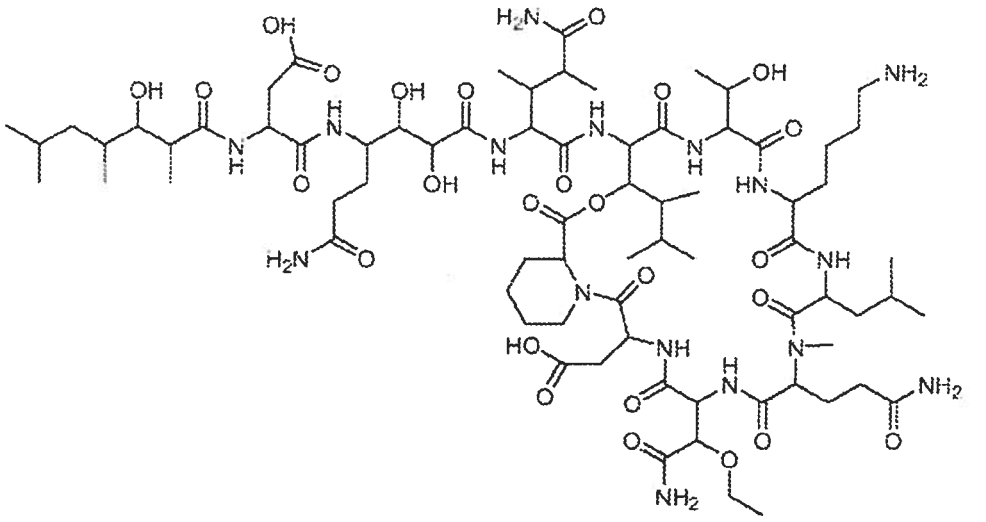
AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

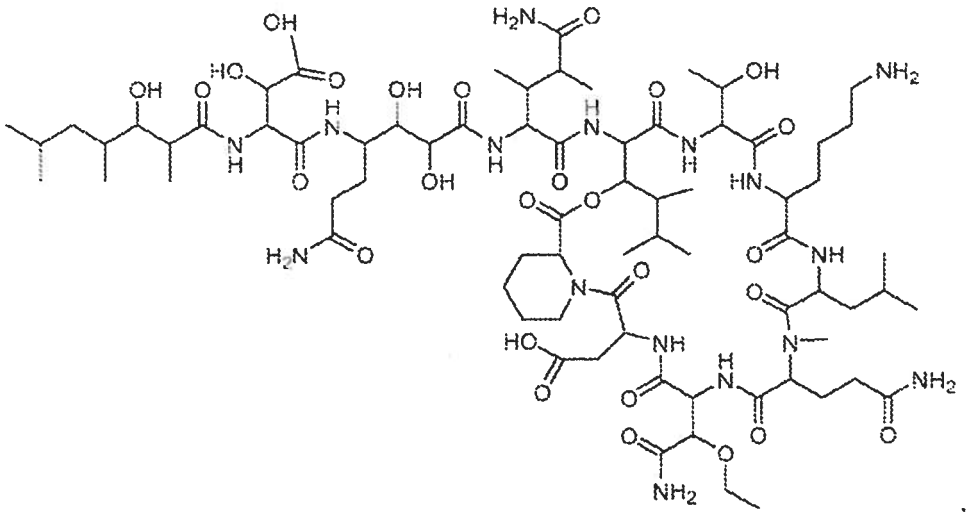
1-25. (Cancelled)

26. (Currently Amended) [[A]] A purified compound selected from the group consisting of: Pipecolidepsin A, Pipecolidepsin B and Pipecolidepsin C, or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof; wherein the structure of Pipecolidepsin A is:



