EXHIBIT 30

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NEURELIS, INC.,	)	
	)	
Plaintiff,	)	
	)	
v.	)	C.A. No. 24-562 (MN)
	)	
PADAGIS LLC, PADAGIS US LLC and PADAGIS ISRAEL PHARMACEUTICALS LTD.,	)	
	)	
Defendants.	)	

DECLARATION OF MAUREEN DONOVAN, PH.D. IN SUPPORT OF DEFENDANTS' RESPONSIVE CLAIM CONSTRUCTION BRIEF

I. INTRODUCTION

1. I, Maureen Donovan, submit this declaration in support of Defendants' Responsive Claim Construction Brief submitted in the above-captioned proceeding. I have been retained in this matter by Polsinelli ("Counsel") on behalf of Padagis LLC, Padagis US LLC, and Padagis Israel Pharmaceuticals, Ltd (collectively "Padagis" or "Defendants"). I have been retained to provide my opinions on the meaning of certain claim language in U.S. Patent Nos. 8,895,546 ("the '546 patent"), 11,241,414 ("the '414 patent"), and 11,793,786 ("the '786 patent"), (collectively "the Asserted Patents") as of the earliest priority date of the Asserted Patents. I understand that Plaintiff Neurelis, Inc. ("Neurelis") contends that the earliest priority date of the Asserted Patents is March 2008, which appears to correlate with the filing of U.S. Provisional Pat. App. No. 61/040,558 filed March 28, 2008. I disagree, as it is my opinion that the earliest possible priority date for the Asserted Patents is the filing date of U.S. Pat. App. No. 12/413,439 ("the '439 application") on March 27, 2009. However, regardless of whether the earliest priority date for the Asserted Patents is determined to be March 2008 or March 2009, my opinions and analysis provided herein are the same.

2. I make this declaration based on my personal knowledge. I am over the age of 21 and am competent to make this declaration.

3. If called as a witness, I could competently testify to the truth of each statement herein.

4. I reserve the right to supplement or amend this declaration based on any new information that is received that is relevant to my opinions, including any additional claim construction briefing from or expert declarations on behalf of Neurelis Inc. ("Neurelis" or "Plaintiff").

5. I am being compensated for my time working on this case at my ordinary and customary rate of $685 per hour for all work performed on the case. My compensation is in no way contingent on the nature of my findings, the presentation of my findings in testimony, or the outcome of this or any other proceeding. I have no financial interest in this proceeding, and the potential for any future financial benefit is unaffected by the content of my testimony or the outcome of this proceeding.

II. BASIS FOR OPINIONS

6. In forming my opinion, I have relied on my own education, work experiences and knowledge and my review of the following documents:

a) U.S. Patent Nos. 8,895,546 ("the '546 patent"), 11,241,414 ("the '414 patent"), and 11,793,786 ("the '786 patent") (collectively, the "Asserted Patents")

b) File History for each of the Asserted Patents, including the File History for U.S. Patent Application, No. 12/413,439 ("the '439 application"), which is a parent application to each of the Asserted Patents

c) Plaintiff Neurelis, Inc.'s Claim Construction Brief and Joint Appendix to Claim Construction Brief

d) The Declaration of Dr. Jason T. McConville, Ph.D. in Support of Plaintiff Neurelis, Inc.'s Claim Construction Brief

III. BACKGROUND AND QUALIFICATIONS

7. I am qualified by education and experience to testify as an expert in the field of nasally administered pharmaceutical formulations, including the nasal administration of benzodiazepine compounds, including diazepam. Attached, as Appendix A, is a copy of my

curriculum vitae, detailing my experience and education. Additionally, I provide the following overview of my background as it pertains to my qualifications for providing expert testimony in this matter.

8. I am a Professor in the Department of Pharmaceutical Sciences and Experimental Therapeutics at the University of Iowa College of Pharmacy. I have more than 40 years of education and experience working, teaching and conducting research in the field of pharmaceutics and pharmaceutical science. I received my Bachelor of Science in Pharmacy from the University of Minnesota College of Pharmacy in 1983 and my Ph.D. in Pharmaceutics from the University of Michigan in 1989.

