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UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN FRANCISCO DIVISION

THE REGENTS OF THE UNIVERSITY OF MICHIGAN, and THE UNIVERSITY OF SOUTH FLORIDA BOARD OF TRUSTEES, Plaintiffs, v. NOVARTIS PHARMACEUTICALS CORPORATION, Defendant.	Case No. 3:22-cv-04913-AMO **PLAINTIFFS THE REGENTS OF THE UNIVERSITY OF MICHIGAN AND THE UNIVERSITY OF SOUTH FLORIDA BOARD OF TRUSTEES' OPENING CLAIM CONSTRUCTION BRIEF**

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I. INTRODUCTION

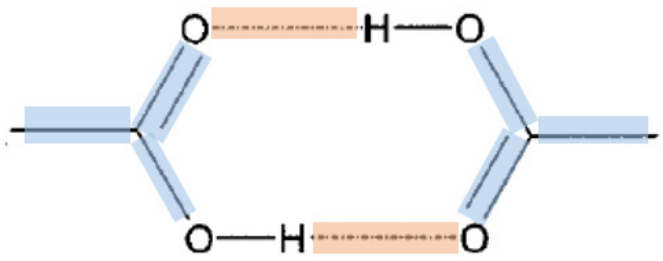
Plaintiffs The Regents of the University of Michigan and The University of South Florida Board of Trustees (collectively, "Plaintiffs") submit this Opening Claim Construction Brief regarding the proper construction of disputed terms of U.S. Patent No. 10,633,344 ("the Asserted Patent" or "the '344 Patent," attached as **Exhibit A**). Plaintiffs' proposed construction reflect the plain and ordinary meaning of these terms as understood by the intrinsic record. In contrast, Defendant Novartis Pharmaceuticals Corp. ("Novartis") seeks to inject new limitations into the claims to attempt to manufacture noninfringement defenses via claim construction. Plaintiffs respectfully submit that this Court should reject Novartis's proposed constructions as contrary to law and should instead adopt Plaintiffs' straightforward understanding of the terms' ordinary meaning.

II. SCIENTIFIC BACKGROUND AND THE ASSERTED PATENT

In the pharmaceutical industry, it is important for drugs to be both effective and accessible. A drug's therapeutic benefit can be limited due to its chemical properties. Ex. A, '344 Patent, at 2:25-29. For example, a drug's chemical properties can make it less soluble, poorly absorbed, or more easily broken down in the body. *Id.* The properties of a crystalline solid of a drug depend upon the internal arrangement of its components. *Id.* at 2:13-15. The '344 Patent relates to the design of new crystalline versions of drugs having chemical and physical properties that improve functional characteristics, like solubility, dissolution rate, and stability. *Id.* at 2:20-24, 2:67-3:28.

A fundamental building block in chemistry is the atom. Atoms interact with one another through the formation of bonds to create molecules. Molecules then can interact with other molecules or atoms to form larger molecules or compounds through covalent or non-covalent bonds. Covalent bonds are typically the strongest chemical interactions; non-covalent bonds (e.g. ionic bonds or hydrogen bonds) are among the weakest. Examples of such interactions are shown below, with the covalent bonds (highlighted in blue) represented via a hard line (-, single bond) or lines (=,

double bond) between atoms in a molecule (e.g., C (carbon)[1], O (oxygen), H (hydrogen), N (nitrogen)), and the non-covalent hydrogen bonds (highlighted in orange) represented by a dashed line (---).

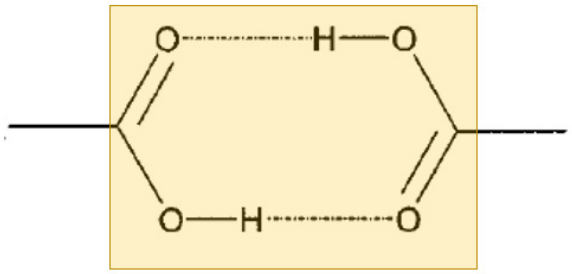


Scientists can form a crystalline solid by engineering specific non-covalent bonds between or among its components.[2] Ex. A, '344 Patent, at 1:48-50. When composed of different components, the crystalline solid can be considered "a multiple component crystal." For example, a multiple-component pharmaceutical crystal would be comprised of at least one molecular component that is an active pharmaceutical ingredient and another, complementary component called a "coformer." *Id.* at 3:12-28. Such non-covalent interactions in a crystalline solid—along with the "chemical functionalities" or the group of atoms on each molecular component that interacts with similar or different groups—are referred to as a supramolecular synthon. Put differently, a supramolecular synthon consists of two or more chemical functionalities and the non-covalent bond(s) between them. These supramolecular synthons contribute to the formation of a discrete supramolecular entity or polymeric structure. *Id.* at 9:66-10:4.

An example of a supramolecular synthon is shown in the yellow box in the figure below. In this example, it is formed by the hydrogen bonds between the carboxylic acid groups (-C(=O)OH) of each molecule. Supramolecular synthons can include the same functionalities or different

[1] The carbon atoms in the figure are denoted at the end of the line or lines (e.g., C—C, C—O, C=O), but are typically removed to simplify the chemical drawings of the type shown above.
[2] A solid is one of several different phases of matter. *See* Ex. A, '344 Patent, at 3:30-32.

functionalities. When the functionalities are the same, it is called a homosynthon. When they are different, it is called a heterosynthon. So in the example below, the supramolecular synthon is a homosynthon because both chemical functionalities are carboxylic acid groups.



The internal arrangement of the components within a crystalline solid can affect its solubility, dissolution rate, chemical stability, and/or bioavailability, making the understanding of the interactions between the components important—particularly for pharmaceutical crystals. *Id.* at 2:13-18, 2:25-31. 2:40-44, 2:66-3:4. For instance, multiple-component pharmaceutical crystals "can exhibit physical and/or chemical properties that are the same or different from the parent pharmaceutical ingredient as a direct result of alternative molecular recognition patterns." *Id.* at 3:19-28.

