

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

UNITED THERAPEUTICS
CORPORATION,

Plaintiff,

v.

LIQUIDIA TECHNOLOGIES, INC.,

Defendant.

C.A. No.: 1:20-cv-00755-RGA

HIGHLY CONFIDENTIAL

SUPPLEMENTAL DECLARATION OF ROBERT R. RUFFOLO, PH.D.

I, Robert R. Ruffolo, Ph.D., declare as follows:

1. I have been retained by counsel for United Therapeutics Corporation (“UTC”) as an expert consultant to UTC, Plaintiff in the above-captioned litigation.

2. I submitted a declaration (“Opening Declaration”) in support of UTC’s Opening Claim Construction Brief with Respect to U.S. Patent Nos. 9,593,066 and 9,604,901, which was dated February 5, 2021.

3. In my Opening Declaration, I set forth my opinion that a POSA would understand the plain and ordinary meaning of the claim term “contacting the solution comprising treprostinil from step (b) with a base to form a salt of treprostinil” that appears in claims 1 and 8 of the ’901 patent, and that this term is not given any special meaning or definition. *See* Opening Declaration, ¶¶ 94-96.

4. I have reviewed Liquidia’s Answering Claim Construction Brief, in which Liquidia contends that (i) statements by UTC in *Inter Partes* Review (“IPR”) proceedings before the Patent Trial and Appeal Board (“PTAB”) require a departure from plain and ordinary meaning according to its proposed construction: “contacting the solution comprising treprostinil from step (b) with a base to form a salt of treprostinil, wherein the salt is formed without isolation of treprostinil after alkylation and hydrolysis”; and (ii) that it “provided UTC with

documentary evidence that tadalafil in Liquidia’s LIQ861 is isolated prior to salt formation and cannot infringe.” See Liquidia’s Answering Claim Construction Brief (“Resp. Br.”) at 21-24 (citing to Exs.¹ 7-9, 28) (emphasis omitted).

5. As explained below, I do not agree that a POSA would understand the statements on which Liquidia relies to require a departure from plain and ordinary meaning according to Liquidia’s proposed construction. Furthermore, Liquidia’s proposed construction would exclude a preferred embodiment, and would thus be inconsistent with a POSA’s understanding of the ’901 patent specification, prosecution history and IPR proceedings.

6. This declaration is intended to supplement (not replace) my Opening Declaration; my relevant background and qualifications may be found in my Opening Declaration (¶¶ 3-29) and accompanying exhibits thereto.

I. SUMMARY OF OPINIONS

7. It is my opinion that the following terms from the ’066 and ’901 patents should have the following constructions:

Claim Term	Patent(s) and Claims	Construction
“a process”	’066 patent, claims 1 and 8	plain and ordinary meaning
“ambient temperature”	’066 patent, claims 6 and 8; ’901 patent, claim 6	plain and ordinary meaning
“stored” / “storing” / “storage”	’066 patent, claims 6 and 8; ’901 patent, claim 6	“require that the stored material possesses stability sufficient to allow manufacture and which maintains integrity for a sufficient period of time to be useful for the preparation of a pharmaceutical composition or a pharmaceutical product”
“pharmaceutical batch”	’901 patent, claims 1-4, 6, and 8	“a specific quantity of tadalafil (or its salt) that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture,

¹ “Ex.” refers to the exhibits attached to the Declaration of Douglas W. Cheek in Support of Defendant’s Answering Claim Construction brief unless otherwise noted.

Claim Term	Patent(s) and Claims	Construction
		wherein the uniform character and quality is such that it still contains impurities resulting from the method by which it is produced”
“contacting the solution comprising treprostinil from step (b) with a base to form a salt of treprostinil”	’901 patent, claims 1 and 8	plain and ordinary meaning

II. LEGAL STANDARDS

8. As set forth in my Opening Declaration, I understand that the meaning of claim terms is a legal issue for the court to decide. I also understand that the court determines the meaning of the claims based on the perspective of a person of ordinary skill in the art (“POSA”) as of the filing date of the patent application. I also understand that the court relies on the claims, patent specification and prosecution history of the patent to determine the meaning of the claim terms. I also understand that the court can consider expert testimony regarding how a POSA would understand the claim terms in view of the claims, patent specification and prosecution history. In this declaration, I offer my opinions about how a POSA would have understood the meaning of the claim terms in view of the claims, patent specification and prosecution history, as well as the IPR proceedings cited by Liquidia.

9. I understand that Liquidia has argued that “UTC’s statements amount to a clear and unmistakable acknowledgement that the claims of the ’901 patent do not permit isolation of treprostinil prior to salt formation.” Resp. Br. at 21. I understand from counsel that claim scope is not disavowed unless the patentee clearly and unambiguously surrenders it. I understand that the standard for finding disavowal has been described as “exacting” and that courts consider a POSA’s understanding after reading the claims, specification and prosecution history.

III. POSA'S UNDERSTANDING OF THE CLAIM TERM

A. "contacting the solution comprising treprostinil from step (b) with a base to form a salt of treprostinil"

10. The claim term "contacting the solution comprising treprostinil from step (b) with a base to form a salt of treprostinil" appears in claims 1 and 8 of the '901 patent. The claims state:

- Claim 1: "A pharmaceutical batch consisting of treprostinil or a salt thereof and impurities resulting from (a) alkylating a benzindene triol, (b) hydrolyzing the product of step (a) to form a solution comprising treprostinil, (c) *contacting the solution comprising treprostinil from step (b) with a base to form a salt of treprostinil*, (d) isolating the salt of treprostinil, and (e) optionally reacting the salt of treprostinil with an acid to form treprostinil, and wherein the pharmaceutical batch contains at least 2.9 g of treprostinil or its salt." Ex. 2 at Claim 1 (emphasis added).
- Claim 8: "A method of preparing a pharmaceutical batch as claimed in claim 1, comprising (a) alkylating a benzindene triol, (b) hydrolyzing the product of step (a) to form a solution comprising treprostinil, (c) *contacting the solution comprising treprostinil from step (b) with a base to form a salt of treprostinil*, (d) isolating the salt of treprostinil, and (e) optionally reacting the salt of treprostinil with an acid to form treprostinil." *Id.* at Claim 8 (emphasis added).

11. As discussed in my Opening Declaration (¶¶ 95-96), a POSA would understand this term according to its plain and ordinary meaning.

12. In its Responsive Brief, Liquidia cited to statements made in the context of an IPR concerning the '901 patent. These underlying IPR documents were attached to Liquidia's Brief as exhibit 7 (the Patent Owner's Preliminary Response), exhibit 8 (Rehearing Request), exhibit 9 (Patent Owner's Response), and exhibit 28 (Rehearing Request Denial). Liquidia relies on a handful of statements from these documents, which were not expert opinions, to contend that a POSA would understand the '901 patent claims to require an additional limitation

that is not recited in the claims. In my opinion, Liquidia's assertions are not consistent with how a POSA would understand the cited statements in their complete context, and in view of the patent claims, specification, prosecution history, and the training and knowledge of a POSA.

13. As an initial matter, Liquidia submitted no opinion from any expert in support of its Answering Brief in order to support its proposed construction.

14. Liquidia further ignores that a POSA reviewing documents filed in connection with the '901 proceedings would consider the declarations of Prof. Pinal, UTC's expert. Prof. Pinal's assessment is unambiguous. He states:

It is noteworthy that in Dr. Winkler's [Liquidia's expert in the IPR proceedings] analysis, opposite actions, such as isolating vs. not isolating treprostinil, operate in the same direction. I note that this isolation limitation Dr. Winkler seems to try to be addressing is actually a limitation from the '066 patent—*not isolating the treprostinil before contacting it with a base is not an explicit limitation of claim 1 of the '901 patent.*

Ex 10, ¶157 (emphasis added). Liquidia's interpretations of attorney statements in the '901 IPR proceedings are not consistent with Prof. Pinal's unambiguous opinion concerning the '901 patent's claim scope, and they are not consistent with how a POSA would interpret those statements in their full context and in light of Prof. Pinal's opinion and the '901 patent specification and claims.

15. I disagree with a number of statements and assertions in Liquidia's Responsive Brief. For example, Liquidia cites to UTC's Patent Owner's Response as purportedly supporting its proposed construction that would require "contacting the solution comprising treprostinil from step (b) with a base to form a salt of treprostinil, wherein the salt is formed without isolation of treprostinil after alkylation and hydrolysis." The language on which Liquidia relies states:

Claim 1 requires "contacting the solution comprising treprostinil from step (b) with a base to form a salt of treprostinil." The claim's preamble requires the pharmaceutical batch be one "consisting of" what results from the recited steps. Together, this language means treprostinil is not isolated from the solution formed in step (b) before forming a salt in step (c). Just as in the '901 patent's Example 3 (reactor charged with treprostinil

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