9. I have held various positions at the University of Iowa College of Pharmacy. I was promoted to the position of Professor in 2008, and I currently hold this position. From 2008 until 2013, I was Head of the Division of Pharmaceutics, and from 2013 until 2019, I served as the Associate Dean for Undergraduate Programs.

10. Throughout my nearly 35 years as a faculty member, I have taught undergraduate, professional and graduate students about principles of pharmaceutics, including drug solubility, equilibria processes; pre-formulation and formulation approaches for pharmaceutical product development or extemporaneous compounding; and advanced of drug delivery system design including approaches to utilize alternative routes of administration including administration to the nasal cavity.

11. I have published over 150 articles, book chapters, abstracts and patents in the area of pharmaceutics, drug formulation, drug absorption, drug delivery, and materials characterization, and I have given numerous invited national and international presentations at universities and

scientific conferences. I am also frequently asked to provide seminars and consulting services to both large and small pharmaceutical companies.

12. I have over 40 peer-reviewed publications describing mechanisms of nasal absorption and nasal drug delivery along with over 75 abstracts and presentations on similar topics related to nasal drug administration.

13. I have supervised over 60 PharmD, MS, PhD, post-doctoral and visiting scholars in my laboratories. Many of my MS and PhD students are employed by both small and large pharmaceutical companies, regulatory agencies or hold academic positions and are active in the development and evaluation of new drug products or delivery systems.

14. My research program has been funded by the NIH, NCI, and FDA. I have also engaged in numerous joint investigations sponsored by pharmaceutical companies to assist with formulation development, absorption evaluation, and druggability assessment. My research team has developed formulations and evaluated drug absorption following delivery to the corneal, conjunctival, nasal, buccal, gastrointestinal and vaginal mucosae and topical delivery to the skin.

15. I have served on numerous grant review panels, including for various divisions of the NIH and NSF and served as chair of the NIH Study Section: Small Business: Drug Discovery for Aging, Neuropsychiatric, and Neurologic Disorders for three terms (various official panel names) along with numerous additional ad hoc study sections. I served as an appointed member of the FDA Pharmaceutical Science and Clinical Pharmacology Advisory Panel and a temporary member of the FDA Anesthetic and Analgesic Drug Products Advisory Committee.

IV. THE PERSON OF ORDINARY SKILL IN THE ART

16. I have been informed that "a person of ordinary skill in the art", a POSA, is not a specific, real individual, but rather a hypothetical individual or team of individuals working closely

together, who is presumed to have known the relevant art at the time of the invention. In defining the POSA, I have considered factors such as the educational level and years of experience not only of the person or persons who have developed the invention that is the subject of the case, but also others working in the pertinent art at the time of the invention; the types of problems encountered in the art; the teachings of the prior art; patents and publications of other persons or companies; and the sophistication of the technology.

17. I have assessed the level of ordinary skill in the art based upon my review of the Asserted Patents, the prior art, and my own long-standing career of working in the field of delivery of pharmaceutical dosage forms, including intranasal dosage forms.

18. It is my opinion that a POSA would have been a pharmaceutical scientist, chemist, or biologist involved in the research and development of pharmaceutical formulations and/or delivery, and would have at least a Bachelor's degree with at least 5 years of experience, or a Master's, Ph.D. or Pharm.D. degree with several years of experience. In addition, it is my opinion that a POSA would have had knowledge of benzodiazepine structure and function, and would further have knowledge and practical experience working with intranasal and transmembrane formulations, including knowledge of the physiology and anatomy of the nasal cavity, with relevant experience in developing intranasal formulations. I meet or exceed these qualifications and qualify as a POSA with respect to the Asserted Patents.

19. It is my understanding that Neurelis has asserted that a person of ordinary skill in the art holds a Master's degree with many years of experience, or a Ph.D. or Pharm.D degree with several years of experience or its equivalent experience in the field of pharmaceutical research and development. Op. Brief at 5, McConville Decl. at ¶6. I also understand that Neurelis has asserted that the skilled artisan would have knowledge of benzodiazepine structure and function, including

physicochemical characteristics of benzodiazepines generally, and would further have knowledge and practical experience developing and working with intranasal formulations, including knowledge of the physiology and anatomy of the nasal cavity and methods of administering drugs intranasally. *Id*. Finally, Neurelis asserts that a person of ordinary skill would have knowledge concerning clinical aspects of bioavailability, tolerability, and patient acceptability of intranasal formulations and the difficulty of administering drugs by other routes during an event like a seizure. *Id*.