Here, the '344 Patent relates to "multiple-component solids having at least one active pharmaceutical ingredient" to achieve crystalline assemblies with "improved drug solubility, dissolution rate, stability[,] and bioavailability." *Id.* at 3:12-28. To achieve these claimed multi-component solids, the '344 Patent teaches that supramolecular synthons are formed between an active pharmaceutical ingredient (API) and a coformer based on their complementary chemical functionalities. *Id.* at 3:29-37, Fig. 24.

The '344 Patent issued on April 28, 2020, from an original utility application (the '956 Application), filed on March 3, 2003. It also claims priority to a provisional application (Application No. 60/360,768) filed March 1, 2002. Plaintiffs assert one independent claim (claim

10) and three dependent claims (claims 11, 16, and 18) from the '344 patent. Independent claim 10 is included with the disputed terms in bold:

> **10**. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of **a co-crystal** comprising supramolecular synthons, each supramolecular synthon formed from stoichiometric amounts of at least one **active pharmaceutical ingredient (API)** and at least one **co-former**,
> wherein **the API** has a first chemical functionality that **permits formation of API homosynthons** through non-covalent hydrogen bonding when **the API** is in its pure form,
> wherein **the co-former has a second chemical functionality complimentary** to the first chemical functionality via non-covalent hydrogen bonding,
> wherein **said co-former** is a sold at room temperature and atmospheric pressure when **the co-former** is in its pure form,
> wherein supramolecular synthons are formed via non-covalent hydrogen bonding between the first chemical functionality of **the API** and the second chemical functionality of **the co-former**, and
> wherein the first chemical functionality is (i) **a carboxamide**, (ii) a carbonyl, or (iii) an amine.

III. LEGAL STANDARDS OF CLAIM INTERPRETATION

This is a patent infringement lawsuit brought by Plaintiffs. Patent infringement is determined by a "two-step process" that first requires interpretation of the claims of the patent by the Court. *See Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (*en banc*), *aff'd*, 517 U.S. 370 (1996). The factfinder then compares the claims as interpreted to the products accused of infringement to determine whether infringement has occurred. *Id*. The interpretation of a patent claim is a question of law for the Court; it may involve subsidiary factual findings. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 331-32 (2015).

Claim terms generally are given their ordinary and customary meaning, which is to say "the meaning that the term would have to a person of ordinary skill in the art [(POSITA)] in question at the time of the invention, i.e., as of the effective filing date of the patent application[.]" *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (*en banc*). "There are only two exceptions to this general rule: 1) when a patentee sets out a definition and acts as his own lexicographer, or 2) when the patentee disavows the full scope of a claim term either in the specification or during prosecution." *Thorner v. Sony Comput. Ent. Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012). "The

patentee is free to choose a broad term and expect to obtain the full scope of its plain and ordinary meaning unless the patentee explicitly redefines the term or disavows its full scope." *Id.* at 1367. Disavowal of claim scope exists when the patentee's statement is "clear and unmistakable," and not "amenable to multiple reasonable interpretations." *CUPP Computing AS v. Trend Micro Inc.*, 53 F.4th 1376, 1382 (Fed. Cir. 2022); *see also Genuine Enabling Tech. LLC v. Nintendo Co.*, 29 F.4th 1365, 1374 (Fed. Cir. 2022) (reversing district court's determination of a broad disavowal where "the only disavowal of claim scope that is clear and unmistakable [was] disavowal of signals below the audio frequency spectrum.").

The Court must construe claim terms as they would have been understood by a POSITA at the relevant time period. *See Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004) ("A court construing a patent claim seeks to accord a claim the meaning it would have to a person of ordinary skill in the art at the time of the invention."). A POSITA reads claim terms in the context of the entire patent, including the specification. *See Phillips*, 415 F.3d at 1313 ("[T]he person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification."). In determining the level of ordinary skill in the art, various factors may be considered, including the "type of problems encountered in art; prior art solutions to those problems; rapidity with which innovations are made; sophistication of the technology; and educational level of active workers in the field." *Custom Accessories, Inc. v. Jeffrey-Allan Indus., Inc.*, 807 F.2d 955, 962 (Fed. Cir. 1986).

When interpreting a claim, the Court looks first to the intrinsic evidence of record, *i.e.* the patent itself, including the specification and the claims, as well as the prosecution history. *See Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). "Such intrinsic evidence is the most significant source of the legally operative meaning of disputed claim language." *Id.* A Court may not rely on extrinsic evidence, such as expert testimony, when such intrinsic evidence is sufficient to construe the meaning of a claim term. *See id.* The Federal Circuit has stated that the patent specification is the most important source of evidence when construing patent claims. *See*

Phillips, 415 F.3d at 1315 (stating that a patent specification "[u]sually is dispositive; it is the single best guide to the meaning of a disputed term.").

IV. PROPOSED INTERPRETATION OF DISPUTED CLAIM TERMS

A. "co-crystal" ('344 Patent, Claim 10)

Plaintiffs' Construction	Novartis's Construction
"A multiple-component, single crystalline phase, having a fixed stoichiometry of its component compounds"	"a crystalline solid containing more than one molecular component (at least one API and at least one co-former) comprising stoichiometric, non-covalent interactions between chemical functionalities of the molecular components, where the crystalline solid is not a salt (i.e., a solid comprising cations and anions)"

The term "co-crystal" is not expressly defined in the '344 Patent or its file history. To skilled artisans working in the field of the invention in 2002-03, and even today, the term is broadly understood to have multiple meanings. *See* Ex. B, Childs Tr., at 59:19-60:4; Ex. C, Rogers Tr., at 20:22-23:23. Therefore, the meaning to be ascribed the term should be guided by the intrinsic record. *See Vitronics Corp.*, 90 F.3d at 1582 ("[I]ntrinsic evidence is the most significant source of the legally operative meaning of disputed claim language.").

Plaintiffs' construction is consistent with the intrinsic record. First, a "co-crystal" is a "multiple-component" object. The specification of the Asserted Patent describes the claimed invention as "multiple component solids, such as multiple-component crystal," a "multiple-component phase composition," and "multiple-component solid phases, such as multiple-component crystals[.]" Ex. A, '344 Patent, at 3:19-26, 5:6-11, 7:19-22. Thus, a multiple-component crystal is a type of multiple-component phase composition.