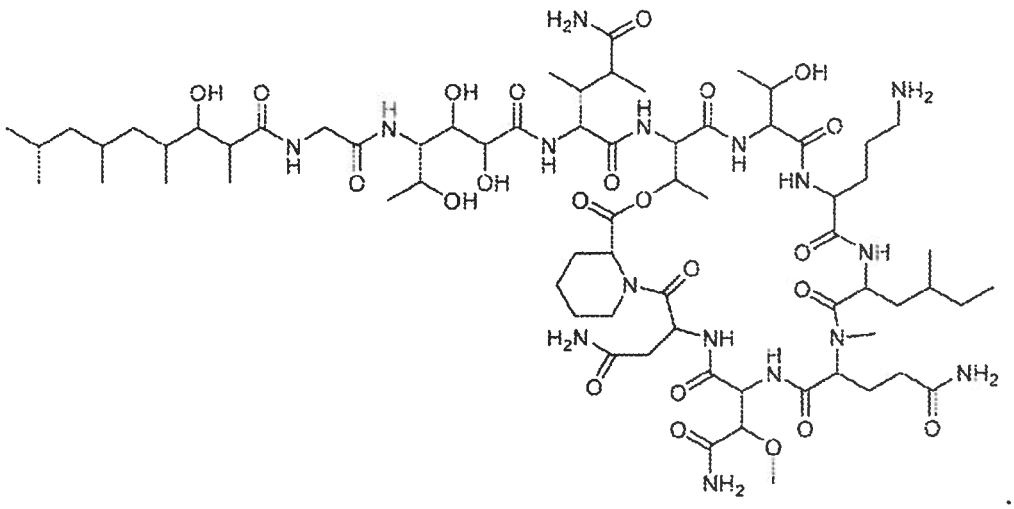
;

wherein the structure of Pipecolidepsin B is:



; and

wherein the structure of Pipecolidepsin C is:



27. (Currently Amended) A pharmaceutical composition comprising [[a]] the purified compound according to claim 26, or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof, and a pharmaceutically acceptable carrier or diluent.

28-29. (Cancelled).

30. (Currently Amended) A method of treating a patient affected by cancer which comprises administering to said affected individual in need thereof a therapeutically effective amount of a the purified compound ~~as defined in~~ according to claim 26, or a pharmaceutically acceptable salt,

tautomer or stereoisomer thereof, wherein said cancer is selected from lung cancer, colon cancer, and breast cancer.

31. (Currently Amended) The purified compound according to claim 26, wherein the purified compound is Pipecolidepsin A or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

32. (Currently Amended) The purified compound according to claim 26, wherein the purified compound is Pipecolidepsin B or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

33. (Currently Amended) The purified compound according to claim 26, wherein the purified compound is Pipecolidepsin C or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

34. (Currently Amended) The pharmaceutical composition according to claim 27, wherein the purified compound is Pipecolidepsin A or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

35. (Currently Amended) The pharmaceutical composition according to claim 27, wherein the purified compound is Pipecolidepsin B or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

36. (Currently Amended) The pharmaceutical composition according to claim 27, wherein the purified compound is Pipecolidepsin C or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

37. (Currently Amended) The method of treating a patient affected by cancer according to claim 30, wherein the purified compound is Pipecolidepsin A or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

38. (Currently Amended) The method of treating a patient affected by cancer according to claim 30, wherein the purified compound is Pipecolidepsin B or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

39. (Currently Amended) The method of treating a patient affected by cancer according to claim 30, wherein the purified compound is Pipecolidepsin C or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

40. (New) The purified compound according to claim 26, wherein the compound is sufficiently purified for use in a pharmaceutical composition for treating humans.

41. (New) The purified compound according to claim 40, wherein the sufficiently purified compound is Pipecolidepsin A or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

42. (New) The purified compound according to claim 40, wherein the sufficiently purified compound is Pipecolidepsin B or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

43. (New) The purified compound according to claim 40, wherein the sufficiently purified compound is Pipecolidepsin C or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

44. (New) The pharmaceutical composition according to claim 27, wherein the purified compound, or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof, is present in said pharmaceutical composition in amount suitable for treating cancer in humans.

45. (New) The pharmaceutical composition according to claim 44, wherein the purified compound is Pipecolidepsin A or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

46. (New) The pharmaceutical composition according to claim 44, wherein the purified compound is Pipecolidepsin B or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

47. (New) The pharmaceutical composition according to claim 44, wherein the purified compound is Pipecolidepsin C or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

48. (New) The method of treating a patient affected by cancer according to claim 30, wherein the patient is a human

49. (New) The method according to claim 48, wherein the purified compound is Pipecolidepsin A or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

50. (New) The method according to claim 48, wherein the purified compound is Pipecolidepsin B or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

51. (New) The method according to claim 48, wherein the purified compound is Pipecolidepsin C or a pharmaceutically acceptable salt, tautomer or stereoisomer thereof.