20. I qualify as a POSA under either definition. I reserve the right to modify my opinions should the Court adopt a different POSA definition.

V. LEGAL UNDERSTANDING

21. I have been informed that claim terms are interpreted according to their ordinary and customary meaning as understood by a POSA, in light of the specification of the patent in which they appear and also in light of the prosecution history pertaining to the patent. However, I have also been advised that certain terms may be construed in a manner other than their ordinary and customary meaning if defined in a particular way by the inventors.

22. I have been informed that there is a generally-understood legal meaning of the scope of "consisting of" as a transitional phrase, which excludes any elements, steps, or ingredients not specified in the claim. I understand that, in the words of a decision by the U.S. District Court for the District of Delaware, the exceptions to this exclusionary rule "are narrow—the Federal Circuit has only mentioned impurities or aspects truly unrelated to the invention." *Shire Dev. Inc. v. Cadila Healthcare Ltd.*, No. CV 10-581 (KAJ), 2015 WL 4596410, at *7 (D. Del. July 28, 2015).

23. I have been informed that the U.S. Patent laws require a patent applicant to distinctly claim the invention with particularity and definiteness. I have been informed that a patent

is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention. I have been informed that the analysis to determine if a claim is invalid for indefiniteness examines the claims, specification, and prosecution history to ascertain if they convey to one of skill in the art with reasonable certainty the scope of the invention claimed.

VI. OPINIONS

24. It is my understanding that Neurelis, supported by its expert, Dr. Jason McConville, Ph.D., has argued in its opening brief that the "consisting of" transition phrase allows for the inclusion of additional unrecited components in the claimed solution, including "impurities" and other additional components that are "unrelated to the invention." Op. Brief. at 9-11, 14; McConville Decl. at ¶¶38-39. It is also my understanding that Neurelis and Dr. McConville argue that the Asserted Patents do not exclude water from the scope of the Asserted Claims, because water is an "impurity ordinarily associated" with the components of the claimed invention. Op. Brief at 10-11; McConville Decl. at ¶36.

25. I disagree with the arguments set forth by Neurelis and its expert Dr. McConville, as it is my opinion that a POSA would not consider water to be an "impurity" within the context of the Asserted Patents, and a POSA would recognize that water content within the claimed solutions is not "unrelated to the invention," because it can directly impact the solubility of benzodiazepine drug compounds. Additionally, if the claims of the Asserted Patents are construed in a manner that allows for the Asserted Claims to include additional unrecited components such as water and oil (which I do not agree to be the correct interpretation), it is my opinion that a POSA cannot reasonably ascertain what additional components (and in what amounts) may be present within the claimed solutions, and the claims are indefinite.

A. Water Content within the Claimed Solutions is not an "Impurity" and is not "Unrelated to the Invention"

26. It is my opinion that water content (even very small amounts of water) is not an "impurity ordinarily associated" with the claimed solution, and that water content is not "unrelated to" the alleged invention. Consequently, based on the case law cited by Neurelis and Dr. McConville, it is my opinion that the "consisting of" transition language of the Asserted Patents does not allow for the inclusion of small amounts of water. The basis for this determination is provided in the sections that follow.

1. The Specification of the Asserted Patents Makes Clear that Very Small Amounts of Water Were Contemplated as a Component, But Were Not Claimed

27. The Asserted Patents are directed to formulations of benzodiazepines, which have significant solubility issues. Specifically, benzodiazepines can be difficult to dissolve in aqueous solutions, and because of this limited aqueous solubility, benzodiazepines can be also be difficult to formulate in suspensions. The Asserted Patents acknowledge these difficulties in formulating benzodiazepines, stating that the ability to develop benzodiazepine formulation is "significantly limited due, in many cases, to solubility challenges," '546 patent at 1:49-51,[1] and "most benzodiazepines are so slightly soluble in water that a therapeutically effective amount cannot be dissolved in a volume of aqueous solvent that is amenable to application to a mucosal membrane." *Id*. at 18:50-53. As known by a POSA, and as acknowledged by the Asserted Patents, the components and their respective concentrations within benzodiazepine formulations are critical to ensuring that the benzodiazepine is adequately solubilized and that the benzodiazepine can be effectively delivered to a patient.

[1] All citations to the '546 patent in this declaration are considered exemplary, and the same disclosure can also be found in the '414 and '786 patents.

28. The specification of the Asserted Patents discloses numerous alternative benzodiazepine formulations including a variety of active ingredients, tocopherols or tocotrienols, alcohols, and alkyl glycosides. The Asserted Patents further state that possible formulations may include other active ingredients, enhancers, excipients, pH adjusters, buffers, and other agents to prevent degradation or to improve appearance, odor, or taste. *See* '546 patent at 6:26-30.

29. The Asserted Claims themselves are far narrower, reciting only a pharmaceutical solution "consisting of" (a) a benzodiazepine drug (or diazepam, specifically); (b) one or more natural or synthetic tocopherols or tocotrienols (in some claims, limited to a specific list); (c) one or more alcohols (or in some cases, specifically at least benzyl alcohol, or specifically ethanol and benzyl alcohol); and (d) an alkyl glycoside (or n-dodecyl beta-D-maltoside, specifically).

30. Although the Asserted Claims recite only four specific types of ingredients, the specification of the Asserted Patents is much broader. A wide variety of other possible ingredients are contemplated, *including water*. In the context of the Asserted Patents, these other ingredients—including water—are not "impurities." They are components that can contribute to and affect the properties of the carrier system (e.g., the diazepam solubility in the carrier system). Whether and how much a specific ingredient is used in a particular formulation is a reflection of intentional design choices. Given the "solubility challenges" of benzodiazepines, altering the ingredients or their relative amounts can significantly affect the suitability of a formulation.

31. In particular, the claims of the Asserted Patents are all directed to a "pharmaceutical ***solution***," meaning that the benzodiazepine drug must be fully solubilized in the claimed formulation. Any components of a benzodiazepine formulation that impact the solubility of the benzodiazepine within that formulation (and the ability to form a "pharmaceutical ***solution***" of the benzodiazepine) are important aspects of the formulation. Consequently, the inclusion of certain

components, such as water, that impact the relative solubility of the benzodiazepine in the formulation are not "unrelated to" the alleged invention described in the Asserted Claims.

32. In fact, the specification of the Asserted Patents expressly contemplates various alternative formulations which contemplate the inclusion of water as a component of the formulation (even when present in very small concentrations). The specification of the Asserted Patents state:

> In some embodiments, the composition comprises a benzodiazepine drug that is fully dissolved in a solvent comprising a natural or synthetic tocopherol or tocotrienol, and an alcohol or glycol. In some embodiments, the composition comprises a benzodiazepine drug that is fully dissolved in a solvent comprising a natural or synthetic tocopherol or tocotrienol and an alcohol or glycol, ***wherein the solution is at least substantially free of water. (In some embodiments, "substantially free of water" indicates that the solution contains less than about 1%, less than about 0.5%, less than about 0.25% or less than about 0.1% water***.) In some embodiments, the composition consists essentially of a benzodiazepine drug that is fully dissolved in a solvent consisting of one or more natural or synthetic tocopherols or tocotrienols, one or more alcohols or glycols, and optionally one or more alkyl glycosides. In some embodiments, the composition consists essentially of a benzodiazepine drug that is fully dissolved in a solvent consisting of one or more natural or synthetic tocopherols or tocotrienols, one or more alcohols or glycols, and optionally one or more alkyl glycosides ***wherein the solution is at least substantially free of water. (In some embodiments, "substantially free of water" indicates that the solution contains less than about 1%, less than about 0.5%, less than about 0.25% or less than about 0.1% water***.) In some embodiments, the composition consists of a benzodiazepine dissolved in a solvent consisting of one or more natural or synthetic tocopherols or tocotrienols, one or more alcohols or glycols, and optionally one or more alkyl glycosides. In some embodiments, the composition consists of a benzodiazepine dissolved in a solvent consisting of one or more natural or synthetic tocopherols or tocotrienols, one or more alcohols or glycols, and optionally one or more alkyl glycosides, ***wherein the solution is at least substantially free of water. (In some embodiments, "substantially free of water" indicates that the solution contains less than about 1%, less than about 0.5%, less than about 0.25% or less than about 0.1% water.***).

'546 patent at 11:24-59 (emphasis added).

33. A POSA reading the passage above would understand that the Asserted Patents expressly contemplated multiple scenarios where the solution is "substantially free of water," which the Asserted Patents define as containing "less than about 1%, less than about 0.5%, less than about 0.25% or less than about 0.1% water." The Asserted Patents even describe one embodiment of the composition "consists of a benzodiazepine dissolved in a solvent consisting of one or more natural or synthetic tocopherols or tocotrienols, one or more alcohols or glycols, and optionally one or more alkyl glycosides, ***wherein the solution is at least substantially free of water***." In my opinion, this suggests to a POSA that the Asserted Patents did not view the presence of small amounts of water to be an "impurity ordinarily associated" with the claimed solutions. To the contrary, if the applicants for the Asserted Patents intended for the claimed solutions to include small amounts of water as "impurities ordinarily associated" with the claimed solution, they could have drafted the claims in the exact manner described in the specification, namely to recite a pharmaceutical solution consisting of a benzodiazepine drug, one or more natural or synthetic tocopherols or tocotrienols, one or more alcohols or glycols, and optionally one or more alkyl glycosides, ***wherein the solution is at least substantially free of water***. But the applicants intentionally drafted the claims to omit the qualifier that "the solution is at least substantially free of water." In my opinion, this suggests to a POSA that the claimed solutions did not intend for even very small amounts of water (e.g., less than about 0.1%) to be present in the claimed solutions.

34. In addition, it is my understanding that an additional patent in the same family as the '414 and '786 patents recently issued as U.S. Patent No. 12,268,664 ("the '664 patent"). It is my understanding that the '664 patent is a continuation application of the '786 patent, and includes a specification that is identical to the '786 and '414 patents. The '664 patent includes claim language reciting a pharmaceutical composition "wherein the pharmaceutical composition is a

solution **and contains less than 1% water**." '664 patent at 54:23-25 (emphasis added). In my opinion, unlike the language of the Asserted Patents, the language of the '664 patent accounts for very small amounts of water to be present in the claimed solution, as a POSA would expect from reading the specification of the Asserted Patents.

35. In view of the express disclosure provided in the specification of the Asserted Patents, as well as the claim language of the recently issued '664 patent, I disagree with Neurelis and its expert Dr. McConville, and it is my opinion that a POSA would not view small amounts of water to simply be "impurities ordinarily associated" with the claimed solutions, or that the amount of water present in the solution is "unrelated to" the alleged invention described in the Asserted Claims.

2. The Prosecution History of the Asserted Patents Indicates to a POSA that the Applicants for the Asserted Patents Viewed Water and Oil Content as Components of the Claimed Solution, Not as "Impurities" or "Unrelated to the Invention"

36. In addition to the express disclosure in the specification of the Asserted Patents, it is my opinion that the prosecution history for the Asserted Patents further underscores the understanding that water and oil content are not simply "impurities" or "unrelated to the invention" within the context of the Asserted Claims. Rather, the prosecution history emphasizes that the absence of water and oil are the defining the characteristics that distinguished the prior art cited by the Examiner. In my opinion, this further indicates to a POSA that even very small amounts of water and oil cannot simply be considered an "impurity ordinarily associated" with the solution, or "unrelated to the invention."

37. The '546 patent is the earliest filed of the Asserted Patents, having been filed on June 13, 2012, as Application No. 13/495,942. The '546 patent claims priority as a continuation-in-part of Application No. 12/431,439, filed on March 27, 2009, which claims priority to

Provisional Application No. 61/497,017, filed June 14,2011, and Provisional Application No. 61/570,110, filed on December 13, 2011. The ’546 patent issued on November 25, 2014.

38. The ’414 patent was filed on May 27, 2021, as Application No. 17/332,800. The ’414 patent does not claim priority directly to the ’546 patent, but among its parent applications is Application No. 12/431,439. The ’414 patent issued on February 8, 2022.

39. The ’786 patent was filed on April 12, 2021, as Application No. 17,228,514. The ’786 patent also does not claim priority directly to the ’546 patent, but among its parent applications is Application No. 12/431,439. The ’786 patent issued on October 24, 2023.

40. All of the Asserted Patents claim priority through a lineage that includes the ’439 application.

41. I reviewed the file histories of the Asserted Patents and the ’439 application. I summarize below particularly relevant events and statements during the prosecution of the Asserted Patents and the ’439 application that impact how a POSA would interpret the claim language.

42. During prosecution of the ’439 application, the original claims of the ’439 application recited a pharmaceutical composition for nasal administration (or a method treating a patient with such a composition) “***comprising*** a benzodiazepine drug, one or more natural or synthetic tocopherols or tocotrienols, or any combinations thereof, in an amount from about 30% to about 95% (w/w), and one or more alcohols or glycols, or any combinations thereof, in an amount of about 10% to about 70% (w/w).” Appx376. As stated, it is my understanding that the “comprising” transition phrase is “open-ended” and allows for the inclusion of other unrecited components. Consequently, in addition to the aforementioned components expressly recited in the

claims, the original claims of the ’439 application reciting a composition “comprising” the recited components would allow for the inclusion of other unrecited components, such as water.

43. On March 18, 2011, the USPTO issued a non-final office action rejecting the elected claims as, among other things, obvious in view of teachings of tocopherol compositions to deliver biologically active agents that are sparingly soluble in water, such as diazepam, and the use of absorption enhancers such as alkyl glycoside. Appx391-395.

44. On September 19, 2011, the applicants for the ’439 application responded to the office action by amending the claims to require that the pharmaceutical composition be a “solution” and that it be “consisting of” the specifically listed ingredients. Appx249. In the remarks accompanying the amendment, the applicants argued: “the solution recited in claim 20 consists of a benzodiazepine drug, one or more natural or synthetic tocopherols or tocotrienols, one or more alcohols or glycols and optionally one or more alkyl glycosides. In other words, the recited solution contains: each of a benzodiazepine drug; one or more tocopherols or tocotrienols; one or more alcohols or glycols; and optionally one or more alkylglycosides; and **the solution excludes anything else. In particular, the solution excludes water and oil**.” Appx257 (emphasis added).

45. In additional remarks accompanying the September 19, 2011 amendment, the applicants argued: “Sonne teaches specific benzodiazepine formulations in Examples 1-3, 7-11, 17-19 and 22-23. Of these, Examples 1-3, 7-11, 17, 19 and 22-23 each describe an oil-in-water emulsion of the benzodiazepine. Such emulsions are specifically excluded from the instant claims, which recite solutions (not emulsions) and **exclude any ingredients (such as water and oil) not included within the group of benzodiazepine drugs, tocopherols or tocotrienols, alcohols or glycols, and optionally alkylglycosides**.” Appx258 (emphasis added).

46. In remarks accompanying the November 19, 2014 response to an office action, the applicants argued: "The method comprises administering a nasal solution. The recited nasal solution consists of each of: a benzodiazepine drug; one or more tocopherols or tocotrienols; one or more alcohols or glycols; and one or more alkylglycosides, each in specific proportions. **The solution excludes anything else, including water and oil**." Appx272 (emphasis added).

47. In further remarks accompanying the November 19, 2014 response, the applicants argued: "while Sonne teaches emulsions and solutions, all the emulsions taught therein include water and oil, and all the disclosed solutions require oil. In contrast, the instant claims require solutions, and thus specifically exclude Sonne's emulsions. The instant claims also recite specific ingredients, while excluding others through the recitation of 'consisting of' language. **In particular, both water and oil are excluded from the instant claims, as they are not one of the recited ingredients**." Appx272 (emphasis added).

48. During prosecution of the '414 patent, in a statement for the reasons for allowance of the '414 patent, the Examiner stated: "The prior art does not reasonably teach or suggest the recited combination of components while excluding all non-recited components as required by the 'consisting of' transitional phrase." Appx401.

49. Consistent with how a POSA would view the components of a benzodiazepine formulation, all of these statements and arguments provided during prosecution of the '439 application and the '414 patent underscore the understanding that the inclusion of specific components, particularly water and oils, are not unrelated to the alleged invention, as the applicants repeatedly emphasized the absence of these components as the primary basis for distinguishing the prior art. Consequently, it is my opinion that the prosecution history for the Asserted Patents supports my understanding that water content and oil content are not simply "impurities" that can

be included within the scope of the claimed solutions, and certainly are not "unrelated to the invention," as the water content and oil content (more specifically, the absence of water and oil) was repeatedly asserted by the applicants of the Asserted Patents to be the primary basis for distinguishing the prior art cited by the Examiner.

B. If the Claims of the Asserted Patents are Construed to Allow for the Inclusion of Unrecited Components, Including Water and Oil, the Claims are Indefinite

50. As I discussed in the section on legal principles, it is my understanding a patent is invalid for indefiniteness if its claims, when read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention. For the reasons I have articulated previously, it is my opinion that water content (even very small amounts of water) is not an "impurity ordinarily associated" with the claimed solution, and that water and oil content are not "unrelated to" the alleged invention, meaning that the "consisting of" transition phrase does not allow for small amounts of water in the claimed solutions. However, should the claims of the Asserted Patents be construed to allow for the inclusion of water (and other components), it is my opinion that a POSA cannot reasonably ascertain what is within the scope of the invention, and what is outside the scope of the invention, and the claims are indefinite.

51. As I discussed previously, the Asserted Patents are directed to formulations of benzodiazepines, which have known water solubility issues. The Asserted Patents acknowledge these difficulties in formulating benzodiazepines, stating that the ability to develop benzodiazepine formulation is "significantly limited due, in many cases, to solubility challenges," '546 patent at 1:49-51, and "most benzodiazepines are so slightly soluble in water that a therapeutically effective amount cannot be dissolved in a volume of aqueous solvent that is amenable to application to a mucosal membrane." *Id.* at 18:50-53. As known by a POSA, and as acknowledged by the Asserted

Patents, the components and their respective concentrations within benzodiazepine formulations are critical to ensuring that the benzodiazepine is adequately solubilized and that the benzodiazepine can be effectively delivered to a patient.

52. Consequently, the amount of water present in the claimed solutions is a very important factor, as it impacts the solubility of the benzodiazepine within the claimed solution. Dr. McConville repeatedly states that a POSA would expect residual solvents (such as water) to be present in "trace amounts," and to be carried forward into the final ingredients of the formulation, *see* McConville Dec at ¶¶35-36, 38, 41, and 44, but not one time does Dr. McConville define what amount or concentration of a residual solvent constitutes a "trace amount." Additionally, Neurelis appears to draw a distinction between "trace amounts" of impurities that are allowed to be present within the claims, and "additional ingredients" that are not allowed to be in the claimed solution. *See, e.g.*, Op. Brief at 14, 16. But again, nowhere does Neurelis or Dr. McConville define what amount of a residual solvent (such as water) must be present to constitute an "ingredient" as compared to a "trace amount" of an impurity. Based on this, a POSA does not have any level of certainty regarding the amount of water that would be considered a "trace amount," which is allowed to be present within the claimed solution, and the amount of water that constitutes an "additional ingredient" that is excluded from the scope of the claimed solutions including the "consisting of" transition language.

53. This determination is further complicated by the fact that the specification of the Asserted Patents explicitly contemplates the inclusion of water as an additional ingredient/component of the solutions described therein. The Asserted Patents recognize that water may be a component of the formulations, stating, for example, that "[i]n some embodiments, a carrier system in such a composition includes water." '546 patent at 13:45-46. Additionally, as I

discussed previously, the specification of the Asserted Patents also contemplates embodiments whereby the composition "consists of a benzodiazepine dissolved in a solvent consisting of one or more natural or synthetic tocopherols or tocotrienols, one or more alcohols or glycols, and optionally one or more alkyl glycosides, ***wherein the solution is at least substantially free of water. (In some embodiments, 'substantially free of water' indicates that the solution contains less than about 1%, less than about 0.5%, less than about 0.25% or less than about 0.1% water.***)." '546 patent at 11:51-59 (emphasis added). Here, the specification of the Asserted Patents clearly views the "substantially free of water" language as an additional "ingredient"/requirement of the solution, and indicates that the water may be included in an amount of "less than about 0.1% water." But the specification places no lower limit on "less than about 0.1% water." For example, under the express language of the specification, 0.0000001% water is "less than 0.1% water," and would be considered part of the "substantially free of water" ingredient/requirement of the claims. The Asserted Patents have provided no guidance regarding a threshold amount that distinguishes a "trace amount" of residual solvent and what rises to the level of an "ingredient" of the claimed solution.

54. Furthermore, Neurelis and Dr. McConville's positions open up the claimed solutions to include any "trace impurities" and other components that are "unrelated to the claimed invention." The Asserted Patents indicate that numerous other components may also be present in the solutions, stating "In some embodiments, the composition comprises at least one additional ingredient selected from the group consisting of: active pharmaceutical ingredients; enhancers; excipients; and agents used to adjust the pH, buffer the composition, prevent degradation, and improve appearance, odor, or taste." '546 patent at 6:26-30. Under Neurelis' position that additional components or steps unrelated to the invention are not excluded from the claimed

solutions, a POSA does not have any clarity or certainty as to which additional excipients (including those recited in the Asserted Patents and others known in the field) are "unrelated to the invention" and may be added to the solution, and which additional excipients are "related to the invention" and must be excluded. For example, is an excipient that "improve[s] appearance" of the claimed solutions (which is called out as a potential excipient in the specification of the Asserted Patents) "unrelated to the invention" or "related to the invention"? This determination is arbitrary, and will vary from one POSA to another, yet this arbitrary determination dictates whether the additional component may be present in the claimed solutions or not.

55. I also note that Dr. McConville argues that the distinction between "ethanol" and "ethanol (dehydrated, USP)" in the Asserted Patents suggests to a POSA that the claimed components, including the claimed "ethanol" must allow for some amount of water to be present. *See* McConville Decl. at ¶¶38-40. Dr. McConville also asserts that a POSA knows that "there is always some trace water present in benzyl alcohol," and that "[t]he USP reflects and allows for this." *Id*. at ¶41. But Dr. McConville's statements and positions are problematic when trying to ascertain the meaning and scope of the Asserted Claims. If water can be present in the claimed solutions, how much? The Asserted Patents acknowledge that benzodiazepine drugs are poorly soluble in water, so the amount of water in the claimed solutions is a critical aspect of the formulation. Yet neither the Asserted Patents nor Dr. McConville provide any guidance regarding how much water may be present and still fall within the scope of the claimed solutions.

56. In addition, the Asserted Patents explicitly acknowledge that the alcohol components (including, e.g., ethanol and benzyl alcohol) may be present in dehydrated, USP forms. '546 patent at 7:27-28 ("[i]n some embodiments, the alcohol or glycol is free of water (dehydrated, USP)." By Dr. McConville's own admission, the USP standard allows for a specific

amount of water to be present in the component. *See* McConville Dec at ¶¶38-42. However, despite this well-known knowledge within the art, the Asserted Claims do not recite that the ethanol or benzyl alcohol components are required to be USP grade. Consequently, it is my opinion that the knowledge and recognition that the alcohol components may be USP grade (and the subsequent decision to not claim the ethanol and/or benzyl alcohol as USP grade) only further enhances the ambiguity as to what amount of water, if any, can be included within the claimed solutions.

57. Taken together, it is my opinion that the Asserted Patents do not provide any guidance regarding what additional unrecited components (whether it be water or other excipients) are "unrelated to the invention" and are allowed in the claimed solutions or are "related" to the invention and are excluded from the claimed solutions. Such a determination is arbitrary and will likely vary from one POSA to another. Additionally, the Asserted Patents do not provide any guidance regarding what amount of water (or other unrecited components) constitutes a "trace amount" and may be present in the claimed solutions, or what amount of water (or other unrecited components) rise to the level of an "ingredient" and is excluded from the claimed solutions. For at least these reasons, it is my opinion that a POSA does not have reasonable certainty as to what is within the scope of the Asserted Patent claims, and the claims are indefinite.

VII. CONCLUSION

58. I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct to the best of my knowledge.

Maureen D. Donovan

Maureen Donovan, Ph.D.

Dated: July 11, 2025