Second, a "co-crystal" is a "single crystalline phase, having a fixed stoichiometry of its component compounds." In the context of the Asserted Patent, a "multiple-component phase" is "any solid material (phase) that is sustained by intermolecular interactions between at least two independent molecular entities, *in any stoichiometric ratio*, wherein at least one of the independent molecular entities is a pharmaceutical entity." *Id.* at 9:10-15 (emphasis added); *see also* Ex. D, '956

Application File History, at UM00014729 ("By definition, and as presently claimed, a co-crystal being a single crystalline entity, has a fixed stoichiometry of component molecules."). Plaintiffs' proposed construction of co-crystal thus accounts for the required elements of a multiple-component phase having multiple (i.e. two or more) component compounds (i.e. molecular entities) with a fixed stoichiometric ratio in a crystalline phase (i.e. solid material phase). Novartis' claim construction expert agrees. *See* Ex. E, Rogers Decl., at 26, ¶ 65 ("I agree with Plaintiffs that a co-crystal is a crystalline phase that contains multiple components (more than one component) and that has a fixed stoichiometry (or ratio) of those components.").

Plaintiffs' proposed construction accurately captures how a POSITA would understand the term co-crystal in light of the intrinsic record. Novartis's proposed construction, however, goes further, requiring two additional elements—that at least one of the components in the co-crystal be a pharmaceutical entity and another a co-former, and that the co-crystal be sustained by "non-covalent interactions between chemical functionalities." While these additional elements Novartis proposes might make sense in the context in which the term co-crystal appears in Claim 10—which requires that the claimed co-crystal have "at least one active pharmaceutical ingredient (API)" and the components interact via an intermolecular interaction (i.e. hydrogen bond))—it is improper to include it in the *definition* co-crystal. *E.g., Phillips*, 415 F.3d at 1314 ("[T]he context in which a term is used in the asserted claim can be highly instructive. To take a simple example, the claim in this case refers to 'steel baffles,' which strongly implies that the term 'baffles' does not inherently mean objects made of steel."). The claimed invention relates to pharmaceutical co-crystals; a POSITA would understand "co-crystal" is broader than that. *See, e.g.*, Ex. F, Appeal Br., at UM00000550 (classifying pharmaceutical co-crystals as a type of co-crystal).

The parties' remaining dispute concerning the construction of co-crystal is essentially two-fold: (1) how to characterize the "component[s]" within the co-crystal and (2) to what extent the applicant disclaimed certain material(s) during the '344 Patent's prosecution history. Outside of those issues, the parties' proposed constructions differ only in form, not substance.

1. "Component Compound" More Accurately Captures the Components of a Co-Crystal as Opposed to Novartis's Term, "Molecular Components"

The parties agree that a "co-crystal," as that term is used in the '344 Patent, would have multiple components, but dispute whether those constituent components are "compounds" (as Plaintiffs contend) or if they are limited to molecules (as Novartis suggests). Plaintiffs' construction is more closely aligned with how a person of ordinary skill would understand the term.

The patent explains in the Background of the Invention section that the problem to which the invention is directed is improved molecular compounds in the pharmaceutical space. Ex. A,'344 Patent, 1:37-43 ("[T]he existence of more than one crystalline form of a given *molecular compound*, typically in the form of solvates, represents a problem and an opportunity. This is particularly true for the pharmaceutical industry.") (emphasis added); *id*. at 2:36-39. Thus, in the Brief Summary of the Invention the inventors describe a "design of new pharmaceutical phases that contain more than one *molecular component*"—as opposed to simply stating more than one *molecule*. *Id.* at 3:9-11 (emphasis added). Among the molecular components described in the specification is a pharmaceutical molecule, examples of which provided in the specification are chemical *compounds*—including carbamazepine, phenyloin, and acetaminophen. *See id.* at 3:14-19. The '344 Patent specification nowhere limits the components of the co-crystal just to molecules, nor does it say the components *cannot* be compounds. *See* Ex. C, Rogers Tr., at 140:23-141:24. In fact, the intrinsic record shows that persons of ordinary skill would have understood the components could be compounds. *See*, *e.g.*, Ex. F, '344 Patent File History, Appeal Br. at UM00000550 ("[P]harmaceutical cocrystals exploit the supramolecular chemistry of the API to create a new crystal form through formation of a multiple-component crystal that comprises of the API and a second *compound* or 'cocrystal former'[.]") (emphasis added); *id.* (defining cocrystal as "a multiple component crystalline formed in a stoichiometric ratio between two *compounds* that are crystalline solids under ambient conditions") (emphasis added); Ex. I, U.S. Patent No. 6,559,293 (Almarsson) at 9:24-28 (describing "co-crystals" consisting of topiramate salts "with other *compounds*, as well as with other salts or forms of topiramate") (emphasis added).

Plaintiffs' use of the term "component compound" to describe the co-crystal components more accurately captures the distinction that co-crystal components are molecular *entities*, not just molecules, and thus can include compounds. The specification consistently describes the co-crystal components as "molecular components" or "molecular entities." *See, e.g.*, Ex. A, '344 Patent, at 3:8-11; 4:62-67; 5:4-13; 8:49-54; 9:10-19. Here, the use of "molecular" serves as a descriptor to show the entities relate to or consist of molecules, not that it is limited to a single molecule alone. The specification confirms this understanding when stating that a pharmaceutical entity, which serves as a component in the co-crystal, also "include[s the] pharmaceutically acceptable salts of [that] pharmaceutical entity[.]" *Id.* at 9:10-15, 40-43. A person of ordinary skill in the art in 2002 would have had an understanding of what a co-crystal component would be—a "component compound" or "complete[, net-neutral] entity that can exist in nature independently and [is] formed from at least two pieces brought together." Ex. G, Childs Decl. at ¶¶ 31, 32. "For example, a molecule is a compound with atoms brought together by covalent bonds, and a simple salt of an API is an example of an ionic compound containing one kind of anion and one kind of cation, where the ions are brought together by the requirement of charge balance." *Id.* at ¶ 32. Indeed, the United States Patent and Trademark Office's Patent Trial and Appeal Board (PTAB), having considered the Asserted Patent's specification and prosecution history, understood the components of the co-crystal to be "compounds." *See*, *e.g.*, Ex. M, '344 Patent File History, Appeal Decision, at UM00000631 ("Appellants' invention involves forming a crystal by combining a pharmaceutically active *compound* with a second *compound*, termed a 'co-crystal former.'") (emphasis added).