REMARKS

A. Status of the Claims

Claims 26, 27 and 30-39 are pending and rejected by the Examiner. Without waiver or prejudice, claims 26, 27 and 30-39 are amended herein to recite a "purified compound." Support for these amendments is found in the as-filed specification corresponding to U.S. Pre-grant Publication No. 2011/0237520, e.g., the description that "Pipecolidepsins A, B and C were isolated from a sponge of the order Lithistida, family Neopeltidae, genus Homophymia, species *Homophymia lamellose*" at ¶¶ [0024], [0054] and Examples 1-3 at ¶¶ [0066]-[0069]; [0070]-[0074] and [0077]-[0082] which disclose methods of isolating and purifying the claimed compounds and using the purified compounds in cell assays to detect cytotoxicity. The term "purified" is used to indicate that the claimed compound has been isolated and purified from its endogenous environment so that it is therapeutically useful, or may be formulated to be therapeutically useful, but should not be construed as limiting the source of the compound. No new matter is added.

New dependent claims 40-43 are added to specifically claim the compound which is sufficiently purified for use in a pharmaceutical composition for treating humans; dependent claims 44-47 are added to claim pharmaceutical compositions for treating humans; and dependent claims 48-51 are added to specifically recite methods of treating humans. The specification supports pharmaceutical compositions and methods for treating humans at [0021] and [0058]-[0061].

B. Claim Rejections.

Rejection under 35 U.S.C. § 101

Claims 26, 27, and 30-39 are rejected under 35 U.S.C. § 101, as allegedly not being directed to patent eligible subject matter. The Examiner contends that "[b]ased upon an analysis with respect to the claim as a whole, claim(s) 26, 27, and 30-39 do not recite something significantly different than a judicial exception. The rationale for this determination is … based on the analysis presented in the USPTO's 'Guidance For Determining Subject Matter Eligibility Of Claims Reciting Or Involving Laws of Nature, Natural Phenomena, & Natural Products' dated March 4, 2014

(hereafter 'Guidance,' refer to the flow chart in Section I of the Guidance)." See, Office Action at pages 2-3. Applicants respectfully traverse this rejection.

The USPTO's Guidance states to address "the impact of *Association for Molecular Pathology v. Myriad Genetics*, Inc., 569 U.S. _, 133 S. Ct. 2107, 2116, 106 USPQ2d 1972 (2013) ('*Myriad*'), on the Supreme Court's long-standing 'rule against patents on naturally occurring things', as expressed in its earlier precedent including *Diamond v. Chakrabarty*, 447 U.S. 303 (1980) ('*Chakrabarty*'), and *Mayo Collaborative Services v. Prometheus Laboratories*, Inc., 566 U.S. __, 132 S. Ct. 1289, 101 USPQ2d 1961 (2012) ('*Mayo*'). See *Myriad*, 133 S. Ct. at 2116." Guidance at 1. According to the Guidance, "natural products" are among the judicial exceptions, which, if present in a claim under examination, requires the Examiner to ask "[d]oes the claim as whole recite something *significantly different* than the judicial exception(s)?" *Id.* At 2. The Guidance provides several factors to be weighed for or against drawing a conclusion that a significant difference from the judicial exception exists to qualify the claim as covering eligible subject matter. Applicants disagree with the Examiner's conclusion that the factors weigh against a conclusion that the pending claims qualify as covering patent eligible subject matter. In addition, the Guidance analogizes the factors to be weighed for patent eligibility to the *Wands* factor-based analysis for enablement, Guidance at 4, however, even the *Wands* enablement factors are only "illustrative" guides that are not mandatory.

> "In addition, it is not necessary that a court review all the Wands factors to find a disclosure enabling. They are illustrative, not mandatory."

Amgen. Inc., v. Chugai Pharmaceutical Co., Ltd., 927 F.2d 1200, 1213 (Fed. Cir. 1991). Accordingly, as explained below, Applicants claims cover patent eligible subject matter that meets the requirements of 35 U.S.C. §101.

Applicants have amended the claims to specifically recite that they claim "purified" compounds, pharmaceutical compositions comprising such purified compounds and methods of treating cancer with the purified compounds. As presently claimed, the compounds are clearly removed and separated from their natural environment, a marine sponge, giving the compounds a new and significant utility as a cancer therapeutic which is significantly different from the function and characteristic of the compounds as they exist in the marine sponges. In addition, all of the claims have additional elements besides the "judicial exception" such that the each claim as a whole relates to subject matter that is significantly different from the natural product. As

explained below, none of the cases which are relied upon by the USPTO as the basis of the Guidance support a rejection of the pending claims. Accordingly, as the Guidance itself is not legal authority on which to reject the claims, and for the reasons discussed below, Applicants respectfully request that the current grounds of rejection relying on the Guidance be withdrawn.

Purified Compound Claims 26 and 31-33 are Directed to Subject Matter Significantly Different From the Natural Product

The Examiner contends that claims to Pipecolidepsin A, B and C are not significantly different from the judicial exception and does not meet Factor "a" supporting patent eligibility of the Guidance "because there is no structural difference between the Pipecolidipsins A, B and C claimed and the Pipecolidepsins A, B and C found in nature." Applicants have amended the claims to specifically recite that the claimed compounds are purified, meaning that they have been removed from their natural environment, the marine sponge. As amended, the claims do relate to subject matter that is structurally significantly different from that which exists in nature. According to the Merriam-Webster Dictionary, a definition of "structure" is "5: the aggregate of elements of an entity in their relationships to each other." *Webster's Ninth New Collegiate Dictionary*, Merriam-Webster Inc., Springfield, MA, 1990. As recognized by the Examiner, as natural products, Pipecolidepsin A, B and C, are found in the marine sponge of the order Lithisdida, family Neopeltidae, genus Homophymia, species *Homophymia lamellosa* at depths of from 3 to 7 meters. To further illustrate the elements naturally found with Pipecolidepsin A, B and C, attached is a photograph of the marine sponge from which the purified compounds may be obtained. Exhibit 1. Purification of the claimed products involves multiple extractions in aqueous and organic solvents as well as at least five separate chromatography steps. See, Examples 2-3. The final purified products are white amorphous solids which are significantly different from their endogenous form in the marine sponges as shown in the photograph of the marine sponge. Whether the purified product is present as a white solid or is further treated and formulated for use as a therapeutic, the purified products are present in a vastly different environment from their native one which imparts a new aggregate structure. This new aggregate structure, provides for the new utility of treating cancer associated with the claimed purified compounds which do not exist in nature in the form as they are claimed.

The Examiner also contends that Factors b though f of the Guidance are not relevant "because the claims do not include any elements in addition to the natural product." As amended to include the element "purified" in the claims, all of the claims of the present application either specifically recite that the claimed compound is purified, or depend from such a claim. The purified product therefore differs from that which exists in nature in a "significant way" (factor c) which is not only "nominally, insignificantly, or tangentially related to the judicial exception" because the claimed product is in a completely different environment and is separated from other molecules endogenous to the marine sponge. As a purified compound, Applicants have provided a product having a completely new and useful function - to treat cancer.

The purified product, which is removed from other substances associated with the marine organism and is able to be formulated to provide controlled dosage to treat cancer, has utility that is not at all possible when the Pipecolidepsins are present in the marine sponge in the ocean. It was only through the inventive work of Applicants that the claimed compounds were discovered, structurally characterized and rendered sufficiently pure to have utility as cancer therapeutics. Moreover, as purified compounds, having unique and novel attributes because of their removal from their natural environment, and therefore having a different structure as defined above by the aggregate of elements with which the compounds would naturally associate, there is no legal basis to require that the compounds themselves have significantly different molecular structures from the compounds existing in the marine sponge.

When the purified compound claims are viewed as whole, including the recitation of "purified", the claims relate to subject matter that differs from the natural product in significant ways. The claims as a whole, therefore, including all of their elements, encompass products that are more than nominally or insignificantly different than the compounds as they naturally occur in the marine sponge.

Products purified from natural sources have been recognized as patentable subject matter for over a hundred years and none of the cases relied on by the USPTO as the basis of the Guidance has changed that law. The identification and isolation of a particular molecule with a substantial real-world utility has long been held an "invention" under 35 U.S.C. § 101. Although not exhaustive, examples of patents covering important therapeutic products purified from natural sources include: U.S. Patent No. 730,176 issued June 2, 1903 covering adrenaline

purified from suprarenal glands; U.S. Patent No. 1,469, 994 issued October 9. 1923, covering insulin purified from fresh pancreatic or related glands; U.S. Patent No. 1,898,199, issued February 21, 1933, covering digitalis extracted from the leaves of digitalis lanata; and U.S. Patent No. 2,562,794, issued August 7, 1951, covering vitamin B_{12} isolated from fungus. Examples of other patents issued covering molecules purified from natural sources having therapeutic application include U.S. Patent No. 4,324,887 issued covering a purified polysaccharide from type II group B streptococci and U.S. Patent No. RE 32,011 issued covering Factor VIII:C, an important protein necessary for clotting used to treat patients with hemophilia. See, Newman et al., "Natural Products as Sources of New Drugs over the Period 1981-2002,", *J. Nat. Prod.* 66:1022-1037 (2003).

Courts have long endorsed the issuance of such patents covering purified products such as those presently claimed, upholding the patentability of extracts or isolates of natural products having significant utility and different characteristics than the natural material from which they were obtained. *See*, e.g., *Kuehmstead v. Farbenfabriken of Elberfeld Co.*, 179 F. 701 (7th Cir. 1910) (aspirin); *In re Kratz*, 592 F.2d 1169 (C.C.P.A. 1979) (substantially pure 2-methyl-2-pentenoic acid (2M2PA)—the molecule that imparts strawberries' distinctive flavor and odor—mixed with an adjuvant); *In re Bergstrom*, 427 F.2d 1394 (C.C.P.A. 1970) (substantially pure PGE2 and PGE3 (prostaglandins)); *Merck Co. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156 (4th Cir. 1958) (purified vitamin B12 obtained from extracts of streptomyces cultures); *Parke-Davis & Co. v. H.K. Mulford & Co.*, 196 F. 496 (2d Cir. 1912) (substantially pure adrenalin derived from cow glands).

Prior to the Guidance, the USPTO itself relied on the well established law relating to purified natural products as a basis to support the patentability of isolated DNA in its own Utility Guidelines, published in the Federal Register /Vol. 66, No. 4, in 2001, well after the *Chakrabarty's* 1980 decision. Although *Myriad*, may have changed the law relating to DNA, the underlying law relating to purified natural products as explained by the USPTO in its own Utility Guidelines has not changed.

> Patenting compositions or compounds isolated from nature follows well-established principles, and is not a new practice. For example, Louis Pasteur received U.S. Patent 141,072 in 1873, claiming "[y]east, free from organic germs of disease, as an article of manufacture." Another example is an early patent for

> adrenaline. In a decision finding the patent valid, the court explained that compounds isolated from nature are patentable: "even if it were merely an extracted product without change, there is no rule that such products are not patentable. Takamine was the first to make it [adrenaline] available for any use by removing it from the other gland-tissue in which it was found, and, while it is of course possible logically to call this a purification of the principle, it became for every practical purpose a new thing commercially and therapeutically. That was a good ground for a patent." *Parke-Davis & Co. v. H. K. Mulford Co.*, 189 F. 95, 103 (S.D.N.Y. 1911) (J. Learned Hand).
>
> In a more recent case dealing with the prostaglandins PGE2 and PGE3, extracted from human or animal prostate glands, a patent examiner had rejected the claims, reasoning that "inasmuch as the 'claimed compounds are naturally occurring' * * * they therefore 'are not 'new' within the connotation of the patent statute.' " *In re Bergstrom*, 427 F.2d 1394, 1397, 166 USPQ 256, 259 (CCPA 1970). The Court reversed the Patent Office and explained the error: "what appellants claim—pure PGE2 and PGE3—is not 'naturally occurring.' Those compounds, as far as the record establishes, do not exist in nature in pure form, and appellants have neither merely discovered, nor claimed sufficiently broadly to encompass, what has previously existed in fact in nature's storehouse, albeit unknown, or what has previously been known to exist." *Id.* at 1401, 166 USPQ at 261–62. Like other chemical compounds, DNA molecules are eligible for patents when isolated from their natural state and purified or when synthesized in a laboratory from chemical starting materials.

The decision in *Myriad*, rejecting the patentability of an isolated human gene based on the information contained in the isolated DNA being the same as non-isolated DNA, does not change the long standing law that isolated/purified natural products having markedly different characteristics and substantial utility upon their isolation are patent eligible subject matter. *Myriad* itself affirmatively limits its application only to genes and the information they encode:

> We merely hold that genes and the information they encode are not patent eligible under §101 simply because they have been isolated from the surrounding genetic material.

Myriad, Slip Op., at 18. *Myriad* is not about the patent eligibility of purified natural products generally, but is about whether isolated DNA with the information it imparts is patentable subject matter. It is because the sequence information, according to *Myriad*, provides the real

value to the claim and not the chemical entity itself that the Court in *Myraid* held the claims to the isolated DNA invalid.

> Myriad's claims are simply not expressed in terms of chemical composition, nor do they rely in any way on the chemical changes that result from the isolation of a particular section of DNA. Instead, the claims understandably focus on the genetic information encoded in the BRCA1 and BRCA2 genes. If the patents depended upon the creation of a unique molecule, then a would be infringer could arguably avoid at least Myriad's patent claims on entire genes (such as claims 1 and 2 of the '282 patent) by isolating a DNA sequence that included both the BRCA1 or the BRCA2 gene and one additional nucleotide pair. Such a molecule would not be chemically identical to the molecule "invented" by Myriad. But, Myriad obviously would resist that outcome because its claim is concerned primarily with the information contained in the genetic *sequence*, not with the specific chemical composition of a particular molecule.

Myriad, Slip Op., at 14-15. Simply put, according to *Myriad*, had the molecule itself been important to claim because of its utility as a chemical entity, rather than because of the sequence information, one could avoid infringement by isolating a different chemical entity, one with an additional nucleotide pair. By highlighting that the claims in *Myriad* are "primarily concerned with the information contained in the genetic *sequence*, not with the specific chemical composition of a particular molecule", *Myriad* distinguishes claims to isolated DNA from claims to other types of isolated molecules. Rather than arguing against the patentability of isolated and purified non-DNA molecules, *Myriad* acknowledges the patentability of claims to chemical entities based on structure and not "information" and distinguishes them from claims to DNA because infringement may be avoided by making a minor change to the chemical structure, whereas a change to the sequence information of DNA is not possible without losing the value of the DNA itself. Unlike the DNA sequence claims of *Myriad*, Applicants' claim 26 specifically recites the word "structure" three times and provides the molecular structural drawings to specifically describe the newly discovered and claimed purified Pipecolidepsin A, B and C compounds.

Finally, ending its decision by stating that it was "merely" about "genes and the information they encode," the Supreme Court confirms that, despite considerable discussion regarding the patentability of other isolated and purified products during the *Myriad* oral

argument at the Supreme Court, argument that included the hypothetical therapeutic Amazon product exemplified in the Guidance, the Court affirmatively states that its decision does not relate to non-DNA products. In fact, when counsel for Petitioners was asked by the Court whether an extracted product would be patentable, counsel for Petitioner confirmed such an extracted product would be patent eligible:

> Mr. Hansen: No, that may well be eligible because you have now taken what was in nature and you've transformed it in two ways. First of all, you've made it substantially more concentrated than it was in nature; and second, you've given it a function. If it doesn't work in the diluted form but does work in a concentrated form, you've given it a new function. And the – by both changing its nature and by giving it a new function, you may well have patent --

Myriad, