IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF WEST VIRGINIA

ACTELION PHARMACEUTICALS LTD.,

Plaintiff,

v. **CIVIL ACTION NO. 1:20CV110**
(Judge Keeley)

MYLAN PHARMACEUTICALS, INC.;

Defendant.

MEMORANDUM OPINION AND ORDER ADOPTING PLAINTIFF'S PROPOSED CLAIM CONSTRUCTION

This patent infringement case involves two United States Patents owned by Actelion Pharmaceuticals Ltd. ("Actelion"), U.S. Patent Nos. 8,318,802 (the "'802 patent") and 8,598,227 (the "'227 patent") (collectively, the "patents-in-suit") (Dkt. No. 1). The pharmaceutical composition and methods described in these patents are used to produce VELETRI®, a drug indicated for the treatment of pulmonary arterial hypertension (Dkt. No. 1 at 4).

The parties dispute the construction of one claim term: "a pH of 13 or higher." For the reasons that follow, the Court adopts Actelion's proposed construction of this term.

I. BACKGROUND

In this first-filed Hatch-Waxman suit, Actelion alleges that the defendant, Mylan Pharmaceuticals Inc. ("Mylan"), has infringed the patents-in-suit (Dkt. No. 1 at 5-7). Actelion holds approved New Drug Application No. 022260, under which the United States

Food and Drug Administration ("FDA") granted approval on June 27, 2008 for epoprostenol sodium for injection, eq. 1.5 mg/vial, and on June 28, 2012 for epoprostenol sodium for injection, eq. 0.5 mg/vial, both marketed in the United States under the trade name VELETRI®. (Dkt. No. 1 at 4). The patents-in-suit are listed in the FDA's Orange Book, Approved Drug Products with Therapeutic Equivalence Evaluations, for VELETRI®. Id. After receiving notice and certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) that Mylan had filed Abbreviated New Drug Application No. 213913, seeking FDA approval to manufacture and sell generic epoprostenol sodium for injection, 1.5 mg/vial and 0.5 mg/vial, Actelion sued Mylan for infringement. Id. at 5.

After the parties had briefed their respective positions as to how the Court should construe the disputed claim term in the patents-in-suit, the Court held a Markman hearing on August 11, 2021, (Dkt. No. 95). The matter is now ripe for decision.

II. LEGAL STANDARDS

The construction of patent claims is a matter of law governed by federal statutes and the decisions of the Supreme Court of the United States and the United States Court of Appeals for the Federal Circuit. See Markman v. Westview Instruments, Inc., 52 F.3d 967, 979 (Fed. Cir. 1995). When interpreting the meaning of a claim, a court may consider the context, the specification, and

the prosecution histories as intrinsic evidence. Id. (quoting Unique Concepts, Inc. v. Brown, 939 F.2d 1558, 1561 (Fed. Cir. 1991)). "It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." Phillips v. AWH Corp., 415 F.3d 1303, 1312 (Fed. Cir. 2005) (internal quotation marks omitted). The description of an invention in the claims, therefore, limits the scope of the invention. Id. "[T]here is no magic formula or catechism for conducting claim construction." Id. at 1324. Instead, the Court is free to attach the appropriate weight to appropriate sources "in light of the statutes and policies that inform patent law." Id.

"[T]he words of a claim are generally given their ordinary and customary meaning [which is] the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." Id. at 1312-13 (internal citations and quotation marks omitted). "[T]he ordinary meaning of a claim term is its meaning to the ordinary artisan after reading the entire patent." Id. at 1321 (citing Medrad, Inc. v. MRI Devices Corp., 401 F.3d 1313, 1319 (Fed. Cir. 2005) ("We cannot look at the ordinary meaning of the term ... in a vacuum. Rather, we must look

at the ordinary meaning in the context of the written description and the prosecution history.")

When construing patent claims, then, a court must consider the context of the entire patent, including both asserted and unasserted claims. Id. at 1314. Because a patent will ordinarily use patent terms consistently, "the usage of a term in one claim can often illuminate the meaning of the same term in other claims." Id. Accordingly, "[d]ifferences among claims" can provide insight into "understanding the meaning of particular claim terms," and "the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." Id. at 1314-15 (citing Liebel-Flarsheim Co. v. Medrad, Inc., 358 F.3d 898, 910 (Fed. Cir. 2004)).

Pursuant to 35 U.S.C. § 112(a), an inventor must use the patent specification to describe the claimed invention in "full, clear, concise, and exact terms." The patent specification therefore "is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996).

"[T]he specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would

otherwise possess. In such cases, the inventor's lexicography governs." Phillips, 415 F.3d at 1316. "Even when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." Hill-Rom Servs., Inc. v. Stryker Corp., 755 F.3d 1367, 1372 (Fed. Cir. 2014) (quoting Liebel-Flarsheim, 358 F.3d at 906) (internal quotation marks omitted).

Nevertheless, a court may not import a limitation into the claims from the specification. Phillips, 415 F.3d at 1323. The Federal Circuit has "repeatedly warned" against limiting the claims to the embodiments specifically described in the specification. Id. In other words, a court should not construe the patent claims as being limited to a single embodiment simply because the patent describes only one embodiment. Id. (citing Gemstar-TV Guide Int'l Inc. v. Int'l Trade Comm'n, 383 F.3d 1352, 1366 (Fed. Cir. 2004)).

A court "should also consider the patent's prosecution history, if it is in evidence." Markman, 52 F.3d at 980. The prosecution history, which is "intrinsic evidence," "consists of the complete record of the proceedings before the PTO [Patent and Trademark Office] and includes the prior art cited during the

examination of the patent." Phillips, 415 F.3d at 1317. "[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." Id.

"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 correction construction." Renishaw PLC v. Marposs Societa' per Azionio, 158 F.3d 1243, 1250 (Fed. Cir. 1998). It follows that "a claim interpretation that would exclude the inventor's device is rarely the correct interpretation." Osram GmbH v. Int'l Trade Comm'n, 505 F.3d 1351, 1358 (Fed. Cir. 2007) (quoting Modine Mfg. Co. v. U.S. Int'l Trade Comm'n, 75 F.3d 1545, 1550 (Fed. Cir. 1996)).

A court thus begins its analysis by looking to the "actual words of the claim," Becton, Dickinson and Co. v. Tyco Healthcare Group, LP, 616 F.3d 1249, 1254 (Fed. Cir. 2010), as well as the context in which the disputed term appears. Phillips, 415 F.3d at 1314. Patent claims come in two general forms, independent and dependent. 35 U.S.C. § 112(c). Independent claims do not refer to another claim of the patent and are read separately to determine their scope. Inamin, Ltd. v. Magnetar Tech. Corp., 623 F. Supp. 2d

1055, 1065 (C.D. Cal. 2009). Dependent claims, by contrast, refer to at least one other claim, include all of the limitations of the claim to which they refer, and specify a further limitation on that claim. 35 U.S.C. § 112(d); see also Monsanto Co. v. Syngenta Seeds, Inc., 503 F.3d 1352, 1357 (Fed. Cir. 2007).

With these legal principles in mind, the Court turns to the construction of the disputed term in the asserted claims of the patents-in-suit.

III. DISCUSSION

As a preliminary matter, the parties no longer contest a claim term that previously had been in dispute, that is, "adjusting the pH of the bulk solution to greater than 13," and agree that no further construction is needed (Dkt. No. 67). Turning to the disputed claim term, Actelion contends that it should be construed according to its plain and ordinary meaning, "i.e., a pH of 13, or a pH higher than 13." (Dkt. No. 56 at 1). Mylan agrees that this term should be construed according to its plain and ordinary meaning but proposes that this means "the bulk solution has a pH greater than or equal to 13, not less than 13, prior to lyophilization." Id.

A. The Claims

1. The '802 Patent

Independent claim 1 of the '802 patent reads:

> A lyophilized pharmaceutical composition comprising:
> (a) a unit dose of 0.5 mg or 1/5 mg of epoprostenol or a salt thereof;
> (b) arginine; and
> (c) sodium hydroxide,
> wherein said lyophilized pharmaceutical composition is (I) formed from a bulk solution having a pH of 13 or higher and (ii) capable of being reconstituted for intravenous administration with an intravenous fluid.

(Dkt. No. 63-4 at 18:45-54).

Independent claim 11 reads:

> A lyophilisate formed from a bulk solution comprising:
> (a) epropostenol or a salt thereof;
> (b) arginine;
> (c) sodium hydroxide; and
> (d) water,
> wherein the bulk solution has a pH of 13 or higher, and wherein said lyophilisate is capable of being reconstituted for intravenous administration with an intravenous fluid.

Id. at 19:13-20.

2. The '227 Patent

Independent claim 16 reads:

> A method for treating a patient suffering from a disease selected from the group consisting of cardiovascular disease, atherosclerosis, arteriosclerosis, congestive heart failure, angina pectoris, and hypertension, said method comprising the steps of (1) combining an intravenous fluid with an effective amount of a lyophilized pharmaceutical composition comprising:
> (a) a unit dose of 0.5 mg or 1.5 mg of epoprostenol or a salt thereof;
> (b) arginine; and
> (c) sodium hydroxide,
> wherein said lyophilized pharmaceutical composition is formed from a bulk solution having a pH of 13 or higher;

and (2) administering the resulting intravenous fluid of step (1) to a patient in need thereof.

Dkt. No. 63-5 at 19:40-54.

Independent claim 22 reads:

> A method for treating a patient suffering from a disease selected from the group consisting of cardiovascular disease or disorder, atherosclerosis, arteriosclerosis, congestive heart failure, angina pectoris, and hypertension, said method comprising the steps of (1) combining an intravenous fluid with an effective amount of a lyophilized pharmaceutical composition comprising:
> (a) a unit dose of 0.5 mg or 1.5 mg of epoprostenol or a salt thereof;
> (b) 50 mg of arginine;
> (c) Mannitol or sucrose; and
> (d) sodium hydroxide.
> wherein said lyophilized pharmaceutical composition is formed from a bulk solution having a pH of 13 or higher; and [sic] (2) [sic] and (2) administering the resulting intravenous fluid of step (1) to a patient in need thereof.

Id. at 20:3-19.

Independent claim 32 states:

> A method for treating a patient suffering from a disease selected from the group consisting of cardiovascular disease, atherosclerosis, arteriosclerosis, congestive heart failure, angina pectoris, and hypertension, said method comprising the steps of (1)(I) reconstituting an effective amount of a lyophilized pharmaceutical composition comprising:
> (a) a unit dose of 0.5 mg or 1.5 mg of epoprostenol or a salt thereof;
> (b) 50 mg of arginine;
> (c) Mannitol or sucrose; and
> (d) sodium hydroxide,
> in 5 mL [sic] of water for injection or 0.9% sodium chloride solution to form a reconstituted solution,

> wherein said lyophilized pharmaceutical composition is formed from a bulk solution having a pH of 13 or higher, (1)(ii) diluting the reconstituted solution of step (1)(I) with a second diluent to form a diluted solution; and (2) administering the resulting diluted solution of step (1)(ii) to a patient in need thereof.

Id. at 20:43-60.

Finally, independent claim 40 states:

> A method for treating a patient suffering from a disease selected from the group consisting of cardiovascular disease, atherosclerosis, arteriosclerosis, congestive heart failure, angina pectoris, and hypertension, said method comprising the steps of (1)(I) reconstituting an effective amount of a lyophilized pharmaceutical composition comprising:
> (a) a unit dose of 0.5 mg or 1.5 mg of epoprostenol or a salt thereof;
> (b) 50 mg of arginine;
> (c) Mannitol or sucrose; and
> (d) sodium hydroxide,
> in 5 mL [sic] of water for injection to form a reconstituted solution, wherein said lyophilized pharmaceutical composition is formed from a bulk solution having a pH of 13 or higher; (1)(ii) diluting the reconstituted solution of step (1)(I) with water for injection to form a diluted solution; and (2) administering the resulting diluted solution of step (1)(ii) to a patient in need thereof.

Id. at 21:10-27.

B. The Specification

The specification in the '802 patent provides in pertinent part:

> The present inventor has unexpectedly found that epoprostenol solution in the presence of an alkalinizing agent, and high pH (>11) is very stable compared to

> Flolan. Accordingly, one object of the present invention is to provide pharmaceutical compositions containing epoprostenol or a salt thereof, and at least one alkalizing agent at pH>11. The composition is characterized by improved stability upon reconstitution with commercially available intravenous (IV) fluids.
>
> ***
>
> The composition is preferably a lyophile produced by freeze drying (lyophilizing) a bulk solution containing epoprostenol, or a salt thereof, and arginine. The pH of the bulk solution is preferably adjusted to about 12.5-13.5, most preferably 13, by the addition of sodium hydroxide.
>
> ***
>
> The pH of the bulk solution is adjusted to >11 with sodium hydroxide prior to lyophilization. In another embodiment, the composition of the present composition contains epoprostenol (or a salt thereof, such as epoprostenol sodium), and arginine. The composition may also include a base. . . . The base is added so that the pH of the bulk solution is greater than 11, preferably greater than 12, and most preferably 13 or higher.
>
> ***
>
> In another embodiment . . . [t]he pH of the bulk solution is adjusted to 13.0 with the base.
>
> ***
>
> In the next stage of development, we screened several lyophilized formulations with the pH of bulk solution for lyophilization adjusted between 10.5 and 13 in the presence of different excipients. . . . As shown in the Table 8 above, the stability of epoprostenol is better at pH 13 compared to lower pH samples.
>
> ***

> As seen from the data above, epoprostenol is most stable in mannitol/arginine containing formulations when the pH of the bulk solution [is] adjusted to 13.

(Dkt. No. 63-4 at 4:8-15; 5:29-43; 6:63-7:5; 7:6-17; 10:62-11:55; 14:26-28).

C. Patent Prosecution History

Although the prosecution history of the '277 patent is not in evidence, the file history of the '802 patent is instructive because those two patents share a specification. See Capital Mach. Co. v. Miller Veneers, Inc., 524 Fed. App'x 644, 649 (Fed. Cir. 2013) ("We have held that the prosecution history regarding a claim term is pertinent when interpreting the same term in both later-issued and earlier-issued patents in the same family."). Pursuant to 35 U.S.C. §§ 112, 102, and 103, the Examiner initially rejected several claims of the '802 patent because the phrase, "wherein the composition is reconstituted, the pH of the reconstituted solution is greater than 11," lacked clarity and was indistinguishable from the prior art (Dkt. No. 62-4). In response, Actelion amended the claims so that the pH of the solution was "greater than 12," but the Examiner was still unpersuaded.

The claims eventually were allowed once Actelion amended the claims at issue to include the term "a pH of 13 or higher." According to the Examiner:

> Applicant has demonstrated unexpected results with respect to compositions made with solutions of pH 13 or higher as shown in tables 8 and 9 of the specification (example 4, paragraphs [0057-0058]). The stability of the composition is greatly increased when reconstituted versus compositions with a pH of 12 or lower. This is an unexpected result as the prior art does not teach pH of 13 as having advantages over pH 11 or 12.

Id.

D. Analysis

The central conflict involves the weight given to the integers used to express "a pH of 13 or higher," i.e., 13 or 13.0, in the patent specification. To give this term its ordinary meaning, the Court begins, as it must, with the language of the claims at issue. Prima Tek II, L.L.C. v. Polypap, S.A.R.L., 318 F.3d 1143, 1148 (Fed. Cir. 2003) ("Claim construction begins with the words of the claim."). In the claims at issue, Actelion consistently expressed "a pH of 13" with two significant figures. See Dkt. Nos. 63-4 at 18:45-54, 19:13-20; 63-5 at 19:40-54, 20:3-19, 20:43-60, 21:10-27. This claim language provides no basis for inferring any higher level of precision. Accordingly, under its conventional significant figure meaning, the term a "pH of 13" would ordinarily encompass those values that round up or down to 13, 12.5 to 13.4. Viskase Corp v. American Nat'l Can Co., 261 F.3d 1316, 1320 (Fed. Cir. 2007) (recognizing the "standard scientific convention" of significant figures).

But the Court must also read the claims at issue in view of both the written description and prosecution history. AstraZeneca AB v. Mylan Pharms. Inc., 19 F.4th 1325, 1330 (Fed. Cir. 2021). "On the one hand, claims 'must be read in view of the specification, of which they are a part.'" Liebel-Flarsheim Co. v. Medrad, Inc., 358 F.3d 898, 904 (Fed. Cir. 2004) (quoting Markman v. Westview Instruments, Inc., 52 F.3d 967, 979 (Fed. Cir. 1995). On the other hand, "there is sometimes a fine line between reading a claim in light of the specification, and reading a limitation into the claim from the specification." Comark Comm'ns, Inc. v. Harris Corp, 156 F.3d 1182, 1186-87 (Fed. Cir. 1998); accord Anchor Wall Sys., Inc. v. Rockwood Retaining Walls, Inc., 340 F.3d 1298, 1307 (Fed. Cir. 2003). As the Federal Circuit has explained, "an inherent tension exists as to whether a statement is a clear lexicographic definition or a description of a preferred embodiment. The problem is to interpret claims 'in view of the specification' without unnecessarily importing limitations from the specification into the claims." E-Pass Techs., Inc. v. 3Com Corp., 343 F.3d 1364, 1369 (Fed. Cir. 2003).

Here, within the specification, Actelion expressed pH and, specifically, "a pH of 13," with varying degrees of precision. For example, it used two significant figures to the describe the invention's significantly high degree of acidity and to compare

the pH of the invention with the pH of the early invented product, Flolan. See Dkt. No. 63-4 at 4:39-40 ("the present epoprostenol formulation is administered at a high pH (>11)"), and Dkt. No. 63-4 at 4:9-10 ("The present inventor has unexpectedly found that epoprostenol solution in the presence of an alkalizing agent, and high pH (>11) is very stable compared to Flolan."). Actelion further reported that its prototype formulations used for batch testing were created from a bulk solution "with the pH . . . adjusted to 13." Id. at 11:58-12:34.

But Actelion also stated pH to three significant figures within the specification, such as to express the pH of the bulk solutions used in other experiments: to test the stability of Flolan, it "adjusted the pH of the diluent to 10.5," Id. at 8:3-5, Example 1; to measure the stability of epoprostenol with arginine, it adjusted the pH of the bulk solutions to 11.9, 11.2, and 13.0, Id. at Example 2; and, to measure the stability of the reconstituted lyophile, "the pH of the solution containing epoprostenol and arginine was adjusted to 13.0 with sodium hydroxide, and lyophilized," Id. at 9:50-57, Example 3. Moreover, Actelion demonstrated in the specification that it could measure the pH of the bulk solution with increased precision, up to four significant figures. See Id. at Tables 19, 21, 27, and 29

(recording results of testing conducted with bulk solutions having pH values of 11.58, 11.55, 11.63).

Notably, when describing the preferred embodiment of its invention, Actelion expressed the pH of the bulk solution with both two and three significant figures. See e.g., Id. at 5:41-43 ("The pH of the bulk solution is preferably adjusted to about 12.5-13.5, most preferably 13, by the addition of sodium hydroxide."); id. at 5:35-38 ("Preferably, the base is added so that the pH of the bulk solution is greater than 11, preferably greater than 12, and most preferably greater than 13."); id. at 7:16-17 ("The pH of the bulk solution is adjusted to 13.0 with a base."). Actelion also used mixed references to describe the pH of the reconstituted solution. Id. at 7:26-31 ("When reconstituted and/or diluted, the pH of the reconstituted solution is greater than about 11, preferably greater than about 11.3, more preferably greater than about 11.5, and most preferably greater than about 11.8.").

"[W]hen a patentee uses a claim term throughout the entire patent specification, in a manner consistent with only a single meaning, he has defined that term 'by implication.'" Bell Atl. Network Servs., Inc. v. Covad Commc'ns Grp., Inc., 262 F.3d 1258, 1271 (Fed. Cir. 2001) (citing Vitronics, 90 F.3d at 1582). But, here, Actelion did not consistently use any particular numerical convention to express "a pH of 13." Thus, there is nothing to

indicate that Actelion intended to import any higher degree of precision to "a pH of 13" as it is articulated in the claims at issue and the Court must avoid reading additional limitations not explicitly intended by Actelion from the patent specification into the claim terms.

Likewise, the Court is unpersuaded that the prosecution history requires it to read an increased degree of precision into the claim language. The file history of the '802 patent clearly shows that Actelion retreated from "a pH of greater than 11" to "a pH of greater than 12" and, ultimately, to "a pH of 13 or higher." Nevertheless, Actelion and the Examiner consistently expressed the pH value of the bulk solution with two significant figures. In the "Reasons for Allowance," the Examiner explained that Actelion "ha[d] demonstrated unexpected results with respect to compositions made with solutions of pH 13 or higher as shown in tables 8 and 9 of the specification . . . The stability of the composition is greatly increased when reconstituted versus compositions with a pH of 12 or lower." (Dkt. No. 63-4 at 17). Importantly, in Tables 8 and 9, the pH value of 13 is reported with only two significant figures. Therefore, it is evident from the patent prosecution that, although pH values of 11 and 12 were not allowable, a pH of "13 or higher" was allowable, with no reservation further narrowing this pH value or expressing it with

increased precision. Furthermore, Actelion's change in language during the amendment process, from "greater than 11" and "greater than 12" to "13 or higher" indicates that it understood the phrases "greater than 13" and "13 or higher" to carry different meanings. While the first draws a line in the sand forfeiting any value below 13, the second leaves that door open to rounding.

According to Mylan, the specification lists three contenders for "13," those being "13," "13.0," and "13.00." Although "13" is found both in the claim terms and throughout the specification, Mylan contends that only "13.0" and/or "13.00" remain after Actelion's apparent disavowal of any pH lower than 13, and the handful of references to "13.0" and "13.00" in the specification, most of which deal with data. But neither the prosecution history, nor the specification's variations in expressing "a pH of 13," constitute the disavowal necessary to support Mylan's argument that Actelion abandoned pH values between 12.5 and 13.

The words of a claim are not given their ordinary and customary meaning only if (1) the patentee sets out a definition and acts as his own lexicographer, or (2) the patentee "disavows the full scope of a claim term either in the specification or during prosecution." Thorner v. Sony Computer Entertainment America LLC, 669 F.3d 1362, 1365 (Fed. Cir. 2012) (citing Vitronics, 90 F.3d at 1580. Pertinent here is the "exacting"

standard for disavowal of claim scope. Thorner, 669 F.3d at 1366. "Where the specification makes clear that the invention does not include a particular feature, that feature is deemed to be outside the reach of the claims of the patent, even though the language of the claims, read without reference to the specification, might be considered broad enough to encompass the feature in question." SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc., 242 F.3d 1337, 1341 (Fed. Cir. 2001). "The patentee may demonstrate intent to deviate from the ordinary and accustomed meaning of a claim term by including in the specification expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope." Teleflex, Inc. v. Ficosa N. Am. Corp., 299 F.3d 1313, 1325 (Fed. Cir. 2002); see also Home Diagnostics, Inc. v. LifeScan, Inc., 381 F.3d 1352, 1358 (Fed. Cir. 2004) ("Absent a clear disavowal in the specification or prosecution history, the patentee is entitled to the full scope of its claim language.").

Here, Actelion did not manifestly restrict the scope of the term "a pH of 13 or higher" to exclude those values between 12.5 and 13. Accordingly, the Court declines Mylan's invitation to choose which iteration of "13" it apparently believes is the most correct based on the specification and prosecution history, and will not construe the term as if it had been written with increased precision.

Finally, the Court notes that both parties invoke the Federal Circuit's holding in AstraZeneca AB v. Mylan Pharm., Inc., 19 F.4th 1325 (Fed. Cir. 2021), in support of their construction. In AstraZeneca, this Court construed the claim term, 0.001% of PVP, to mean "0.001% within one significant figure (encompassing a concentration of PVP in the range of 0.0005% to 0.0014%)." AstraZeneca AB v. Mylan Pharm., Inc., 2020 WL 4670401 at * 7 (N.D.W. Va. Aug. 12, 2020). The Federal Circuit subsequently vacated this construction. AstraZeneca, 19 F.4th at 1329.

The Federal Circuit recognized that 0.001%, expressed with one significant figure, would ordinarily encompass a range from 0.0005 to 0.0014%, but found that intrinsic evidence impacted the term's plain and ordinary meaning. Id. at 1335. The specification had emphasized the importance of the increased stability of the new compound to the claimed invention and "testing evidence in the written description and prosecution history show[ed] that very minor differences in the concentration of PVP—down to the ten thousandth of a percentage (fourth decimal place)—impact stability." Id. at 1330. The prosecution history also established that AstraZeneca had made significant amendments to the PVP concentration during patent prosecution. Id. at 1332-33. Thus, "taken as a whole, the intrinsic record support[ed] a narrower construction of 0.001%," and "[t]o reflect the level of exactness

the inventors used in the written description," the Federal Circuit construed 0.001% of PVP "as that precise number with only minor variations, i.e., 0.00065% to 0.00104%." Id. at 1330.

Unlike AstraZeneca, the intrinsic record in this case does not support a narrower construction of the disputed claim term because neither the specification nor prosecution history demonstrates that the inventor intended to employ a more precise level of exactness for the term "a pH of 13 of higher." First, in AstraZeneca, the test results in the specification demonstrated that slightly different concentrations of PVP greatly impacted the stability of the product. AstraZeneca, 19 F.4th at 1333. For example, a formulation with a PVP concentration of 0.0005%, a concentration that would have been encompassed by 0.001% had the ordinary rules of rounding applied, was much more unstable when compared to a formulation with a PVP concentration of exactly 0.001%. Id.

But, here, the specification does not indicate that slight variations in pH would undermine the product. The specification includes data from Actelion's testing to compare the stability of the products when made from bulk solutions with pH values of 10.5, 11, 12, and 13. Dkt. No. 63-4 at Tables 8 and 9. While this testing showed that "the stability of epoprostenol is better at pH 13 compared to lower pH samples," it did not indicate that slight

variations of pH ranges, such as those that would fall within "a pH of 13" under the ordinary rules of rounding, 12.5-13.4, would greatly impact the stability of the product. In point of fact, the specification's description of the preferred embodiment indicates that these ranges also would create a stable product. Specifically, it states that the product would be derived from a bulk solution with a pH "greater than 11, preferably greater than 12, and most preferably greater than 13," id. at 5:35-38, and that "[t]he pH of the bulk solution is preferably adjusted to about 12.5-13.5, most preferably 13. . . .", id. at 5:41-43.

Second, unlike AstraZeneca, the intrinsic record does not demonstrate that Actelion disavowed pH values below 13 during patent prosecution. In AstraZeneca, amendments to the disputed claim term during the patent prosecution included exchanging a range of PVP concentration for the exact 0.001% value, eliminating the term "about" before the PVP concentration, and citing to testing establishing that variations in the PVP concentration to the fourth significant digit impacted the invention's stability. AstraZeneca, 19 F.4th at 1333-34. Here, however, Actelion did not forgo a pH range for an exact pH value; nor did it define the disputed term with more precision during patent prosecution. Nothing in the file history indicates that Actelion intended to

use a more exacting level of measurement or to forfeit the use of ordinary rounding rules.

Therefore, after considering the claims, the entirety of the specifications of the patents-in-suit, and the prosecution history of the '802 patent, to determine the proper construction of the challenged claim term, the Court concludes that Actelion's proposed construction, specifically, that "a pH of 13 or higher" is to be construed in accordance with its plain language, is correct.

IV. CONCLUSION

The Court **ADOPTS** Actelion's proposed construction of "a pH of 13 or higher" and **CONSTRUES** it consistent with its plain and ordinary meaning, that is, a pH of 13, or a pH higher than 13.

It is so **ORDERED.**

The Clerk **SHALL** transmit copies of this Order to counsel of record.

DATED: February 14, 2022

/s/ Irene M. Keeley
IRENE M. KEELEY
UNITED STATES DISTRICT JUDGE