Plaintiffs' use of the term "component compound," clarifies that a co-crystal component encompasses, for example, an API molecule, where more than one type of atom are brought together via covalent bonds, and the pharmaceutically-acceptable salt of that API molecule, where two ions, including the ionized API molecule, are brought together via ionic bond(s) and the ions' charges are balanced resulting in a net-neutral charge. *See* Ex. G, Childs Decl. at ¶ 32. In other words, the term "component compound" is a more inclusive term than "molecular component" or "molecular

entity," because it encompasses pharmaceutical entities and their pharmaceutically-acceptable salts as co-crystal components, as contemplated by the '344 Patent specification.

2. Not All Salts Were Given Up During Prosecution

There is no real argument whether the '344 Patent specification and claims include salts; they do. *See* Ex. C, Rogers Tr., 150:17-152:21; Ex. M, '344 Patent prosecution history, Appeal Decision, at UM00000632 ("The Specification explains further that a crystal co-former may include a functional group that is identical to a functional group on the pharmaceutical compounds also present in the two-component or multiple-component salt."). Indeed, the patentees intended for ions to be included in the claimed co-crystals. *See, e.g.*, Ex. A, '344 Patent, at 9:10-15, 40-43; *see also* Ex. F, '344 Patent File History, Appeal Br., at UM00000487 (describing figure showing "cocrystal structure, *e.g.,* a repeating array of molecules or ions in three dimensions"). A person of ordinary skill in the art would understand that what the inventors gave up in the prosecution history was a specific type of salt—"simple salts." The inventors did not give up *all* salts, as Novartis argues.

"[W]here the patentee has unequivocally disavowed a certain meaning to obtain his patent, the doctrine of prosecution disclaimer attaches and narrows the ordinary meaning of the claim congruent with the scope of the surrender." *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1324 (Fed. Cir. 2003) (emphasis added). In order to rise to the level of disavowal of claim scope, the statement must be "clear and unmistakable," and not "amenable to multiple reasonable interpretations." *CUPP Computing AS*, 53 F.4th at 1382; *see also Genuine Enabling Tech. LLC*, 29 F.4th at 1374 (reversing district court's determination of a broad disavowal where "the only disavowal of claim scope that is clear and unmistakable [was] disavowal of signals below the audio frequency spectrum").

Novartis says the inventors disavowed all salts by distinguishing their invention over certain prior art. That is not right. In order to understand what the inventors gave up, one has to look at the actual references the inventors were distinguishing when making the statements in the prosecution history that Novartis relies upon. During prosecution of the '344 Patent, the Examiner rejected then-pending claims in view of two prior art references: Huffman (U.S. Patent No. 3,664,858, Ex. H) and

Almarsson (U.S. Patent No. 6,559,293, Ex. I). The PTAB concluded the Huffman patent is not analogous art (meaning it cannot be the basis of a proper rejection) because it relates to heat-sensitive copy-sheet coatings, rather than the field of pharmaceutical arts. *See, e.g.,* Ex. M, Appeal Decision, at UM00000640. Even if it could be considered analogous art, the inventors told the examiner that "Huffman provides no teaching or suggestion to make co-crystals, as recited the present claims[,]" it "makes salts rather than cocrystals[,]" and that "one of ordinary skill in the art will readily appreciate that the amines disclosed in Huffman will deprotonate the carboxylic acids disclosed in Huffman to make salts" whereas "[t]he present claims recite co-crystals." *See, e.g.*, Ex. F, '344 Patent File History, Appeal Br., at UM00000490-91. Regarding Almarsson, the inventors stated that the passage the examiner cited to and relied upon in the rejection "relate[d] to the formation of salts, not crystals comprising at least one pharmaceutical ingredient (API) and a co-crystal former." *See*, *e.g.,* Ex. J, '956 Application File History, at UM00014282-285. But a POSITA would have understood the Huffman and Almarsson references disclose simple salts.

"A simple salt is formed by reacting two elements or molecules to form an ionic compound with a net neutral charge that cannot be further reduced to a less complex compound with a net neutral charge." Ex. G, Childs Decl. at ¶ 34. A POSITA also would know that, as a result, a simple salt can be a component of a co-crystal but cannot form a co-crystal on its own since its components are charged. *See id.* at ¶ 37. In other words, the components of a simple salt cannot serve as components of the co-crystal because they are charged. Those charges must be neutralized by another ion of equal and opposite charge. A POSITA would understand that a complex salt, on the other hand, is a type of salt that "has more than two different ions," permitting them to be "co-crystals." *Id.* at ¶¶ 34, 37. For example, a complex salt could be a co-crystal when component one is a simple salt (A^-B^+) and component two is also simple salt (C^-B^+) because there are three types of ions, and the two net-neutral simple salts serve as components of the co-crystal.

Co-crystals containing simple salts as components were known by those of skill in the art as of 2002/2003. *See, e.g.*, Ex. I, U.S. Patent No. 6,559,293 (Almarsson), at 9:24-32 (describing co-crystals having salts of topiramate "with other compounds, as well as with other salts or forms of

topiramate"). Indeed, in 1998, even Novartis' expert Dr. Rogers authored a paper titled "Molecular Tweezers and Pentameric Aggregates: Convergent Hydrogen-Bonded Self-Assembly of 2:1 and 2:3 *Cocrystals* of Phthalazine:Phthalic Acid" that describes a cocrystal containing two different component compounds: a simple salt comprised of a phthalic acid anion and phthalazine cation, and a neutral phthalic acid molecule. *See* Ex. N, Rogers Dep., Ex. 3, at 255, 260 (emphasis added). Similarly, in 1996, Dr. Rogers authored a paper describing a compound comprising a neutral trimesic acid molecule and three unique diethylammonium simple salts of trimesic acid anions as "effectively a cocrystal." Ex. K, Rogers Dep., Ex. 2, at 2214.

Read in context, a person of ordinary skill in the art in 2002/03 would have understood that the applicant's statements were distinguishing the claimed co-crystals from *simple* salts, not all "solid[s] containing cations and anions," which would include complex salts, as Novartis suggests. *See* Ex. G, Childs Decl. at ¶¶ 40-43. Almarsson describes binary, stoichiometric combinations of a base and an API acid (topiramate) (i.e. simple salts), that cannot be subdivided into two or more independent (net-neutral) component compounds. *See id.* at ¶ 41; *see also,* Ex. I, U.S. Patent No. 6,559,293, at (57), 6:5-8, 7:6-24, 14:28-44, 25:23-33:16. "Similarly, the salts described in Huffman are simple salts generated from the reaction of amines with aromatic hydroxy compounds or other acids" at least because the starting materials described therein have a difference in pKa value greater than three, thereby indicating proton transfer will occur. Ex. G, Childs Decl. at ¶ 42; *see also,* Ex. H, U.S. Patent No. 3,664,858, at 2:23, 3:1-5:47; cl. 1 (claiming combination of "*a* basic organic amino compound and *an* organic acid compound") (emphasis added).

Thus, when considered in view of the references about which the inventors' statements were made, a POSITA would know they were limited only to the specific types of salts described in those references—simple salts—not all solids comprising cations and anions. That is to say, a person of ordinary skill in the art would understand that "complex salts" are still encompassed in the definition of "co-crystal," making Novartis's exclusion of "all solids comprising cations and anions" inconsistent with the intrinsic record and a person of ordinary skill's understanding.

B. "co-former" / "the co-former" / "said co-former" ('344 Patent, Claim 10)

Plaintiffs' Construction	Novartis's Construction
"A co-crystal former i.e. a component compound of a co-crystal"	"molecular component of the co-crystal; for clarity, the terms "co-former," "the co-former" and "said co-former" describe the same molecular component having the same chemical formula"

The issue in dispute here largely is the same as the compound/molecule argument discussed above regarding the term co-crystal. The meaning of the term(s) "co-former" / "the co-former" / "said co-former" is clear on a review of the intrinsic record—a "co-former" is simply a co-crystal former, that is, a component compound of a co-crystal. Novartis improperly reads in limitations requiring the co-crystal former to be a "molecular component" of the co-crystal and that the co-crystal has the "same chemical formula," neither of which can be found in the intrinsic record.

Independent Claim 10 requires that the co-crystal being comprised of an API and a co-former. There are two additional limitations that bound the definition of a co-former: it must have a chemical functionality complementary to the API's chemical functionality via non-covalent hydrogen bonding, and it must be a solid at room temperature and pressure when it's in its pure form. The claim requires nothing further of the co-former, and the claim certainly does not limit the co-former to molecules. Thus, the plain reading of Claim 10 supports Plaintiffs' construction, not Novartis' construction.

Plaintiffs' construction is supported by the patent specification, too. First, there can be no dispute that the phrases "co-former"/ "the co-former" / "said co-former" refer to a co-crystal former. *See* Ex. A, '344 Patent, at Fig. 24, 3:19-26, 4:10-12, 4:28-30, 7:59-61, 8:10-12, 8:29-31, 8:32-35. Second, a "co-former" is a component compound of a co-crystal, for the same reasons as explained above. *See supra*, §IV.A.1. The '344 Patent describes its invention as containing "multiple-component crystals" which comprise, among other things, co-formers:

> Multiple-component solids, such as multiple-component crystals, containing these pharmaceutical ingredients and complementary molecules (*hereafter referred to as "co-crystal formers"*) have been characterized by various techniques and can exhibit

> physical and/or chemical properties that are the same or different from the parent pharmaceutical ingredient as a direct result of alternative molecular recognition patterns.

Ex. A, '344 Patent, at 3:19-26. Figure 24 further supports that the described "multiple component crystals" comprise co-formers. *Id.* at Fig. 24 (noting that "multiple component crystals with the API and one or one cocrystal formers" are prepared using various methods of preparation, including crystallization from solution). As exemplary embodiments, "[t]he identified co-crystal formers can be, for example, a different API, a GRAS compound, a food additive, a low toxicity organic, or a metal-ion complex." *Id.* at 8:35-38.

Novartis's alternative construction adds the limitation "the same molecular component having the same chemical formula"—language that is not supported by the specification. This introduction of a new claim limitation devoid of intrinsic support is improper and contrary to how a person of ordinary skill in the art would understand the claim. As Plaintiffs' expert, Dr. Childs explained, a person of ordinary skill in the art would understand that "[t]he claims require that the API have a first chemical functionality that non-covalently hydrogen bonds to the second chemical functionality of the coformer. *See*, *e.g.*, [*id.* at] claim 10. Nothing in the claim excludes other interactions the API and coformer may have with other components of the crystal structure." Ex. G, Childs Decl. at ¶ 47. This is evident from the patent specification itself which recognizes that the term "API" may include pharmaceutically acceptable salts or ions of the API:

> As used herein, these pharmaceutical entities are intended to include pharmaceutically acceptable salts of a given pharmaceutical entity that retain all or a portion of their pharmaceutical activity. Pharmaceutical molecules or ions are inherently predisposed for such crystal engineering studies since they already contain molecular recognition sites that bind selectively to biomolecules, and they are prone to supramolecular self-assembly.

Ex. A, '344 Patent, at 9:40-47. "The above passage reflects that the 'API' or 'coformer' encompasses not only the pharmaceutically acceptable salt version of the pharmaceutical entity (or API) but also pharmaceutical ions which may result from the transfer of a proton generating the pharmaceutically acceptable salt." Ex. G, Childs Decl. at ¶ 49. As Dr. Childs agreed, the term

"coformer" is, therefore, not limited to having the "same chemical formula" as Novartis's proposed construction requires. *Id.*

C. "API homosynthons" ('344 Patent, Claim 10)

Plaintiffs' Construction	Novartis's Construction
"Synthons formed between identical and complementary chemical functionalities of the API"	"synthons formed between identical and complementary chemical functionalities of the API[3]"

The parties' dispute concerning the term "API homosynthons" arises from the parties' dispute concerning the term "compl[e]mentary," which appears in both parties' constructions. The parties' dispute regarding "API homosynthons" will therefore be resolved by the Court's construction of "compl[e]mentary." *See infra*, § IV.D.

D. "compl[e]mentary" ('344 Patent, Claim 10)

Plaintiffs' Construction	Novartis's Construction
"Plain and ordinary meaning of complementary, which is corresponding geometry/shape and molecular recognition that allows for interaction"	"[chemical functionalities] that, from the perspectives of geometry/shape and molecular recognition, can and do in fact interact [with one another] under certain conditions"

Plaintiffs' proposed construction of the term "compl[e]mentary" is supported by the intrinsic evidence. The patent says Figure 24 "shows an exemplified scheme for preparing multi-component phase compositions of the subject invention." Ex. A, '344 Patent, 7:13-15. In Step 2 of Figure 24, the specification teaches that chemical functionalities in the API are "suitable" if they are "complementary from the perspectives of geometry/shape and molecular recognition." Plaintiffs' proposed construction was derived directly from the definition of complementary provided in Figure 24.

[3] "Novartis understands that the only dispute between the parties with respect to the claim construction of 'API homosynthons' is the proper meaning of 'complementary' that appears therein. Novartis further understands that the Court's construction of the term 'compl[e]mentary [chemical functionalities]' / 'compl[e]mentary' will resolve the dispute regarding the construction of 'API homosynthons.'" D.I. 73-1 (Ex. A to Joint Claim Construction and Prehearing Statement) at 6, n.2.

The prosecution history also supports Plaintiffs' proposed construction. For example, Plaintiffs responded to an Office Action by clarifying that the invention "relates to the application of the concepts of crystal engineering towards the design of new pharmaceutical phases. In terms of superstructure, there are three likely ways in which a drug molecule *might interact* with another molecule: Binary compounds in which superstructure is generated by two or more molecules, both of which are integral components of the network and complementary." Ex. J, '956 Application File History, Aug. 3, 2007 Affidavit, Ex. 2 at UM00014301 (emphasis added). This statement made by the inventors supports Plaintiffs' position that complementary simply means "allows for interaction."

Novartis's construction is wrong because it reads in the requirement that the claimed chemical functionalities "can *and do in fact* interact…." This additional requirement ignores the claim as a whole, which recites that the "supramolecular synthons *are formed*" between the first chemical functionality and second chemical functionality if and when additional limitations are met. Ex. A, '344 Patent, at cl. 10 (emphasis added). In other words, if "compl[e]mentary" means the chemical functionalities "do in fact interact" as Novartis's proposed construction requires, claim 10's requirement of "supramolecular synthons are formed" between the first and second chemical functionalities would be superfluous. Ignoring the surrounding claim language is a *no-no*. *See Huawei Techs., Co., Ltd. v. Samsung Elecs. Co., Ltd.*, No. 3:16-cv-02787-WHO, 2017 WL 7058419, at *16 (N.D. Cal. Aug. 31, 2017) (rejecting a proposed construction that "would ignore the surrounding claim language"); *Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1186 (Fed. Cir. 1998) ("The appropriate starting point ... is always with the language of the asserted claim itself."). Not only is it improper to ignore the surrounding claim language, but it is also improper to render claim language redundant or superfluous, as Novartis's proposed construction does. *See Mfg. Res. Int'l, Inc. v. Civiq Smartscapes, LLC*, No. 17-269-RGA, 2018 WL 4627661, at *5 (D. Del. Sept. 27, 2018) (rejecting a proposed construction that "create[d] redundant limitations"); *Wasica Finance GmbH v. Continental Auto. Sys., Inc.*, 853 F.3d 1272, 1288 n.10 (Fed. Cir. 2017) ("It is highly disfavored to construe terms in a way that renders them void, meaningless, or superfluous.");

Mformation Techs., Inc. v. Rsch. in Motion Ltd., 764 F.3d 1392, 1399 (Fed. Cir. 2014) (favoring a construction that does not render another limitation "superfluous").

Novartis's construction is also improper because it reads in a limitation that is not supported by the claim language. The claim language does not require that the chemical functionalities "do in fact interact." Reading in such a limitation from the specification into the claims is prohibited. *See Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 904 (Fed. Cir. 2004) ("[I]t is improper to read a limitation from the specification into the claims.").

Finally, through the addition of the qualifying language "under certain conditions," Novartis's proposed construction injects ambiguity into the claim where none actually exists. This proposed construction is unhelpful and provides no insight as to what "certain conditions" are being referred to, and the language "certain conditions" appears nowhere in the specification. Given the ambiguity Novartis's proposed construction seeks to introduce into the claim, Novartis's proposed construction should be rejected. *See Mfg. Res. Int'l, Inc.*, 2018 WL 4627661, at *4 (refusing to adopt a construction that inserts more ambiguity than clarity into the claim term).

E. "compl[e]mentary [chemical functionalities]"[4] ('344 Patent)

Plaintiffs' Construction	Novartis's Construction
"No additional construction necessary, beyond the construction of 'compl[e]mentary' discussed above."	"[chemical functionalities] that, from the perspectives of geometry/shape and molecular recognition, can and do in fact interact [with one another] under certain conditions"

The term "compl[e]mentary [chemical functionalities]" is not a claim limitation, and construction of this term is improper. Claim 10 of the '344 Patent claims a co-former that "has a second chemical functionality compl[e]mentary to the first chemical functionality…." *See* Ex. A, '344 Patent, at cl. 10. The Asserted Claims do not contain the term "compl[e]mentary [chemical functionalities]," and Dr. Rogers' argument that construing this longer term provides additional

[4] Plaintiffs believe it is improper to construe the term "compl[e]mentary [chemical functionalities]" because it is not a claim term.

relevant context, Ex. E, Rogers Decl., at ¶ 81, is unavailing because tying the term "compl[e]mentary" to "chemical functionalities" is improper according to the claim language. The parties' argument regarding "compl[e]mentary [chemical functionalities]" is therefore confined to their argument regarding the term "compl[e]mentary," as discussed above in § IV.D.

F. "heterosynthon dimer" ('344 Patent, Claim 11)

Plaintiffs' Construction	Novartis's Construction
"A synthon formed by two different, yet complementary chemical functionalities"	"synthon formed by two different, yet complementary chemical functionalities[5]"

The parties' dispute concerning the term "heterosynthon dimer" arises from the parties' dispute concerning the term "compl[e]mentary," which appears in both parties' constructions. The parties' dispute regarding "heterosynthon dimer" will therefore be resolved by the Court's construction of "compl[e]mentary." The parties' dispute regarding "compl[e]mentary" is discussed in § IV.D.

G. "permits formation of" ('344 Patent, Claim 10)

Plaintiffs' Construction	Novartis's Construction
"can form"	"can and does in fact form under certain conditions"

Plaintiffs' proposed construction stays true to the claim language and is well grounded in the intrinsic record. The claim language "permits formation of" in and of itself means "can form." The claim requirement that the first chemical functionality of the API "permits formation of API homosynthons" must mean that the API homosynthons are capable of being formed, but not actually are formed, as Novartis argues. Ex. A, '344 Patent, at cl. 10.

[5] "Novartis understands that the only dispute between the parties with respect to the claim construction of 'heterosynthon dimer' is the proper meaning of 'complementary' that appears therein. Novartis further understands that the Court's construction of the term 'compl[e]mentary [chemical functionalities]' / 'compl[e]mentary' will resolve the dispute regarding the construction of 'heterosynthon dimer.'" D.I. 73-1 (Ex. A to Joint Claim Construction and Prehearing Statement) at 9, n.5.

The specification confirms Plaintiffs' construction. The chemical functionality of groups commonly found in active pharmaceutical ingredients (APIs) "are capable of forming supramolecular synthons." *Id.* at 3:41-44, 3:51-56, 9:56-62. And the specification explicitly directs the selection of a chemical functionality that is "capable of forming supramolecular synthons" to practice the subject invention. *Id.* at 3:65-67, 4:8-10, 4:50-55, 7:56-59, 8:8-10. There can be no question that the specification describes that the API selected to practice the claimed invention is one that contains a chemical functionality that can form a supramolecular synthon of the API. Without the additional limitations of the claimed API (present elsewhere in claim 10), it is not a requirement that the synthon does in fact form, as Novartis proposes.

Novartis's construction is incorrect because its proposed construction *requiring* formation is not grounded in the claim language or the intrinsic evidence. First, Novartis ignores the plain and ordinary meaning of "permits" as "capable of" and instead suggests that "permits" means "requires." The claim term "permits formation of" is analogous to the accepted and well-understood claim terminology "capable of." Indeed, the specification describes just that. Ex. A, '344 Patent, at 3:41-44, 3:51-56, 3:65-67, 4:8-10, 4:50-55, 7:56-59, 8:8-10, 9:56-62. Courts have routinely found that such functional language is equivalent to reciting capability (not necessity). For example, in *TMI Products, Inc. v. Rosen Entertainment Systems, L.P.*, the Federal Circuit affirmed the lower court's construction of "the housing is structured to *permit selective access* to the input opening" to require that "the housing is structured to *be capable of moving between an accessible and inaccessible orientation*." 610 Fed. App'x 968, 971-72 (Fed. Cir. 2015) (emphasis added). Similarly, the Federal Circuit, in *Cobalt Boats, LLC v. Brunswick Corp.*, accepted its parties' treatment of "*capable of* being rotated 180[deg]" and "*configured to permit* rotation of said step 180[deg]" having the same meaning. 773 Fed. App'x 611, 613-14 (Fed. Cir. 2019) (emphasis added).

Second, Novartis's construction is wrong because it ignores the rest of the claim, which shows the applicants knew how to claim *actual* formation when they wanted to. Claim 10 says, for example, the supramolecular synthons "*are formed* via non-covalent hydrogen bonding" between the first chemical functionality and second chemical functionality when additional limitations are

met. Ex. A, '344 Patent, at cl. 10 (emphasis added). In other words, if "permits formation of" means an API homosynthon in fact is formed as Novartis's proposed construction requires, claim 10's requirement of "supramolecular synthons are formed" between the first and second chemical functionalities would be meaningless. Novartis's construction renders this limitation of claim 10 superfluous and therefore is incorrect. *See VirnetX Inc. v. Apple Inc.*, 792 F. App'x 796, 811 (Fed. Cir. 2019) (holding superfluous claim constructions are "strongly disfavored").

Novartis's expert, Dr. Rogers, makes the same error when he says Figure 24 requires supramolecular synthons to necessarily form. Ex. E, Rogers Decl., at ¶ 91. Yet, the specification discloses the process of "determining whether the API contains chemical functionalities *capable of* forming supramolecular synthons" and identifying a chemical functionality that will (not "does") form a supramolecular synthon. Ex. A, '344 Patent, at 4:17-23; Fig. 24 (emphasis added). Dr. Rogers describes this Step 2 in Figure 24 as requiring both the capability of the first chemical functionality to form a supramolecular synthon and the *actual formation* of a supramolecular synthon between the first chemical functionality and the second chemical functionality (as recited in the last limitation of claim 10). Ex. E, Rogers Decl., at ¶¶ 92-93. Dr. Rogers incorrectly encompasses the entirety of claim 10 into this limitation "permits formation of," rendering the later claim limitation meaningless and impermissibly superfluous.

Likewise, the prosecution history supports the distinction between these concepts of capability and actual formation. Namely, the applicants during prosecution of the parent application to the '344 Patent described the lack of disclosure in the prior art of both the capability of forming, and the actual formation of, such a homosynthon. Ex. L, '956 Application File History, Jan. 14, 2014 Amendment, at UM00017217. Here too, Dr. Rogers melds these two concepts, which are distinct and independently required by claim 10. Ex. E, Rogers Decl., at ¶¶ 92-93.

Third, Novartis's construction injects ambiguity into the claim where none exists. Novartis seeks to impart an additional limitation as a requirement that an API supramolecular synthon is necessarily formed under certain conditions. Novartis's proposed construction is unhelpful for a jury because it provides no insight as to those conditions and how a synthon is formed without

encompassing claim 10 in its entirety into this claim term. While Dr. Rogers attempts to tie those conditions to the remainder of the claim limitation—"wherein the API has a first chemical functionality that permits formation of API homosynthons . . . *when the API is in its pure form*," Ex. E, Roger Decl., at ¶¶ 95-97—this rationale does not resolve the ambiguity of Novartis's construction in light of the rest of the claim, which requires additional conditions and, again, independently recites the actual formation of the supramolecular synthon.

What is clear from the intrinsic evidence is that, based on the first chemical functional group of the API, a supramolecular synthon can be or is capable of being formed. Ex. A, '344 Patent, at 3:41-44, 3:51-56, 3:65-67, 4:8-10, 4:50-55, 7:56-59, 8:8-10, 9:56-62. Thus, to the extent Novartis's proposed construction of "permits formation of" requires the actual formation of the supramolecular synthon, this construction should be rejected as inconsistent with the plain language of the term and the specification. *See, e.g.*, *ERBE Elektromedizin GmbH v. Int'l Trade Comm'n*, 566 F.3d 1028, 1034 (Fed. Cir. 2009) ("We generally do not construe claim language to be inconsistent with the clear language of the specification.").

H. "active pharmaceutical ingredient (API)" / "the API" ('344 Patent, Claims 10, 11)

Plaintiffs' Construction	Novartis's Construction
"Plain and ordinary meaning, which is 'biologically active moiety having a therapeutic effect on a human or animal suffering from a given pathological condition, when administered in a given concentration'"	"biologically active moiety having a therapeutic effect on a human or animal suffering from a given pathological condition, when administered in a given concentration; for clarity, the terms 'active pharmaceutical ingredient (API)' and 'the API' describe the same molecular component having the same chemical formula"

As discussed above in Section IV.B, Novartis's proposed construction adds "the same molecular component having the same chemical formula" – language that appears nowhere in the specification – and is unsupported by the specification and a person of ordinary skill in the art's understanding. For the same reasons that insertion of this language in the construction of "coformer" is improper, this language is also improperly inserted into the construction of "active pharmaceutical ingredient (API) / the API." *See supra*, § IV.B.

I. "a second chemical functionality" / "the second chemical functionality" ('344 Patent, Claim 10)

Plaintiffs' Construction	Novartis's Construction
"No construction necessary; plain and ordinary meaning."	"for clarity, the terms 'a second chemical functionality' and 'the second chemical functionality' describe the same chemical functionality having the same chemical formula"

The terms "a second chemical functionality" / "the second chemical functionality" are understood in the context of the intrinsic record without further construction. Novartis seemingly does not dispute this because its proposed construction does not define "a second chemical functionality" or "the second chemical functionality" at all. Rather, Novartis seeks to insert the same "having the same chemical formula" language as it does for its constructions of "API" and "coformer." For all of the reasons discussed above in Section IV.B, insertion of such language is contrary to the disclosures of the specification and how a person of ordinary skill in the art would understand the term. *See, e.g.*, Ex. G, Childs Decl. at ¶ 50.

J. "carboxamide" ('344 Patent, Claims 10, 18)

Plaintiffs' Construction	Novartis's Construction
"No construction necessary; plain and ordinary meaning"	"-C(=O)NH_2"

Plaintiffs' proposed construction more appropriately encompasses a POSITA's understanding of what "carboxamide" means. A POSA would have understood "carboxamide" could mean: (1) RC(=O)NR_2 (where R is a carbon (C) or hydrogen (H)); or (2) –C(=O)NH_2. *See, e.g.*, Ex. E, Rogers Decl. at ¶¶ 124, 125 (citing to 1995 IUPAC Glossary); Ex. G, Childs Decl. at ¶¶ 54, 56 (referencing same). And nowhere does the 1995 IUPAC Glossary upon which both experts rely indicate that these definitions are mutually exclusive. *See* Ex. E, Rogers Decl., Ex. 18, at NPC-UNIV-028066715. Thus, a POSITA would understand the plain and ordinary meaning of "carboxamide" to include both definitions. Ex. C, Rogers Tr., at 216:14-21 ("Q. [Y]ou agree that a person of ordinary skill

in the art — a person — a chemist in 2002 would have understood that carboxamide can be used in two different ways? A. Yes, a chemist would have understood that."). A person of ordinary skill also would recognize that the inventors did not give up one of the two meanings of carboxamide. *Id*. at 218:18-219:7; Ex. Ex. G, Childs Decl., at ¶¶ 55,56.

Nevertheless, Novartis's construction wrongly limits the definition of "carboxamide" to only one of the two well-understood definitions. Specifically, Novartis's restriction of "carboxamide" to "–C(=O)NH_2" improperly limits the scope of the term to certain examples described in the specification which is improper. *See*, *e.g.*, *EPOS Techs. Ltd. v. Pegasus Techs. Ltd.*, 766 F.3d 1338, 1341 (Fed. Cir. 2014) ("[I]t is improper to read limitations from a preferred embodiment described in the specification – even if it is the only embodiment – into the claims absent a clear indication in the intrinsic record that the patentee intended the claims to be so limited.").

Although certain examples disclosed in the specification may support "-C(=O)NH_2", nothing the specification indicates the claimed carboxamide is *limited* to that singular definition alone. To the contrary, the specification discloses examples which meet both definitions of carboxamide. A POSITA would understand the first example disclosed in the specification describing a co-crystal with acetaminophen, *see* Ex. A, '344 patent, at 11:60-12:23, to be a carboxamide, despite satisfying only the "RC(=O)NR_2" definition. *See* Ex. E, Rogers Decl., at ¶ 130 ("[A] co-crystal including the API acetaminophen [ ] contains a RC(=O)NR_2 group but not a –C(=O)NH_2 group[.]"). Thus, Novartis's proposed construction is too restrictive and should not be adopted.

V. CONCLUSION

For the foregoing reasons, Plaintiffs respectfully request that their proposed constructions above be adopted in their entirety.

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Respectfully Submitted,

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