. Karpinski. Ex. 27, Mar. 14, 2014 Interview Summary ("[W]hen it was authorized to make the crystalline change to claim 105; the Examiner and Mr. Mulkeen agreed that ***such a crystalline form of the recited compound would also be substantially pure***."). Yet, the Examiner rejected Novartis's arguments over Dr. Karpinski's declaration numerous times because Dr. Karpinski's declaration only supported the effort to isolate and characterize crystalline "trisodium … hemipentahydrate." The Examiner only allowed the claims after Novartis agreed that they were limited to crystalline material, and because the material was crystalline, it was also, by definition, substantially pure. Ex. 28, Mar. 14, 2014 Notice of Allowance, at 3-4 ("The [Karpinski] Declaration establishes over 1000 experiments were required to prepare the claimed ***crystalline*** compound. … It is noted the ***recited trisodium hemipentahydrate crystalline*** compound is construed to also be 'substantially pure.'"). Novartis subsequently confirmed that it agreed with the Examiner's reasons for allowance, and that Dr. Karpinski's declaration confirmed that "trisodium … hemipentahydrate" is crystalline. Ex. 29, Oct. 6, 2014 Comments on Reasons for Allowance, at 1 ("In the [Karpinski] Declaration, it was established that 'over 1000 separate experiments were initially required to prepare, purify, and characterize' the ***claimed crystalline trisodium … hemipentahydrate***."); ("[I]t [is] correct to state that much work was required to prepare ***the claimed crystalline trisodium hemipentahydrate***…").

ii) The ’134 Patent

“When multiple patents derive from the same initial application, the prosecution history regarding a claim limitation in any patent that has issued applies with equal force to subsequently issued patents that contain the same claim limitation.” *Elkay Mfg.*, 192 F.3d at 980. The ’134 Patent issued from a division of the application that issued as the ’938 Patent, meaning that the ’134 and ’938 Patents share a specification. The claims of the ’134 Patent are directed to methods of treating cardiovascular disease by administering the same “trisodium … hemipentahydrate” claimed in the ’938 Patent. Accordingly, the ’938 and ’134 Patents are related, they share a common specification, and the prosecution history of the ’938 Patent applies to the ’134 patent.

The Examiner’s Notice of Allowance incorporated by reference the arguments made in the ’938 Patent file history limiting the claims to substantially pure crystalline material.

> The following is an examiner’s statement of reasons for allowance: … ***[T]he obviousness basis in the parent application was overcome by secondary considerations, which would also apply to the sacubitril-valsartan compound administered in the instant claimed treatment method claims. Evidence established that preparation of the sacubitril-valsartan compound was associated with undue technical hurdles***. The Examiner stated in the parent application, in the reasons for allowance, mailed 3/14/2014:
>
> The following is an examiner's statement of reasons for allowance: The Examiner has reconsidered the Declaration of Piotr H. Karpinski… The Declaration establishes over 1000 experiments were required to prepare ***the claimed crystalline compound***. This demonstrates undue technical hurdles and provides evidence of unpredictability. … Since the amended claims, as allowed are commensurate in scope with the Declaration evidence, the obviousness rejection has been withdrawn. ***It is noted the recited trisodium hemipentahydrate crystalline compound*** is construed to also be “substantially pure”, as discussed in the declaration.

Ex. 36, Mar. 21, 2016 Notice of Allowance.

As described above, Dr. Karpinski's declaration was limited in scope to isolating a substantially pure crystalline "trisodium … hemipentahydrate." The same "trisodium … hemipentahydrate" species is claimed in both the '938 and '134 Patents. Because the Examiner and Novartis agreed that Dr. Karpinski's declaration, and thus, the claimed "trisodium … hemipentahydrate," were limited to crystalline forms during prosecution of the '938 Patent, the same is true for the '134 Patent. Novartis's cases diminishing the significance of unilateral examiner statements are inapplicable here because ***Novartis's*** statements, and not just those of the Examiner, limited the claims to the specific, claimed ***crystalline, substantially pure*** "trisodium … hemipentahydrate." The Examiner simply recognized Novartis's surrender of claim scope.

d) The claimed "trisodium … hemipentahydrate" is a supramolecular complex

Despite previously characterizing the claimed inventions of the '938 and '134 Patents as "supramolecular complexes,"[36] Novartis now apparently disputes that the "trisodium … hemipentahydrate" is such a complex. Novartis's opening brief, however, offers no explanation as to why "trisodium … hemipentahydrate" is not a "supramolecular complex," merely making conclusory statements that Defendants' position should be rejected. *See supra* 56-57 (substantively addressing only the "formula units" and "unit cells" aspects of Defendants' construction).

[36] *See, e.g.*, Novartis's Response to Torrent's Motion for Judgment on the Pleadings (D.I. 30) at 1 ("The '134 and '938 patents ***claim***, among other things, a novel ***supramolecular complex*** referred to herein as 'trisodium [valsartan-sacubitril] hemipentahydrate."); *Id.* at 4 ("The ***claimed inventions*** in the '134 and '938 patents relate to a novel ***supramolecular complex*** combining two active pharmaceutical ingredients—valsartan and sacubitril—in a single complex, not simply a new polymorph of a known compound.").

The specification, however, consistently identifies the claimed "trisodium … hemipentahydrate" as a "supramolecular complex," which is distinct from a physical mixture. *See, e.g.*, Ex. 4, '134 Patent, at 5:7-12 ("FIG. 1 shows a pictorial representation of the unit cell of the ***supramolecular complex*** of trisodium … hemipentahydrate."); 19:4-15 ("Trisodium … hemipentahydrate may be considered a sodium ***supramolecular complex*** coordinated by oxygen ligands."); 15:13-18 ("**[*T*]*he complex*** is termed trisodium … hemipentahydrate); 27:1-30:6 (Describing the "trisodium … hemipentahydrate" produced in examples 1-3 as a complex that is distinct from "a simple physical mixture" and having "[s]ignificant spectral peaks."); *see* Butcher Resp. Decl. ¶¶ 67-69. As described below, the named inventors of the '938 and '134 Patents confirm this to be true.

The specification defines a "supramolecular complex," as "an interaction between the two pharmaceutically active agents, the cations and any other entity present such as a solvent, in particular water, by means of noncovalent, intermolecular bonding between them. This interaction leads to an association of the species present in the supramolecular complex distinguishing this complex over a physical mixture of the species." Ex. 4, '134 Patent, at 6:52-60. In addition, the cations present in the supramolecular complex may form "coordinate bonds" with the active agents and water molecules, in lieu of noncovalent, intermolecular bonds. *Id.* at 7:14-19; Butcher Resp. Decl. ¶¶ 67-69. With respect to "trisodium … hemipentahydrate" specifically, the specification explains that it is considered "a sodium supramolecular complex, coordinated by oxygen ligands." Ex. 4, '134 Patent, at 19:10-15.

It is no coincidence that the claimed "trisodium … hemipentahydrate" contains two active agents, sodium cations, and water molecules, which all interact with one another via the interactions (i.e., non-covalent and coordinate bonding) described above. *See* Butcher Resp.

Decl. ¶¶ 67-69. That is to say, the claimed "trisodium … hemipentahydrate" parallels the definition of a "supramolecular complex" laid out in the specification. *See id.* ¶ 68. In view of the specification, a POSA would understand that the species at issue, "trisodium … hemipentahydrate," is a "supramolecular complex" because of the network of interactions involved. *Id.* ¶ 69.

Novartis confusingly characterizes "trisodium … hemipentahydrate" as a "compound." *See supra* 47 ("The '938 and '134 Patents describe trisodium [sacubitril-valsartan] hemipentahydrate as a 'compound,' meaning a chemical substance comprising pharmaceutically active agents, cations, and other entities such as water molecules, which interact via non-covalent chemical bonding."). In doing so, Novartis defines "compound" differently than the specification.

The patentees acted as their own lexicographers by defining both "compound" and "supramolecular complex."[37] Ex. 4, '134 Patent, at 6:22-27; 6:52-60. While characterizing "trisodium … hemipentahydrate" as a compound, Novartis redefines "compound" by merging the express definitions of "compound" and "supramolecular complex" set forth in the specification. Compare the following definitions:

"compound" *Supra* 47	**"compound"** '134 Patent at 6:22-27	**"supramolecular complex"** '134 Patent at 6:52-60
A chemical substance comprising pharmaceutically active agents, cations, ***and other entities such as water molecules, which interact via non-***	A chemical substance comprising covalent bonds within the two pharmaceutically active agents, the ARB and the NEPi molecular moieties, and non-covalent interactions between these two pharmaceutically active agents, the ARB and the NEPi molecular	An interaction between the two pharmaceutically active agents, the cations and ***any other entity present such as a solvent, in particular water, by means of noncovalent,*** intermolecular ***bonding***

[37] Novartis admits that the inventors used clear definitional language with respect to these terms. *Supra* 51.

covalent chemical bonding.	moieties. The active agents may be linked by a linking moiety, such as a cation or a non-covalent bond.	***between them*** … distinguishing this complex over a physical mixture of the species.

Thus, while Novartis facially disputes that the "trisodium … hemipentahydrate" is a "supramolecular complex," it labels "trisodium … hemipentahydrate" with its own mashed-up definition of "compound" that imports some features of the definition of the "supramolecular complex" from the patent. In short, it appears Novartis applies in its new label certain qualities that Novartis denies should apply to the claimed "trisodium … hemipentahydrate."

That the claims are limited to a "supramolecular complex" is not a mere academic exercise; it has practical consequences. Indeed, as noted above, a POSA would understand that the identification of "trisodium … hemipentahydrate" as a "supramolecular complex" itself distinguishes it from a simple physical mixture. *See* Butcher Resp. Decl. ¶¶ 67-69. In addition, a POSA would understand that a "supramolecular complex," as defined in the '938 and '134 Patents, is consistent with a crystalline material. *Id.*

* * *

Accordingly, in view of the specification and file history, a POSA would understand that the claimed "trisodium … hemipentahydrate" is a crystalline supramolecular complex having formula units of trisodium [3-((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, wherein each formula unit in a unit cell of the crystalline complex has 2.5 water molecules and 3 sodium ions.

e) The plain meaning of "trisodium … hemipentahydrate" requires it to be a crystalline solid

Even outside the teachings of the intrinsic evidence, a POSA would have recognized that the plain and ordinary meaning of "trisodium … hemipentahydrate" requires it to be a crystalline

solid. In the field of solid-state chemistry, a "solvate" refers to a crystalline substance that incorporates solvent molecules into the crystal lattice. *See, e.g.*, Butcher Resp. Decl. ¶ 37. A hydrate is a form of solvate where the solvent is water, such that water molecules are incorporated into the crystal lattice. *See, e.g. id.* ¶¶ 37-39. Thus, hydrates named to identify a fixed number of water molecules are recognized as crystalline solids where water molecules are incorporated into the crystal lattice. *Id.* ¶¶ 37-38 (discussing numerous references defining solvates as molecular complexes containing solvent within the crystal structure).

By way of background, there are generally-accepted rules in the art for naming hydrates and crystalline substances. *Id.* ¶¶ 38-39. First, the crystalline substance is named based on the relevant compound or compounds that produce the crystalline lattice in conjunction with other components such as solvents or other ions. Second, crystalline hydrates are named based on the number of water molecules within the crystal lattice, such that a prefix is added before the word "hydrate." For example, a ***mono***hydrate indicates that there is one water molecule per formula unit of a given crystalline substance, a ***di***hydrate has two water molecules per formula unit, and so on. *Id*.

In this case, "trisodium … hemipentahydrate" indicates that there are (1) three sodium cations; (2) anionic forms of the claimed APIs; and (3) 2.5 water molecules per formula unit[38] in the crystal lattice. Thus, a POSA would recognize that the claim language refers to a ratio of the number of sodium ions and water molecules for each molecule of each API. *See* Butcher Resp.

[38] A POSA would understand that the "formula unit" refers to the simplest whole number ratio of sodium, sacubitril, and valsartan ions. The specifications of the '938 and '134 Patents indicate that the term "formula unit" also includes the water molecules. Regardless, a POSA would understand that "trisodium … hemipentahydrate" refers to ratio of the number of sodium ions, sacubitril ions, valsartan ions, and water molecules in the context of a crystalline material. *See* Butcher Resp. Decl. ¶ 62.

Decl. ¶¶ 61-62. In addition, a POSA would recognize that the claimed complex contains negatively and positively charged ions. *Id.* Furthermore, a POSA would recognize that, taken together, these nomenclature choices indicate that the material is of a crystalline nature. *Id.* ¶¶ 59-66. By specifying the number of sodium cations and water molecules per formula unit, a POSA would understand that the charged ions and water molecules interact to produce a crystal structure and lattice. *Id.* ¶¶ 60-63. Were it a non-crystalline material, such as an amorphous material, it would not have a precise number of sodium cations and water molecules throughout the material. *See id.* ¶¶ 42-44, 60-63. Thus, it would not be termed by a POSA as a "trisodium … hemipentahydrate." Instead, it would be explicitly labeled as an amorphous material and the individual components would be listed separately. Indeed, Novartis has done just this in related pending applications, as discussed in detail below. Thus, it follows that the term "trisodium … hemipentahydrate" means that each formula unit includes three sodium cations, one anion of each of the claimed APIs, and 2.5 water molecules, where the formula units cumulatively form the asymmetric unit, unit cell, and the overall crystal lattice. *Id.* ¶¶ 59-66.

Moreover, that the claimed complex is specifically a ***hemipenta***hydrate is strong evidence that a POSA would understand it as a crystalline material. First, as explained above, a skilled artisan would recognize that, generally speaking, defining a substance as a hydrate signals that it is a crystalline material. This conclusion is even stronger when the hydrate is specified as having a fixed amount of water, indicating that there is a precise amount of water incorporated into the crystal structure and lattice. *Id.*[39]

[39] In addition, there is no such thing as half of a water molecule (i.e., there cannot be 2.5 water molecules). Butcher Resp. Decl. ¶ 64. While the specification presents a "simplified structure" of the "trisodium … hemipentahydrate," as stated in the specification, this simplified structure is merely used to calculate a relative molecular mass. Ex. 4, '134 Patent, at 15:19-50. A POSA

On similar facts, the court in *AstraZeneca AB v. Andrx Labs, LLC*, determined that a claimed "trihydrate" refers to a crystalline material and could not encompass amorphous forms. C.A. No. 14-8030 (MLC)(DEA), 2017 WL 111928 (D.N.J. Jan. 11, 2017). At issue was the term "the magnesium salt of the S-omeprazole trihydrate," which appeared in related patents. Claim 1 of the '070 patent did not restrict the form of the compound, whereas claim 1 of the '085 patent was admittedly limited to a crystalline material. *AstraZeneca*, 2017 WL 111928, at *43. Relying principally on extrinsic evidence of an understanding of a POSA, the court determined that hydrates require crystalline material, finding that a POSA understands a hydrate to entail a compound where water is trapped within the crystal lattice. *Id.* at *45-46. The same conclusion is even more compelling here, where the patentee clearly limited its hydrate claims to substantially pure crystalline material during prosecution.[40]

f) Claim differentiation cannot recapture surrendered claim scope

Novartis's argument that claim 1 of the '134 Patent is not limited to crystalline material is based primarily on the presumption of claim differentiation. According to Novartis, because dependent claim 5 is specifically limited to "crystalline" "trisodium … hemipentahydrate," independent claim 1 must be broader. *Supra* 48-50. Novartis further attempts to distinguish claim 1 of the '134 Patent from claim 1 of the '938 Patent because the latter includes the language "in crystalline form." *Id.* at 50-53.

The Federal Circuit, however, has acknowledged on numerous occasions that claim differentiation is merely "a rule of thumb that does not trump the clear import of the

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would understand that this simplified structure, used for calculating relative molecular mass, does not exist. Butcher Resp. Decl. ¶¶ 61-64.

[40] Moreover, as described above, the claimed "trisodium … hemipentahydrate" contains additional descriptors beyond the hydrate language alone that indicates that it is a crystalline material.

specification." *Eon-Net LP v. Flagstar Bancorp*, 653 F.3d 1314, 1323 (Fed. Cir. 2011); *see also Marine Polymer Techs., Inc. v. HemCon, Inc*., 672 F.3d 1350, 1359 (Fed. Cir. 2012) ("[C]laim differentiation is not a hard and fast rule and will be overcome by a contrary construction dictated by the written description or prosecution history.") (citation and quotation omitted); *CardSoft v. Verifone, Inc*., 769 F.3d 1114, 1119 (Fed. Cir. 2014). In other words, the doctrine of claim differentiation cannot be used to override clear statements of claim scope established by the intrinsic evidence. *Toro Co. v. White Consol. Indus., Inc*., 199 F.3d 1295, 1302 (Fed. Cir. 1999). Simply put, claim differentiation cannot broaden claims beyond their correct scope. *Id.* at 1302; *see also Curtiss-Wright Flow Control Corp. v. Velan, Inc.*, 438 F.3d 1374, 1381 (Fed. Cir. 2006).

While a difference between an independent and dependent claim can give rise to claim differentiation, even in that circumstance, the Federal Circuit has held that claim differentiation cannot be used to broaden the independent claim beyond its correct scope. In *Enzo Biochem v. Applera Corp.*, 780 F.3d 1149 (Fed. Cir. 2015), the Federal Circuit considered claims directed to a oligo- or polynucleotide. The claim required some form of detection of a signaling moiety. Independent claim 1 did not specify whether indirect or direct detection was required, but dependent claims 67, 68, and 70 specified direct detection. *Id.* at 1156. Based on the doctrine of claim differentiation, the district court reasoned that because the dependent claims specified direct detection, independent claim 1 must be broader including direct and indirect detection. The Federal Circuit reversed. *Id.* at 1156-57. The Federal Circuit reviewed the plain language of the claims and the specification, which clearly indicated that the patentee had only claimed indirect detection. *Id.* at 1154-56. The patentee could not then broaden claim 1 by the expedient of adding a dependent claim limited to direct detection.

Similarly, in *Retractable Techs., Inc. v. Beckton, Dickinson & Co.*, the Federal Circuit held that the presumption of claim differentiation could not overcome a construction mandated by the specification. 653 F.3d 1296, 1304-05 (Fed. Cir. 2011). There, an independent claim related to a syringe "body," and a dependent claim limited the "body" to a "one-piece body." *Id.* The specification made clear that the claimed "body" was a one-piece body. *Id.* at 1305. The specification distinguished prior art syringes having multiple pieces and touted the advantages of a one-piece body, as well as describing the invention as "featur[ing] a one piece hollow body." *Id.* All the embodiments and all the figures included a one-piece body, and there was no disclosure of a multiple-piece body. *Id.* The Federal Circuit concluded, "[t]hus, a construction of 'body' that limits the term to a one-piece body is required to tether the claims to what the specifications indicate the inventor actually invented." *Id.*; *see also Backyard Nature Prods., Inc. v. Woodlink, Ltd.*, 81 F. App'x 729, 732 (Fed. Cir. 2003) (rejecting claim differentiation argument where the specification and prosecution history clearly limited the claim term "mesh" to "expanded mesh" despite a dependent claim adding the "expanded" limitation).

Similarly, here, the specification describes the claimed "trisodium … hemipentahydrate" as a crystalline solid. Ex. 4, '134 Patent, at 17:41-48. The specification characterizes the "trisodium … hemipentahydrate" as having properties characteristic of a crystalline material incompatible with an amorphous structure. As discussed above, during prosecution, the patentees overcame an obviousness rejection only by arguing that isolating and purifying the specific "trisodium … hemipentahydrate," a crystalline material, required thousands of experiments. As also described above, a POSA would understand that the term hemipentahydrate necessarily entails that a specific quantity of water, namely 2.5 water molecules, are trapped within the crystal lattice as part of a unit cell. In the face of this evidence, the patentee cannot broaden claim

1 of the '134 patent beyond its correct scope by adding the limitation "in crystalline form" to dependent claim 5. *Enzo Biochem Inc.*, 780 F.3d at 1156-57; *see also Wi-LAN USA, Inc. v. Apple Inc.*, 830 F.3d 1374, 1391-92 (Fed. Cir. 2016) (declining to apply claim differentiation to distinguish between "UL connections" and "connections.").

g) Pending applications related to the '938 and '134 Patents support Defendants' proposed constructions

A review of PTO records shows that there are at least three patent applications related to the '938 and '134 Patents currently pending before the USPTO. The file histories of these pending applications reinforce that Novartis intended the term "trisodium … hemipentahydrate" to encompass only crystalline supramolecular complexes here. In its related applications, Novartis is separately pursuing the types of claims it forewent in the '938 and '134 Patents to obtain allowance of the single, crystalline species claimed here. For example, U.S. Pat. App. No. 16/502,811 currently contains one independent claim, which recites "[a] compound comprising" anionic sacubitril, anionic valsartan, sodium cations, and water, wherein a range of molar ratios of the individual components are recited. Ex. 39, Jan. 15, 2020 Claims at 1. U.S. Pat. App. No. 16/502,821 currently contains one independent claim, which recites "[a] compound of formula" having active agents, sodium cations, and water molecules, in certain ratios. Ex. 40, Jan. 7, 2020 Claims at 1. U.S. Pat. App. No. 16/579,581 currently contains one independent claim, which recites "[a]n amorphous solid form of a compound comprising" the active agents and sodium cations, but not water. Ex. 41, Feb. 18, 2021 Claims at 1. Finally, U.S. Pat. App. No. 16/579,591, which was abandoned on March 26, 2021, contained two independent claims, both of which recited "[a] glassy solid [i.e., amorphous] form of a compound" containing the active agents and sodium cations, but not water. Ex. 42, Feb. 5, 2020 Claims at 1-2.

These related applications are notable for several reasons. First, that Novartis has chosen ***not to use*** "trisodium … hemipentahydrate" in any of the four related applications, and instead to broadly claim "compounds," as well as "glassy solid forms" and "amorphous forms" specifically, containing sacubitril, valsartan, sodium cations, and water molecules, contradicts Novartis's position that "trisodium … hemipentahydrate" is not limited to a crystalline supramolecular complex. Second, that Novartis ***has*** chosen to separately recite the individual components in each of the related applications demonstrates that Novartis could have easily done the same in the '938 and '134 Patents. Instead, Novartis chose not to do so because the term "trisodium … hemipentahydrate" is a single species that is explicitly defined as a crystalline supramolecular complex. Finally, the claimed "glassy solid" and "amorphous" forms do not include any water molecules, unlike the hemipentahydrate claimed in the '938 and '134 Patents.

This confirms that the breadth of the disclosure in the '938 and '134 Patents is large, and that Novartis's arguments regarding other forms relate to the genus of compounds that were disclosed but not claimed. Novartis is pursuing those claims separately. It deliberately limited itself in these patents to "trisodium … hemipentahydrate," a specific species.

h) The inventors characterized "trisodium … hemipentahydrate" as a crystalline supramolecular complex

The inventors' own publications confirm that "trisodium … hemipentahydrate" is a crystalline supramolecular complex. After the patent applications that issued as the '938 and '134 Patents were filed, but before the patents issued, the inventors published an article in the journal *Tetrahedron Letters* titled "LCZ696: a dual-acting sodium supramolecular complex" (Ex. 43, "Feng"). Feng is cited on the face of the '938 and '134 Patents. Accordingly, Feng is intrinsic evidence. *V-Formation, Inc. v. Benetton Group SpA*, 401 F.3d 1307, 1311 (Fed. Cir. 2005).

In Feng, the inventors describe and characterize LCZ696, a development code synonymous with "trisodium … hemipentahydrate." The inventors unambiguously state that "trisodium … hemipentahydrate" (the same nomenclature as claimed in the '938 and '134 Patents) is a crystalline supramolecular complex, providing detailed experimental results showing that it is a crystalline material having a unit cell. *See* Ex. 43, Feng at 275 ("The chemical structure of [trisodium … hemipentahydrate] can be described as a sodium supramolecular complex … The crystal structure displays an infinite 3-dimensional network of such sodium-ion based complexes."); *id.* at 276 (Fig. 2 illustrating half of the unit cell of "trisodium … hemipentahydrate."). Thus, the inventors themselves considered the term "trisodium … hemipentahydrate" to refer to a specific crystalline supramolecular complex, and their descriptions align with Defendants' proposed constructions, not Novartis's arguments.

2. The '134 Patent Is Limited to Substantially Pure "Trisodium … Hemipentahydrate"

As detailed above, "trisodium … hemipentahydrate" is a crystalline material. Because it is crystalline, the prosecution history makes clear that substantial purity is also part of the construction. Even though the claims of the '938 Patent do not expressly recite a "substantially pure" limitation, Novartis concedes that the claims are limited to substantially pure crystalline material. *Supra* 57. Novartis has no other option because during prosecution of the '938 Patent, it clearly surrendered subject matter to secure allowance of the claims. For these very same reasons that required Novartis to surrender claim scope and concede to a narrow construction of the claims of the '938 Patent, the '134 Patent, which is a divisional of the '938 Patent, is likewise so limited.

"[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." *Biogen Idec, Inc. v. GlaxoSmithKline LLC*, 713 F.3d 1090, 1094-95 (Fed. Cir. 2013). Thus, when the patentee unequivocally and unambiguously disavows a certain meaning to obtain a patent, the doctrine of prosecution history disclaimer narrows the meaning of the claim consistent with the scope of the claim surrendered. *Biogen Idec, Inc.*, 713 F.3d at 1095. Here, during prosecution of the parent '938 Patent, the patentee unequivocally and unambiguously stated that crystalline material is, by definition, substantially pure.

Novartis has no option but to concede that claims of the '938 Patent are limited to "substantially pure" "trisodium … hemipentahydrate." During prosecution of the '938 Patent described above (*supra* Part II.B.1.c)), the Examiner rejected all pending claims as obvious over a combination of references teaching the use of compositions comprising valsartan and NEP inhibitors. In response, Novartis submitted the Karpinski declaration arguing that the claims were non-obvious because Novartis had achieved unpredictable results based on its substantially pure crystalline hemipentahydrate. Ex. 22, Sept. 9, 2010 Amendment and Response, at 7-8; Ex. 23, Sept. 9, 2010 Declaration ¶ 4.

The Examiner maintained the rejection because Novartis's evidence of unpredictability was not commensurate in scope with the claims. While Dr. Karpinski's declaration focused on Novartis's alleged difficulties in preparing ***substantially pure*** "trisodium … hemipentahydrate," at that time, only claim 102 of the application was limited to "substantially pure" material. Accordingly, the arguments were insufficient to overcome the rejection with respect to the broader claims which were not so limited. Ex. 24, Nov. 3, 2010 Final Rejection.

In a series of amendments, the applicants added a "substantially pure" limitation but then canceled those claims and presented new claims without any "substantially pure" limitation.[41] In further discussion with the Examiner, and to secure allowance of the claims, Novartis agreed that crystalline hemipentahydrate was substantially pure even though there was no express substantial purity limitation in the claims. *See* March 7, 2014 Interview Summary ("such a crystalline form of the recited compound would also be substantially pure").

Following the interview, the Examiner entered an Examiner's amendment and allowed the claims. A statement of the Examiner's reasons for allowance accompanied the amendment, which clearly articulated Novartis's concession of claim scope in exchange for issuance of the '938 Patent, stating in part: "The Declaration establishes over 1000 experiments were required to prepare ***the claimed crystalline compound***. … ***It is noted the recited trisodium hemipentahydrate crystalline compound is construed to also be 'substantially pure', as discussed in the declaration***." Ex. 28, Mar. 14, 2014 Notice of Allowance, at 3-4; *see also supra* Part II.B.1.c).

In the face of this unmistakable surrender of claim scope to obtain the '938 Patent, Novartis has conceded that the claims of the '938 Patent are limited to a ***substantially pure***, crystalline material. *See* D.I. 205, Joint Claim Construction Chart; *supra* 57. The surrender of claim scope legally applies equally to the '134 Patent. *Elkay Mfg. Co.*, 192 F.3d at 980; *Hakim v. Cannon Avent Grp., PLC*, 479 F.3d 1313, 1318 (Fed. Cir. 2007). In addition to the legal application of the prosecution history of a related application, the Examiner made it clear in the '134 Patent file history that the claims of the '134 Patent required both crystallinity and the

[41] *See* Ex. 25, June 23, 2011 Amendment and Response, at 5 (*"**the claims as amended provide for a substantially pure compound**"*); Ex. 26, Dec. 17, 2013 Amendment, at 6.

associated substantial purity by again allowing the claims only in view of the Karpinski declaration and stating: "It is noted the recited trisodium hemipentahydrate crystalline compound is ***construed to also be 'substantially pure***.'" Ex. 36, Mar. 21, 2016 Notice of Allowance at 4. The Notice of Allowance then referenced the same Karpinski declaration and the same arguments that Novartis had made to secure allowance of the '938 Patent based on the difficulty in preparing the hemipentahydrate form described by Karpinski. *Id.* Thus, the Notice of Allowance confirms both the crystallinity of the hemipentahydrate and that the '134 Patent would not have issued but for Novartis's concession that the claims are limited to "substantially pure" hemipentahydrate.

* * *

For all these reasons, the claimed "trisodium … hemipentahydrate" is a substantially pure crystalline solid. The remainder of Defendants' proposed construction flows directly from the specification. Ex. 4, '134 Patent, at 19:4-19 (describing the formula units of the asymmetric unit cell).

C. <u>Novartis's Reply Position</u>:

1. "trisodium [sacubitril-valsartan] hemipentahydrate" By Itself Is Not Limited To Crystalline Form

Defendants' construction limiting "trisodium [sacubitril-valsartan] hemipentahydrate" by itself to "crystalline" violates the presumption of claim differentiation (at its strongest here) and improperly renders superfluous the separate "crystalline form" limitations of '938 Patent claim 1 and '134 Patent claim 5. *Supra* 48-50. Defendants' cited cases explain that this presumption may only be overcome by another construction that is "dictated" or "mandated" by the intrinsic

evidence. *See Marine*, 672 F.3d at 1359; *Retractable*, 653 F.3d at 1304-05; *supra* 74-76.[42] That is not the situation here. *Supra* 45-55; *infra* Sections II.C.1.a-c.

a) The Specification Never Limits The Claimed "trisodium [sacubitril-valsartan] hemipentahydrate" To Crystalline Form

The specification describes the invented novel compounds which "can be in the crystalline, partially crystalline, amorphous, or polymorphous form, preferably [*i.e.*, not exclusively] in the crystalline form," and identifies trisodium [sacubitril-valsartan] hemipentahydrate as most preferred. *Supra* 50-51, 62-63. Defendants attempt to side-step the explicit amorphous form disclosure by alleging that it does not apply to trisodium [sacubitril-valsartan] hemipentahydrate (*supra* 58-59, 62-63) and by pointing to the preferred crystalline form. This attempt is inconsistent with the intrinsic evidence as a whole.

Trisodium [sacubitril-valsartan] hemipentahydrate is first disclosed in the specification as the "most preferred" compound without reference to crystalline form; it is not, as Defendants assert, exclusively described as crystalline. *See, e.g.*, Ex. 4, '134 Patent, 15:1-18 ("In this most preferred example, the complex is termed trisodium [sacubitril-valsartan] hemipentahydrate."), 15:19-50 (simplified structure of trisodium [sacubitril-valsartan] hemipentahydrate not limited to crystalline form), *see also* 14:36-41, 14:50-54 (the dual-acting compound, not limited to crystalline form, may contain 2.5 water molecules which "may contribute to [its] intermolecular structure"); Klibanov Reply Decl. ¶¶ 17-18; *contra supra* 58-62. The specification never excludes from the above "amorphous form" disclosure any compound, much less the most preferred compound. Klibanov Reply Decl. ¶¶ 16, 19-21.

[42] Defendants' other cases likewise each involved clear intrinsic evidence, which is absent here, overcoming the presumption. *Toro*, 199 F.3d at 1298, 1301-02; *Backyard*, 81 F. App'x at 732; *Curtiss-Wright*, 438 F.3d at 1378-81; *Eon-Net*, 653 F.3d at 1321-23; *CardSoft*, 769 F.3d at 1118-19; *Enzo*, 780 F.3d at 1154-57; *Wi-LAN*, 830 F.3d at 1389-92.

The Court should not limit the compound trisodium [sacubitril-valsartan] hemipentahydrate to the "preferred embodiment" crystalline form absent a "clear intention" in the intrinsic evidence as a whole that the patentee intended such a limitation. *Supra* 51. There is no such "clear intention" here. *Id.* Defendants point to statements using non-definitional or exemplary language and therefore such statements, discussed below, do not limit the claims.

First, the grammatical structure of a single phrase ("trisodium [sacubitril-valsartan] hemipentahydrate, a crystalline solid" (*supra* 59-60)) that is prefaced with the non-limiting words "relates to" and does not follow the clear definitional language used elsewhere (*supra* 51-52), does not undermine the inventors' clear intent to claim trisodium [sacubitril-valsartan] hemipentahydrate in any form. Courts have held that "punctuation is not decisive of [statutory] construction," and it should not be decisive here either in view of the inventors' intent as shown elsewhere in the specification. *See Costanzo v. Tillinghast*, 287 U.S. 341, 344 (1932).

Second, the "examples disclosed in the specification" (*supra* 69 *citing* Ex. 4, '134 Patent, Figure 1, 5:7-12, 27:1-30:6) are expressly not limiting. Ex. 4, '134 Patent, 26:64-67 ("[The] examples are disclosed solely by way of illustrating the invention and should not be taken in any way to limit the scope of the present invention.").

Third, the specification descriptions of trisodium [sacubitril-valsartan] hemipentahydrate that mention "unit cell" (*supra* 61 *citing* Ex. 4, '134 Patent, 5:7-14, 17:40-19:19) relate only to an exemplary embodiment—an analysis of a single crystal of trisodium [sacubitril-valsartan] hemipentahydrate—not trisodium [sacubitril-valsartan] hemipentahydrate without limitation.

Fourth, the term "supramolecular complex" used to describe trisodium [sacubitril-valsartan] hemipentahydrate (*supra* 68-69 *citing* Ex. 4, '134 Patent, 5:7-12, 19:4-15, 15:13-18, 27:1-30:6) is not limited to crystalline form. Ex. 4, '134 Patent, 6:52-7:2 ("As a preferred [*i.e.*,

not exclusive] embodiment of the invention, the [supramolecular] complex is crystalline[.]"); Klibanov Reply Decl. ¶¶ 22, 25. Defendants do not argue otherwise. *Supra* 56 n.29, 71 ("supramolecular complex" is "consistent with [*i.e.*, not limited to] a crystalline material").

Finally, Defendants' argument that the specification only enables "trisodium [sacubitril-valsartan] hemipentahydrate" in crystalline form (not amorphous form), is limited to one footnote with no support, which is not clear and convincing evidence. *Supra* 60 n.32. Moreover, enablement should not play a part in claim construction where, as here, the intrinsic evidence is not ambiguous. *See Phillips*, 415 F.3d at 1327; *Idenix*, 2015 WL 9048010, at *4.

b) The '938 Patent File History Does Not Limit The Claimed "trisodium [sacubitril-valsartan] hemipentahydrate" To Crystalline Form

While Novartis limited the '938 Patent claims to "crystalline form," Novartis omitted "crystalline form" from the '134 Patent application claim 1 (issued as claim 1). *Supra* 54-55. Applicants, like Novartis here, commonly "adopt[] an explicit claim-narrowing limitation to achieve immediate issuance of a patent containing the narrowed claims and postpone[] to the prosecution of a continuation application further arguments about claims that lack the narrowing limitation. [T]hat process does not imply a disclaimer. . . ." *Sanofi v. Watson Labs. Inc.*, 875 F.3d 636, 650 (Fed. Cir. 2017). *Elkay* does not change the outcome because, unlike here, there was no significant claim difference between the earlier and later application claims and therefore no basis to construe the claims differently. *See Elkay*, 192 F.3d at 979.

Neither Novartis nor the Examiner indicated during the prosecution of the '938 Patent that the compound trisodium [sacubitril-valsartan] hemipentahydrate alone was "by definition" in crystalline form. *See supra* 53-55; *contra supra* 80. Instead, Novartis told the Examiner that the invention was a "compound having both [valsartan] and [sacubitril] in the same compound structure." Novartis did not say that the invention was limited to one form of that compound. Ex.

22, '938 FH, 2010/9/9 Response at 6. While Novartis agreed to limit the '938 Patent application claims to crystalline form by expressly adding the word "crystalline" to claim 1, there was no such agreement for the '134 Patent. *Supra* 53-55.

None of Defendants' citations to the '938 Patent prosecution history limits claim scope. First, the Examiner's reliance on co-crystal prior art to reject the '938 Patent application claims (*supra* 64-65) does not limit claim scope, because a prior art species (crystalline form) may render obvious a genus (not limited to any form). *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 419-20 (2007). Second, Novartis elected trisodium [sacubitril-valsartan] hemipentahydrate and crystalline form as a species of the invention, but did not restrict every application claim to the elected species (much less subsequent applications having different claim scope). *Contra supra* 63-64, 67; *see* Ex. 38, '938 FH, 2009/12/07 Election Requirement at 6; *Plantronics, Inc. v. Aliph, Inc.*, 724 F.3d 1343, 1350-53 (Fed. Cir. 2013) (patentee's election of species did not surrender claim scope). Indeed, Novartis's response to the restriction requirement included application claims (*e.g.*, 86-95) that were not limited to trisodium [sacubitril-valsartan] hemipentahydrate or crystalline form. Ex. 20, '938 FH, 2010/1/28 Response at 9-10; Klibanov Reply Decl. ¶¶ 35-36. Third, Defendants leave out support that Novartis cited for claims added during the '938 Patent prosecution. *Supra* 65-66. Novartis stated that support for claims to "trisodium [sacubitril-valsartan] hemipentahydrate" in the "solid form" and in "crystalline form" "***can be found throughout the specification***," including the amorphous form disclosure (*supra* 83), and "***[f]urther*** support . . . is found on pages 23, 25-26 and 27, which describe the crystal structure of the claim compound." Ex. 26, '938 FH, 2013/12/17 Amendment at 3, 6; Klibanov Reply Decl. ¶¶ 37-39. Defendants' brief omits the emphasized language.

c) The '134 Patent Prosecution Does Not Limit The Claimed "trisodium [sacubitril-valsartan] hemipentahydrate" To Crystalline Form

Defendants' sole '134 Patent prosecution evidence appears in the Examiner's Notice of Allowance. *Supra* 67-68. The Notice of Allowance for the parent '938 Patent (limited to "crystalline form") should not limit the broader '134 Patent claims, which the Examiner did not require and Novartis did not agree to be limited to "crystalline form." Ex. 36, '134 FH, 2016/03/21 Notice of Allowance at 3; Ex. 26, '938 FH, 2013/12/17 Amendment at 3-5 (claims); Klibanov Reply Decl. ¶¶ 40-43; *supra* 67-68. Instead, the Examiner stated that the "secondary considerations [*i.e.*, Karpinski Declaration] . . . would also apply to the ***sacubitril-valsartan compound*** administered in the . . . method claims." Ex. 36, '134 FH, 2016/03/21 Notice of Allowance at 2-4; Klibanov Reply Decl. ¶ 44.

Even if the Court finds that the Examiner characterized "trisodium [sacubitril-valsartan] hemipentahydrate" as crystalline (Novartis disagrees), an Examiner's single statement does not constitute a clear disavowal of claim scope where, as here, the rest of the prosecution history and intrinsic evidence shows the patentee clearly did not intend to limit the claims. *Supra* 53-55.

d) The Extrinsic Evidence Is Not Persuasive

As the intrinsic evidence shows unambiguously that the claimed "trisodium [sacubitril-valsartan] hemipentahydrate" is not limited to crystalline form, the claim construction analysis should end there, and the Court should not consider Defendants' extrinsic evidence. *Supra* 55; *AstraZeneca*, 2017 WL 111928, *10, *43-45. However, if the Court considers extrinsic evidence, it demonstrates that a POSA as of 2006 would know that amorphous compounds may also be hydrates with a fixed amount of water.[43] Klibanov Reply Decl. ¶¶ 5-13 *citing* Ex. 55, Kaneniwa

[43] Contrary to the information Defendants provided Dr. Butcher (*see* Butcher Resp. Decl. ¶ 15), the '938 and '134 Patents have the same priority date—either April 4 or August 11, 2006—not

1984 at Abstract, 4552-53, 4555-58; Ex. 56. Thus, the ratio of components in trisodium [sacubitril-valsartan] hemipentahydrate (*supra* 72-73) does not limit this compound to crystalline form.[44] Klibanov Reply Decl. ¶¶ 14-15.

Because the extrinsic evidence indicates that a hydrate with a fixed amount of water, like trisodium [sacubitril-valsartan] hemipentahydrate alone, would not be limited to crystalline form, a POSA would rely on the intrinsic evidence, which resolves the crystalline issue in Novartis's favor. Another court held that a claimed active agent "in the form of its monohydrate" was not limited to crystalline form where "[t]he words of [the claim] d[id] not specify any physical state" of the monohydrate, and the intrinsic record indicated the monohydrate was known to exist in a non-crystalline form (*e.g.*, in a solution). *See Abraxis Bioscience, Inc. v. Navinta, LLC*, 640 F. Supp. 2d 553, 565-67 (D.N.J. 2009), *rev'd on other grounds*, 625 F.3d 1359, 1368 (Fed. Cir. 2010). Like *Abraxis*, '134 Patent claim 1 "does not specify any physical state" and the specification discloses the hemipentahydrate may exist in non-crystalline form.

Defendants' reliance on *AstraZeneca* is misplaced. Unlike in *AstraZeneca*, where the intrinsic evidence "left unanswered" "whether the term 'trihydrate' was a crystalline form," the intrinsic evidence here (including the clear claim language) is not ambiguous. *See AstraZeneca*, 2017 WL 111928, at *44-45. The intrinsic evidence in *AstraZeneca* differed from the facts here in several important ways. First, the court found that '070 patent claim 1 reciting a "trihydrate" could be limited to crystalline form without violating claim differentiation, which is not the case

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two different priority dates. *Supra* 7 & n. 10. A POSA's understanding of the disputed claim terms would be the same as of either April 4 or August 11, 2006. *Supra* 46 n.27.

[44] Novartis withdrew its original proposed construction to simplify the issues for this Court. Novartis did not "elect[] not to construe the claim term" or recognize that "fractional water content must relate to the number of water molecules in a unit cell of a crystal lattice" (*contra supra* 61 n.35); the issues in dispute may be resolved without modifying the claim language.

here. *Compare AstraZeneca*, 2017 WL 111928, at *45-46 *with supra* 82-83. Second, the *AstraZeneca* patent specification "fail[ed] to describe the bounds of the term trihydrate" and was "far from clear," whereas the '134 and '938 Patents' specification discloses that the claimed "hemipentahydrate" is not limited to crystalline form. *Compare AstraZeneca*, 2017 WL 111928, at *45 *with* Section II.C.1.a. Third, the *AstraZeneca* file histories "lack[ed] . . . any conclusive statements regarding crystallinity," whereas the file histories here demonstrate that Novartis and the Examiner understood that the "hemipentahydrate" alone is not limited to crystalline form. *Compare AstraZeneca*, 2017 WL 111928, at *45 *with* Sections II.A.1.d & II.C.1.b-c.

e) Novartis Never Admitted That "trisodium [sacubitril-valsartan] hemipentahydrate" Alone Is Limited To Crystalline Form

Defendants improperly replace statements about "LCZ696" (a short form for crystalline LCZ696) in Feng *et al.* (Ex. 43) with the claim language "trisodium [sacubitril-valsartan] hemipentahydrate." *Supra* 79. Feng never suggests that LCZ696 is synonymous with the claimed "trisodium [sacubitril-valsartan] hemipentahydrate"; LCZ696 is one embodiment of the invention, not the *only* embodiment. Klibanov Reply Decl. ¶¶ 26-27 *citing* Ex. 43 at 275.

Defendants also argue that in pending patent applications, Novartis used different language to claim genuses of compounds (not limited to trisodium [sacubitril-valsartan] hemipentahydrate) including the "amorphous" form of those compounds. *Supra* 73, 77-78 *citing* Exs. 39-42. Patent applicants are permitted to seek claims of different scope and use different terminology in later patent applications, *see, e.g.*, *Sanofi*, 875 F.3d at 650, which Novartis did here. Klibanov Reply Decl. ¶¶ 28-30 *citing* Exs. 39-42. And the claims in these pending applications are consistent with trisodium [sacubitril-valsartan] hemipentahydrate by itself not being limited to crystalline form. Klibanov Reply Decl. ¶¶ 31-33 *citing* Exs. 39 and 40.

2. The Claims Should Not Be Limited To A "Supramolecular Complex Having Formula Units" And "Unit Cell[s]"

The question is not, as Defendants argue, "[w]hether 'trisodium [sacubitril-valsartan] hemipentahydrate' is a supramolecular complex" (*supra* 58). Rather, it is whether "trisodium [sacubitril-valsartan] hemipentahydrate" and "crystalline form" are *limited to* Defendants' "supramolecular complex," "formula units," and "unit cell" language. *Supra* 44, 56-57.

That Novartis has characterized "trisodium [sacubitril-valsartan] hemipentahydrate" as a "complex" or "supramolecular complex" does not mean that "supramolecular complex" should be read into the claims. *Contra supra* 68. The specification also expressly defines "supramolecular complex" without reference to crystalline form, formula units, or unit cells. Ex. 4, '134 Patent, 6:52-7:2; Klibanov Reply Decl. ¶ 25; *supra* 69, 84-85. Nothing in Defendants' arguments about "compound" and "supramolecular complex" changes these facts. *See supra* 68-69; Klibanov Reply Decl. ¶¶ 23-24 *citing* Ex. 4, '134 Patent, 6:22-43. Novartis never suggested that the term "compound" in the intrinsic evidence would encompass a physical mixture. Novartis clearly explained the opposite. *See supra* 5, 7. In short, Defendants' proposal to limit "trisodium [sacubitril-valsartan] hemipentahydrate" alone to "a . . . supramolecular complex having formula units . . ., wherein each formula unit in a unit cell . . . has 2.5 water molecules and 3 sodium ions" is another effort to limit the compound to crystalline form, which it is not. Section II.C.1.

3. The '134 Patent Claims Are Not Limited To "Substantially Pure"

While the Examiner and Novartis explicitly agreed that the application claim issuing as '938 Patent claim 1 "should be amended to require a substantially pure compound," there is no similar agreement with the '134 Patent. Prosecution disavowal must be "clear and unmistakable" to overcome the "heavy presumption" that claims mean what they say. *Biogen*, 713 F.3d at 1094-

95. There is no such "clear and unmistakable" disavowal here. *Supra* 57. Novartis omitted the claim limitation "crystalline" from '134 Patent claim 1, so any disclaimer with respect to the narrower '938 Patent claims does not apply. *Supra* 54-55, 87.[45]

Moreover, Defendants' position that the '134 Patent claims are limited to "substantially pure" compound appears to rise and fall with their argument that the compound trisodium [sacubitril-valsartan] hemipentahydrate must be a crystalline material. *Supra* 79 ("Because [trisodium [sacubitril-valsartan] hemipentahydrate] is crystalline, the prosecution history makes clear that substantial purity is also part of the construction"), *see also* 66 (asserting "because the material was crystalline, it was also, by definition, substantially pure"). The compound trisodium [sacubitril-valsartan] hemipentahydrate is not limited to crystalline form. Section II.C.1.

D. <u>Defendants' Sur-reply Position</u>:

Contrary to Novartis's reply, during prosecution of the '938 and '134 Patents, it agreed to limit its claims to a substantially pure, crystalline material. This is evidenced by an extensive back and forth between Novartis and the Examiner in which Novartis conceded that its evidence for patentability was limited to substantially pure, crystalline trisodium … hemipentahydrate. The prosecution history alone is dispositive. Regardless, Defendants' proposed construction is supported by the specification and intrinsic evidence in its entirety. *Supra* 60-61.

[45] Defendants' reliance on *Elkay* is inapposite because in that case, unlike the present case, there was no significant difference between the claim language of the earlier and later applications and therefore no basis to construe the claims differently. *See Elkay*, 192 F.3d at 979. *Hakim* is also inapposite. In *Hakim*, the applicant replaced a claim term, despite emphasizing throughout prosecution of the parent patent that the replaced term distinguished the claimed invention over prior art. *Hakim*, 479 F.3d at 1318. There is no indication that the examiner here allowed the '134 Patent claims because "substantially pure" distinguished the claims over prior art.

1. During Prosecution of the '938 Patent, Novartis Agreed with the Examiner that It Was Entitled to Claim No More than Substantially Pure, Crystalline Trisodium … Hemipentahydrate

During prosecution of the '938 Patent, the Examiner rejected the claims as obvious. Ex. 21, Apr. 7, 2010 Non-final Rejection. The Examiner found that each aspect of the invention was known in the art and it would have been obvious to prepare the co-crystals from solution and to isolate and "characterize the hydrate forms of this co-crystal, including the crystal in the range of 2.5 H_2O molecule equivalents, giving the elected hemipentahydrate …." *Id.* at 13.

Novartis attempted to overcome the rejection, arguing that the prior art did not teach the possibility of a single ARB/NEPi moiety. Ex. 22, Sept. 9, 2010 Amendment, at 6.[46] Concurrently with its Response, Novartis submitted the Declaration of Dr. Karpinski. As discussed in Section II.B, *supra*, Dr. Karpinski argued that it took over 1000 separate experiments to prepare, purify and characterize ***substantially pure*** trisodium … hemipentahydrate. *See supra* 65. According to Dr. Karpinski and Novartis, the "procedure to prepare, purify and characterize this compound was non-routine and required an undue level of experimentation." Ex. 23, Sept. 9, 2010 Karpinski Decl., ¶ 4; Ex. 22, Sept. 9, 2010 Amendment, at 7–8. It was this undue level of experimentation that Novartis argued rendered the claims non-obvious.

The Examiner rejected the Applicant's arguments. Specifically, regarding Dr. Karpinski's Declaration, the Examiner noted that Dr. Karpinski's evidence of alleged undue experimentation was not commensurate in scope with the claims, with the exception of claim 102, which at that time was the only claim limited to substantially pure trisodium … hemipentahydrate.

[46] Notably, Novartis's statement further evidences that the '659 and '331 Patents are directed to a combination of physically separate components, as opposed to a complex, as explained above. *See supra*, Sections I.B, I.D.

Accordingly, the Examiner maintained the obviousness rejection. Ex. 24, Nov. 3, 2010 Final Rejection.

Novartis then took its first step to limit the claims: it amended pending claim 86, adding a "substantially pure" limitation to a claim that previously recited a broad "compound."[47] Additionally, Novartis canceled most other claims. After this amendment, all proposed claims included the "substantially pure" limitation, except claim 99 (and dependent claims 100 and 101), which, in contrast, broadly recited trisodium … hemipentahydrate "in solid form." Notwithstanding this difference, Novartis nonetheless argued in its remarks accompanying the amendment that "the claims as amended provide for a ***substantially pure*** compound and there is no suggestion in any of the cited references disclosing such an embodiment, either expressly or inherently." Ex. 25, June 23, 2011 Amendment, at 5 (emphasis added). Before any action by the Examiner, however, Novartis cancelled ***all*** previously presented claims and proposed new claim 105, which was identical to previously presented claim 99, generally claiming a "solid form."[48] Ex. 26, Dec. 17, 2013 Preliminary Amendment. Thus, after Novartis had just amended the claims to include the "substantially pure" limitation so that the claims would be commensurate in scope with Dr. Karpinski's Declaration, Novartis attempted to remove that same limitation.

During a March 7, 2014 interview, the Examiner again indicated that claim 105 should be amended to include the "substantially pure" limitation "in order to be commensurate in scope

[47] Claim 86 recited "a compound of the formula:" [(ARB)(NEPi)](Cat)$_{1\text{-}3}$ • xH_2O], specifying that the ARB was valsartan, the NEPi was sacubitril, "Cat" was a sodium cation, and "x" was 0 to 3.

[48] New claim 105: "Trisodium [3-((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 the ***solid form***." Ex. 26, Dec. 17, 2013 Preliminary Amendment at 3. In the remarks accompanying the Amendment, Novartis confirmed that claim 105 was identical to previously presented claim 99, which the applicant had previously argued was "substantially pure." *Id.* at 6.

with the Declaration of [Dr.] Karpinski." Ex. 27, Mar. 14, 2014 Interview Summary. Novartis conceded, and amended claim 105 to recite "crystalline" in place of "solid form" in the body of the claim. *Id*. In addition, "the Examiner and [Novartis] agreed that such a crystalline form of the recited compound would also be ***substantially pure***." *Id*.

Following the interview, with Novartis's consent, the Examiner entered an Examiner's amendment and allowed the claims. Ex. 28, Mar. 14, 2014 Notice of Allowance. Claim 105, which issued as claim 1 of the '938 Patent, was amended to change "solid form" to "crystalline form." *Id*. at 3. A statement of the reasons for allowance accompanied the amendment, explaining that the trisodium … hemipentahydrate was crystalline and substantially pure. *Id*.; *see also supra* 67 ("***It is noted the recited trisodium hemipentahydrate crystalline compound*** is construed to also be 'substantially pure', as discussed in the [Karpinski] declaration.").

This extensive back and forth between Novartis and the Examiner shows that Novartis overcame the obviousness rejection only because of the alleged technical hurdles that it faced in preparing the ***substantially pure, crystalline*** trisodium … hemipentahydrate. And Novartis agreed with the Examiner that the claims are limited to a substantially pure, crystalline trisodium hemipentahydrate. *See* Butcher Sur-Reply Decl. ¶¶ 32–40. Indeed, even though the claims of the '938 Patent do not include the words "substantially pure," the evidence of Novartis's disavowal is so unmistakable that Novartis had to concede that the '938 Patent is limited to substantially pure crystalline material.

2. The Examiner Allowed the '134 Patent Based on the Same Agreement with Novartis that Its Claims Were Limited to Substantially Pure, Crystalline Trisodium … Hemipentahydrate

The '134 Patent is similarly limited. The '134 Patent is a division of the '938 Patent and claims methods of using the same trisodium … hemipentahydrate claimed in the '938 Patent.

Most importantly, the Examiner allowed the claims of the '134 Patent only after reciting the same arguments and evidence presented in Dr. Karpinski's declaration in the parent application:

> The following is an examiner's statement of reasons for allowance: … ***[T]he obviousness basis in the parent application was overcome by secondary considerations, which would also apply to the sacubitril-valsartan compound administered in the instant claimed treatment method claims. Evidence established that preparation of the sacubitril-valsartan compound was associated with undue technical hurdles***. The Examiner stated in the parent application, in the reasons for allowance, mailed 3/14/2014:
>
> > The following is an examiner's statement of reasons for allowance: The Examiner has reconsidered the Declaration of Piotr H. Karpinski… The Declaration establishes over 1000 experiments were required to prepare ***the claimed crystalline compound***. This demonstrates undue technical hurdles and provides evidence of unpredictability. … Since the amended claims, as allowed are commensurate in scope with the Declaration evidence, the obviousness rejection has been withdrawn. ***It is noted the recited trisodium hemipentahydrate crystalline compound*** is construed to also be "substantially pure", as discussed in the declaration.

Ex. 36, Mar. 21, 2016 Notice of Allowance. Thus, the Examiner specifically quoted from the same limiting Notice of Allowance that all parties admit narrowed the '938 Patent to both crystalline and substantially pure material ***despite*** the '938 Patent claims not explicitly reciting that limitation.

Novartis downplays the significance of the related prosecution by arguing that the Examiner's Notice of Allowance is a single unilateral statement by the Examiner. *Supra* 87. But as is clear above, Novartis conceded after extensive back-and-forth during the parent prosecution, in connection with the issuance of the '938 Patent, that it was entitled at most to claims to substantially pure, crystalline trisodium … hemipentahydrate, and the Examiner expressly referenced that same agreement before allowing the '134 Patent claims on that basis. *See id.*; *see also* Butcher Sur-Reply. Decl. ¶¶ 32–40.

Biogen Idec, Inc. v. GlaxoSmithKline LLC, 713 F.3d 1090 (Fed. Cir. 2013), is instructive. In *Biogen*, the examiner rejected all pending claims because the specification did not enable a POSA to practice the full scope of the claimed invention, which would have encompassed all "anti-CD20 antibodies," no matter their specificity or affinity for certain tumor cells. The specification only enabled Rituxan® (rituximab), not other anti-CD20 antibodies. In response, Biogen argued that the specification enabled anti-CD20 antibodies with similar affinity and specificity as Rituxan®, conceding that other antibodies directed to the same antigen might have different affinities and functional characteristics. "While the applicants may not have repeated the examiner's language *verbatim et literatim*, it is clear that they were limiting their invention to what the examiner believed they enabled." *Biogen*, 713 F.3d at 1096.

Similarly, here, to overcome an obviousness rejection, Novartis argued that it would require undue experimentation for a POSA to practice the claimed invention. When the Examiner nonetheless maintained the rejection because Novartis's evidence of unpredictability was not commensurate in scope with its claims, Novartis limited the claims to a substantially pure crystalline material. Indeed, a substantially pure crystalline material was all it was entitled to claim in view of the evidence and arguments presented regarding non-obviousness, just as the applicants in *Biogen* limited their claims to only that which they had enabled. *See also UCB, Inc. v. Yeda Research & Dev. Co., Ltd.*, 837 F.3d 1256, 1261 (Fed. Cir. 2016) ("[A] patent applicant cannot later obtain scope that was requested during prosecution, rejected by the Examiner, and then withdrawn by the applicant.").

Novartis argues that it was free to adopt an explicit claim-narrowing limitation to achieve immediate issuance of the '938 Patent and then pursue broader claims in a child patent, such as the '134 Patent. *Supra* 85 (citing *Sanofi v. Watson Labs. Inc.*, 875 F.3d 636, 650 (Fed. Cir.

2017)). But Novartis did not attempt to overcome the basis of the rejection in the '134 Patent such that it could seek broader claims. Quite the opposite, the Examiner specifically referenced Novartis's prior agreement that trisodium … hemipentahydrate is limited to a substantially pure, crystalline material, and noted that it was only on this basis that Novartis had been able to overcome the obviousness rejection. Because the claims at issue in the '134 Patent recite methods of using that same trisodium … hemipentahydrate material, the Examiner allowed the claims. Novartis did not further attempt to traverse the bases for the Examiner's rejection, argue that it had other evidence of undue experimentation, or otherwise argue for broader claims.

While Novartis attempts to disguise this case as one where it did ***not*** acquiesce to the Examiner's statements in the Notice of Allowance, in fact, Novartis did not sit idly by while the Examiner limited its claims. Novartis actively participated, and its silence on this while actively commenting on other issues affirms the Examiner's acknowledgment of Novartis's own prior agreement as to the limits of the claims. As the Federal Circuit recognized in *Biogen*, the acquiescence cases are inapposite where the applicant adopts an examiner's narrow characterization of an invention to overcome a rejection. *Biogen*, 713 F.3d at 1097, n.6; *ACCO Brands, Inc. v. Micro Sec. Devices*, Inc., 346 F.3d 1075, 1078–79 (Fed. Cir. 2003) (holding that the examiner's reliance on the applicant's statements in the Reasons for Allowance shows agreement on claim scope); *Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 979 (Fed. Cir. 1999). Here, Novartis did more than let the Examiner's characterization stand; as described above, it expressly negotiated the limitations. *See TorPharm, Inc. v. Ranbaxy Pharm., Inc.*, 336 F.3d 1322, 1330 (Fed. Cir. 2003) ("[T]he public is entitled to equate an inventor's acquiescence to the examiner's narrow view of patentable subject matter with abandonment of the rest."); *FlatWorld Interactives LLC v. Samsung Elecs. Co. Ltd.*, 77 F. Supp. 3d 378 (D. Del. 2014).

Novartis's argument hinges on claim differentiation based on dependent claim 5 of the '134 Patent, which expressly recites that trisodium … hemipentahydrate is in crystalline form. Claim 5 was not remarked upon by the Examiner during prosecution, and the '134 Patent issued with very little substantive prosecution at all. Nevertheless, the intrinsic record is clear. Novartis engaged in a years-long back and forth with the Examiner that limited its claims to substantially pure, crystalline material as recited in the Karpinski declaration. This culminated with the Examiner referencing this same agreement as the basis to allow the claims of the '134 Patent. Notwithstanding the presumption of claim differentiation, where the intrinsic record is clear, a dependent claim cannot be used to expand the scope of an independent claim beyond its correct scope. *Toro Co. v. White Consol. Indus., Inc.*, 199 F.3d 1295, 1302 (Fed. Cir. 1999); *Enzo Biochem Inc. v. Applera Corp.,* 780 F.3d 1149, 1154–56 (Fed. Cir. 2015).

3. Consistent with the File Histories, the Specification Identifies Trisodium … Hemipentahydrate as a Crystalline Complex

That the claims of the '134 Patent are limited to a crystalline complex is equally clear from the specification, which further debunks Novartis's claim differentiation argument. The specification expressly states: "trisodium … hemipentahydrate, ***a crystalline solid.***" Ex. 4, '134 Patent, at 17:42–46. Against this, Novartis relies on a single generic statement in the specification that various unclaimed dual-acting compounds may exist in different solid forms. Trisodium … hemipentahydrate is a specific crystalline supramolecular complex that is a species of the larger genus of ARB/NEPi dual-acting compounds discussed in the '938 and '134 Patents. Novartis and Dr. Klibanov state that the specification explicitly discloses an amorphous form of trisodium … hemipentahydrate. *Supra* 83; Klibanov Reply Decl. ¶ 16. However, the only cited specification support is the following (Ex. 4, '134 Patent, at 15:63–67):

> The combination or dual-acting compound, in particular, the complex, of the present invention is preferably in the solid form. In the solid state it can be in the crystalline, partially crystalline, amorphous, or polymorphous form, preferably in the crystalline form.

This statement is not specific to trisodium … hemipentahydrate—it expressly refers generally to the "combination or dual-acting compound." As Dr. Butcher explains, this genus of dual-acting compounds encompasses a large number of potential combinations and permutations. Butcher Sur-Reply Decl. ¶¶ 25–31; Ex. 57, Klibanov Dep. Tr. at 73:17–92:11 (agreeing that the number of possible combinations of the dual-acting compound defined in the '134 patent is a large number). A POSA would not understand this generic, boilerplate statement in the specification to mean that every single combination exists in the crystalline, partially crystalline, amorphous, or polymorphous form. Butcher Sur-Reply Decl. ¶¶ 25–31. Novartis's expert, Dr. Klibanov, did not provide any record evidence for the theory that this is how a POSA would understand that statement. Ex. 57, Klibanov Dep. Tr. at 94:17–95:6.

Despite Novartis's and Dr. Klibanov's characterizations, the specification does not state that trisodium … hemipentahydrate may be amorphous. The specification describes trisodium … hemipentahydrate beginning at column 15. It does not refer specifically to crystalline trisodium … hemipentahydrate or an exemplary embodiment of trisodium … hemipentahydrate. Instead it refers to trisodium … hemipentahydrate using the exact language as it appears in the claim and recites specific features of the compound. Butcher Sur-Reply Decl. ¶¶ 14–20.

Novartis relies on this same portion of the specification. For example, the specification describes trisodium … hemipentahydrate as having three sodium cations, one molecule of valsartan, one molecule of sacubitril, and 2.5 water molecules. Ex. 4, '134 Patent, at 15:1–50. Novartis and Dr. Klibanov agree that these are features of the claimed trisodium … hemipentahydrate. The specification further provides a simplified structural diagram, used only

to "formally calculate the relative molecular mass." *Id.* Again, Novartis and Dr. Klibanov admit that this is a feature of the claimed invention (i.e., these are not characteristics of an exemplary embodiment). Ex. 57, Klibanov Dep. Tr. at 102:18–104:11.

The specification further indicates that any dual-acting compound within the scope of the invention may be characterized using X-ray powder diffraction. Ex. 4, '134 Patent, at 16:14–22. Again, using the same language as used in the claim, the specification provides characterization data for the claim term trisodium ... hemipentahydrate. *Id.* at 16:23–67. This characterization data clearly indicates that the claimed material is crystalline, as Dr. Klibanov admitted. Ex. 57, Klibanov Dep. Tr. at 107:10–108:1. The specification further explains, in no uncertain terms, that trisodium … hemipentahydrate is "a crystalline solid which is characterized by the data and parameters obtained from single crystal X-ray analysis and X-ray powder patterns." Ex. 4, '134 Patent, at 17:42–48.

What's more, trisodium … hemipentahydrate has a well-defined unit cell made up of twelve formula units of trisodium … hemipentahydrate, as was determined by the single-crystal X-ray analysis (i.e., it is crystalline). *Id.* at 18:42–58 ("The details for trisodium … hemipentahydrate from the single crystal measurements, especially the atom coordinates, the isotropic thermal parameters, the coordinates of the hydrogen atoms as well as the corresponding isotropic thermal parameters, show that a monoclinic unit cell exists, its cell content of twelve formula units of [trisodium … hemipentahydrate] occurring as a result of two asymmetric units on two-fold positions."); *see also id.* at 18:65–19:3 ("A pictorial representation of the unit cell of the supramolecular complex of trisodium … hemipentahydrate … is shown in FIG. 1."). This is not limited to an "exemplary embodiment," as Novartis argues; rather, it further supports that

trisodium … hemipentahydrate is a single, specific species that is crystalline and has a defined unit cell made up of defined formula units. Butcher Sur-Reply Decl. ¶¶ 21–24.

These crystalline requirements are not isolated references, in stark contrast to the single general snippet on which Novartis relies. As described in Section II.B., *supra*, and Dr. Butcher's Declarations, the specification repeatedly indicates that trisodium … hemipentahydrate is a specific crystalline material. *Supra* 59-62; Butcher Resp. Decl. ¶¶ 31-36, 51–52, 54, 58–79; Butcher Sur-Reply Decl. ¶¶ 14–31.

In addition, Novartis's attempt to dismiss the clear grammatical reading of the specification fails because grammar, including punctuation, can be highly relevant. *See Innovative Commc'ns Techs., Inc. v. Vivox, Inc.*, Nos. 2:12cv7, 2:12cv9, 2012 WL 5331573, at *13 n.4 (E.D. Va. Oct. 26, 2012) (construing claim term, noting the "absence of commas or other punctuation that might otherwise identify either 'temporary' or 'dynamically assigned' as an appositive of the other"—the very sort of comma ***present*** here that defines the claimed compound as "a crystalline solid"); Ex. 4, '134 Patent, at 17:41-48 ("trisodium [sacubitril-valsartan] hemipentahydrate, a crystalline solid"); *see also Niz-Chavez v. Garland*, 141 S. Ct. 1474, 1480–81 (majority), 1490–91 (dissent) (2021) (interpreting statute based on what the dissent deemed the "quotation-mark theory"); *Toshiba Corp. v. Juniper Networks, Inc.*, 248 F. App'x 170, 174 (Fed. Cir. 2007) (relying on grammar and punctuation in claim construction). And Novartis's continued focus on the words "relates to" is a red herring. *Supra* 84. Defendants do not argue that the referenced portion of the specification states that the alleged invention disclosed in the specification is limited to the claimed trisodium … hemipentahydrate, but that the trisodium … hemipentahydrate embodiment is definitionally crystalline. *Supra* 71-73. The words "relates to" are irrelevant to this conclusion.

Accordingly, while Novartis attempts to cast Defendants' argument as relying on non-limiting examples and preferred embodiments, this is not the case. The intrinsic evidence is not ambiguous. Trisodium… hemipentahydrate is only characterized and identified as crystalline.

4. "Trisodium … Hemipentahydrate" Is a Crystalline Material According to Its Plain and Ordinary Meaning as Understood by a POSA

As explained in Section II.B., *supra*, a POSA would understand from the claim term as a whole that trisodium … hemipentahydrate is crystalline. *Supra* 71-74. That is to say, the Court need not rely exclusively on any one portion of the claim term to conclude that trisodium … hemipentahydrate must be crystalline. Rather, that the claim term requires a fixed number of both sodium ions (***tri***sodium) and water molecules (***hemipenta***hydrate), and recites specific stoichiometric ratios of each individual component (i.e., a "formula unit"), is a clear indicator that it is a crystalline material. Butcher Sur-Reply Decl. ¶ 19. Myopically focusing on whether a material with the word "hydrate" in its name can be amorphous, Novartis glosses over this point. The claim term at issue is not "hydrate" in a vacuum—the term as a whole is "trisodium … hemipentahydrate." And Novartis has failed to explain how or why the claim term as a whole, trisodium … hemipentahydrate, is not limited to a specific crystalline supramolecular complex, as Defendants' evidence conclusively establishes.

In any event, as noted in Section II.B., *supra*, and by Dr. Butcher, solvates, including hydrates, with a fixed amount of solvent are defined as crystalline materials where the solvent is incorporated into the crystal lattice. *Supra* 71-74; Butcher Resp. Decl. ¶¶ 37–38 (citing Brittain 1999 (Ex. 44); Wells (Ex. 51); Haleblian (Ex. 47); Khankari (Ex. 50); Byrn 1995 (Ex. 45)); Butcher Sur-Reply Decl. ¶ 14. Solvates and hydrates with a fixed amount of solvent or water are distinguished from amorphous forms. Butcher Resp. Decl. ¶¶ 37–38. Thus, a POSA would understand from the name itself that trisodium … hemipentahydrate is crystalline, with the

solvent incorporated into the crystal lattice. Accordingly, each formula unit in a unit cell of the crystalline complex has 2.5 water molecules [hemipentahydrate] and 3 sodium ions [trisodium].

Despite numerous references that attest to this general understanding of a POSA, Novartis persists that hydrates with a fixed amount of water may be amorphous. But neither Novartis nor Dr. Klibanov even attempts to prove that the numerous references relied upon by Dr. Butcher are incorrect. And in deposition, as in his Reply Declaration, Dr. Klibanov identified only a single reference (Kaneniwa) that disclosed alleged "amorphous hydrates." *Supra* 87-88; Klibanov Reply Decl. ¶¶ 5–13 (citing Kaneniwa 1984). As Dr. Butcher explains, Novartis's reliance on Kaneniwa is unsound. Butcher Sur-Reply Decl. ¶¶ 8–13. Among other shortcomings, the reference lacks reliable and necessary data to confirm that the compounds are amorphous with a fixed amount of water. *Id.* ¶¶ 10–13. Additionally, the various analyses that are included are inconclusive. *Id*. In any event, Kaneniwa is an outlier at best, and certainly cannot overcome the greater weight of evidence supporting a POSA's general understanding that hydrates with a fixed amount of water are necessarily crystalline.

5. Trisodium … Hemipentahydrate is a Supramolecular Complex

As previously explained, trisodium … hemipentahydrate is a "supramolecular complex." *Supra* 68-71; *see also* Butcher Sur-Reply Decl. ¶¶ 41–43. Novartis argues that, even though it has characterized "trisodium … hemipentahydrate" as a "complex" and a "supramolecular complex," these terms should not be read into the claims. *Supra* 90. But, in addition to Novartis's prior characterizations, the specification expressly identifies trisodium … hemipentahydrate as a supramolecular complex. *Supra* 68-69. As Novartis acknowledges, "supramolecular complex" is

defined in the specification.[49] Ex. 4, '134 Patent, 6:52–7:2; *Supra* 90. Contrary to Novartis's assertion, one disputed question ***is*** whether trisodium … hemipentahydrate is a supramolecular complex. Based on the specification's consistent characterization of "trisodium … hemipentahydrate" as a supramolecular complex and Novartis's characterizations of the claimed "trisodium … hemipentahydrate" as a supramolecular complex, the claims should be so limited.

6. The Inventors' Characterization of Trisodium … Hemipentahydrate

Finally, Novartis asserts that "Defendants improperly replace statements about 'LCZ696' … in Feng et al. (Ex. 43) with the claim language 'trisodium [sacubitril-valsartan] hemipentahydrate,'" which Novartis claims "never suggests that LCZ696 is synonymous with the claimed 'trisodium [sacubitril-valsartan] hemipentahydrate.'" *Supra* 89. But Novartis does not dispute that Feng is intrinsic evidence (*supra* 78) or that Feng identifies LCZ696 as trisodium … hemipentahydrate using nomenclature identical to the claim term. Ex. 43, Feng at 275 ("Crystalline LCZ696, ***trisodium … hemipentahydrate***…").

[49] Novartis seemingly concedes that the claimed "trisodium … hemipentahydrate" does not encompass a physical mixture, which is one aspect of the definition of "supramolecular complex." *Supra* 90; Klibanov Reply Decl. ¶ 23.

Dated: May 21, 2021

/s/ Daniel M. Silver
Daniel M. Silver (#4758)
Alexandra M. Joyce (#6423)
MCCARTER & ENGLISH, LLP
Renaissance Centre
405 N. King Street, 8th Floor
Wilmington, Delaware 19801
(302) 984-6300
dsilver@mccarter.com
ajoyce@mccarter.com

Attorneys for Plaintiff Novartis Pharmaceuticals Corporation

OF COUNSEL:

Nicholas N. Kallas
Christina Schwarz
Christopher E. Loh
Susanne Flanders
Jared L. Stringham
Shannon Clark
Laura Fishwick
VENABLE LLP
1290 Avenue of the Americas
New York, New York 10104
(212) 218-2100
nkallas@venable.com
cschwarz@venable.com
cloh@venable.com
slflanders@venable.com
jlstringham@venable.com
skclark@venable.com
lfishwick@venable.com

/s/ Dominick T. Gattuso
Dominick T. Gattuso (#3630)
HEYMAN ENERIO GATTUSO & HIRZEL LLP
300 Delaware Avenue, Suite 200
Wilmington, DE 19801
(302) 472-7311
dgattuso@hegh.law

Attorneys for Defendant Crystal Pharmaceutical (Suzhou) Co., Ltd.

OF COUNSEL:

Scott A. Cunning, II
Elizabeth M. Crompton
PARKER POE ADAMS & BERNSTEIN, LLP
1400 K Street, NW
Suite 1000
Washington, DC 20005
(202) 434-9100
scottcunning@parkerpoe.com
elizabethcrompton@parkerpoe.com

C. Kyle Musgrove
PARKER POE ADAMS & BERNSTEIN, LLP
620 South Tryon Street, Suite 800
Charlotte, NC 28202
(704) 372-9000
kylemusgrove@parkerpoe.com

/s/ Stamatios Stamoulis
Stamatios Stamoulis (#4606)
Richard C. Weinblatt (#5080)
STAMOULIS & WEINBLATT LLC
Two Fox Point Centre
6 Denny Road, Suite 307
Wilmington, DE 19809
(302) 999-1540
stamoulis@swdelaw.com
weinblatt@swdelaw.com

Attorneys for Defendants Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd.

OF COUNSEL:

Autumn N. Nero
PERKINS COIE LLP
33 East Main Street, Suite 201
Madison, WI 53703-3095
(608) 663-7460
ANero@perkinscoie.com

Christopher D. Jones
PERKINS COIE LLP
700 Thirteenth Street, NW, Suite 600
Washington, D.C. 20005-3960
(202) 654-6200
CDJones@perkinscoie.com

Bryan D. Beel
PERKINS COIE LLP
1120 NW Couch Street, 10th Floor
Portland, OR 97209
(503) 727-2000
BBeel@perkinscoie.com

/s/ Eve H. Ormerod
Neal C. Belgam (#2721)
Eve H. Ormerod (#5369)
SMITH, KATZENSTEIN, & JENKINS LLP
1000 West Street, Suite 1501
Wilmington, DE 19801
(302) 652-8400
nbelgam@skjlaw.com
eormerod@skjlaw.com

Attorneys for Defendants Alembic Pharmaceuticals Limited and Alembic Pharmaceuticals, Inc.

OF COUNSEL:

Stuart D. Sender
Frank D. Rodriguez
Amit Singhai
WINDELS MARX LANE & MITTENDORF, LLP
1 Giralda Farms, Suite 100
Madison, New Jersey 07940
(973) 966-3200
ssender@windelsmarx.com
frodriguez@windelsmarx.com
asinghai@windelsmarx.com

/s/ Kenneth Laurence Dorsney
Kenneth Laurence Dorsney (#3726)
Cortlan S. Hitch (#6720)
MORRIS JAMES LLP
500 Delaware Avenue, Suite 1500 Wilmington, DE 19899-2306 (302) 888-6855

OF COUNSEL:

Stephen R. Auten
Richard T. Ruzich
Roshan P. Shrestha

TAFT STETTINIUS & HOLLISTER LLP
111 East Wacker Drive, Suite 2800
Chicago, IL 60601
(312) 527-4000
sauten@taftlaw.com
rruzich@taftlaw.com
rshrestha@taftlaw.com

OF COUNSEL:

Steven J. Moore
James E. Nealon
WITHERS BERGMAN LLP
1700 East Putnam Avenue, Suite 400
Greenwich, Connecticut 06870-1366
(203) 302-4100
(203) 302-6611
steven.moore@withersworldwide.com
james.nealon@withersworldwide.com

kdorsney@morrisjames.com

Attorneys for Defendant Alkem Laboratories Ltd.

/s/ Kenneth Laurence Dorsney
Kenneth Laurence Dorsney (#3726)
Cortlan S. Hitch (#6720)
MORRIS JAMES LLP
500 Delaware Avenue, Suite 1500
Wilmington, DE 19899-2306
(302) 888-6855
kdorsney@morrisjames.com

Attorneys for Defendants Aurobindo Pharma USA Inc. and Aurobindo Pharma Ltd.

/s/ Kenneth Laurence Dorsney
Kenneth Laurence Dorsney (#3726)
Cortlan S. Hitch (#6720)
MORRIS JAMES LLP
500 Delaware Avenue, Suite 1500
Wilmington, DE 19899-2306
(302) 888-6855
kdorsney@morrisjames.com

Attorneys for Defendants Biocon Pharma Limited, Biocon Limited, and Biocon Pharma, Inc.

OF COUNSEL:

Matthew M. Holub
Jillian M. Schurr
KATTEN MUCHIN ROSENMAN LLP
525 West Monroe Street
Chicago, IL 60661
(312) 902-5200
matthew.holub@katten.com
jillian.schurr@katten.com

Jitendra Malik
KATTEN MUCHIN ROSENMAN LLP
550 South Tryon Street, Suite 2900
Charlotte, NC 28202
(704) 444-2000
jitty.malik@katten.com

Christopher B. Ferenc
KATTEN MUCHIN ROSENMAN LLP
2900 K Street NW
Washington, DC 20007
(202) 625-3500
christopher.ferenc@katten.com

/s/ Eve H. Ormerod

OF COUNSEL:

Dmitry V. Shelhoff
Kenneth S. Canfield
Edward D. Pergament
PERGAMENT & CEPEDA LLP
25A Hanover Road, Suite 104
Florham Park, NJ 07932
(973) 998-7722
dshelhoff@pergamentcepeda.com
kcanfield@pergamentcepeda.com
epergament@pergamentcepeda.com

Neal C. Belgam (#2721)
Eve H. Ormerod (#5369)
SMITH, KATZENSTEIN, & JENKINS LLP
1000 West Street, Suite 1501
Wilmington, DE 19801
(302) 652-8400
nbelgam@skjlaw.com
eormerod@skjlaw.com

Attorneys for Defendants Hetero USA Inc., Hetero Labs Limited, Hetero Labs Limited Unit III, Torrent Pharma Inc. and Torrent Pharmaceuticals Ltd.

/s/ Beth A. Swadley

OF COUNSEL:

Nirav N. Desai
Dennies Varughese
Joseph H. Kim
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 New York Avenue N.W.
Washington, DC 20005
(202) 371-2600
ndesai@sternekessler.com
dvarughese@sternekessler.com
josephk@sternekessler.com

Adam Wyatt Poff (#3990)
Beth A. Swadley (#6331)
YOUNG, CONAWAY, STARGATT & TAYLOR LLP
Rodney Square
1000 North King Street
Wilmington, DE 19801
(302) 571-6600
apoff@ycst.com
bswadley@ycst.com

Attorneys for Defendants Laurus Labs Limited and Laurus Generics Inc.

/s/ Alexandra M. Ewing

OF COUNSEL:

William R. Zimmerman
Andrea L. Cheek
Catherine R. Gourash
KNOBBE, MARTENS, OLSON, & BEAR LLP
1717 Pennsylvania Ave. N.W., Ste. 900
Washington D.C. 20006
(202) 640-6400
Bill.Zimmerman@knobbe.com
Andrea.Cheek@knobbe.com
Cassie.Gourash@knobbe.com

Frederick L. Cottrell, III (#2555)
Alexandra M. Ewing (#6407)
RICHARDS, LAYTON & FINGER, P.A.
One Rodney Square
920 N. King Street
Wilmington, DE 19801
(302) 651-7700
cottrell@rlf.com
ewing@rlf.com

Attorneys for Defendants Lupin Atlantis Holdings, S.A., Lupin Limited, Lupin Inc., and

Lupin Pharmaceuticals, Inc.

Carol M. Pitzel Cruz
KNOBBE, MARTENS, OLSON, & BEAR LLP
925 Fourth Avenue, Suite 2500
Seattle, WA 98104
(206) 405-2000
carol.pitzel.cruz@knobbe.com

/s/ John M. Seaman

OF COUNSEL:

A. Neal Seth
Corey Weinstein
WILEY
1776 K St., NW
Washington, D.C. 20036
(202) 719-7000
nseth@wiley.law
cweinstein@wiley.law

John M. Seaman (#3868)
April M. Kirby (#6152)
ABRAMS & BAYLISS LLP
20 Montchanin Road
Suite 200
Wilmington, DE 19807
(302) 778-1000
seaman@abramsbayliss.com
akirby@abramsbayliss.com

Attorneys for Defendants Macleods Pharmaceuticals Ltd. and Macleods Pharma USA, Inc.

/s/ Stamatios Stamoulis

OF COUNSEL:

Ronald M. Daignault (pro hac vice)
Richard Juang (pro hac vice)
rdaignault@daignaultiyer.com
rjuang@daignaultiyer.com
DAIGNAULT IYER LLP
8200 Greensboro Drive, Suite 900
Mclean, VA 22102

Stamatios Stamoulis (#4606)
Richard C. Weinblatt (#5080)
STAMOULIS & WEINBLATT LLC
800 N West Street, Third Floor
Wilmington, DE 19801
(302) 999-1540
stamoulis@swdelaw.com
weinblatt@swdelaw.com

Attorneys for Defendants MSN Pharmaceuticals Inc., MSN Laboratories Private Limited, and MSN Life Sciences Private Limited

/s/ David Ellis Moore

OF COUNSEL:

Robert L. Florence
PARKER POE ADAMS & BERNSTEIN LLP
1075 Peachtree Street, N.E.
Suite 1800
Atlanta, GA 30309
(678) 690-5750

David Ellis Moore (#3983)
Bindu Ann George Palapura (#5370)
POTTER ANDERSON & CORROON, LLP
1313 N. Market St., Hercules Plaza, 6th Flr.
P.O. Box 951
Wilmington, DE 19899-0951
(302) 984-6000
dmoore@potteranderson.com

robertflorence@parkerpoe.com

Tasneem A. Dharamsi
PARKER POE ADAMS & BERNSTEIN LLP
110 East Court Street
Suite 200
Greenville, SC 29601
(864) 577-6370
tasneemdharamsi@parkerpoe.com

OF COUNSEL:

Don J. Mizerk
Femi Masha
HUSCH BLACKWELL LLP
120 South Riverside Plaza, Suite 2200
Chicago, IL 60606
(312) 655-1500
don.mizerk@huschblackwell.com
femi.masha@huschblackwell.com

bpalapura@potteranderson.com

Attorneys for Defendant Mylan Pharmaceuticals Inc.

/s/ Megan C. Haney
John C. Phillips, Jr. (#110)
Megan C. Haney (#5016)
PHILLIPS, MCLAUGHLIN & HALL, P.A.
1200 North Broom Street
Wilmington, DE 19806
(302) 655-4200
jcp@pmhdelaw.com
mch@pmhdelaw.com

Attorneys for Defendant Nanjing Noratech Pharmaceutical Co., Limited

OF COUNSEL:

Alan B. ClementZhibin Li
LOCKE LORD LLP
Brookfield Place, 200 Vesey Street
New York, New York 10281
646-217-7897
aclement@lockelord.com
zhibin.li@lockelord.com

Nina Vachhani
LOCKE LORD LLP
111 South Wacker Drive
Chicago, IL 60606
(312) 443-0700

nvachhani@lockelord.com

/s/ Beth A. Swadley
Adam Wyatt Poff (#3990)
Beth A. Swadley (#6331)
YOUNG, CONAWAY, STARGATT & TAYLOR LLP
Rodney Square
1000 North King Street
Wilmington, DE 19801
(302) 571-6600
apoff@ycst.com
bswadley@ycst.com

Attorneys for Defendant Novugen Pharma (Malaysia) Sdn. Bhd.

OF COUNSEL:

Leora Ben-Ami

/s/ Karen Elizabeth Keller
John W. Shaw (#3362)
Karen Elizabeth Keller (#4489)
Nathan Hoeschen (#6232)

Mira Mulvaney
KIRKLAND & ELLIS LLP
601 Lexington Avenue
New York, NY 10022
(212) 446-4800
leora.benami@kirkland.com
mira.mulvaney@kirkland.com

OF COUNSEL:

Michael J. Gaertner
James T. Peterka
Nina Vachhani
LOCKE LORD LLP
111 South Wacker Drive
Chicago, IL 60606
(312) 443-0700
mgaertner@lockelord.com
jpeterka@lockelord.com
nvachhani@lockelord.com

Zhibin Li
LOCKE LORD LLP
Brookfield Place, 200 Vesey Street
New York, New York 10281
(646) 217-7897
zhibin.li@lockelord.com

SHAW KELLER LLP
I.M. Pei Building
1105 North Market Street, 12th Floor
Wilmington, DE 19801
(302) 298-0700
jshaw@shawkeller.com
kkeller@shawkeller.com
nhoeschen@shawkeller.com

Attorneys for Defendant Teva Pharmaceuticals USA, Inc.

/s/ Beth A. Swadley
Adam Wyatt Poff (#3990)
Beth A. Swadley (#6331)
YOUNG, CONAWAY, STARGATT & TAYLOR LLP
Rodney Square
1000 North King Street
Wilmington, DE 19801
(302) 571-6600
apoff@ycst.com
bswadley@ycst.com

Attorneys for Defendants Zydus Pharmaceuticals (USA) Inc. and Cadila Healthcare Ltd.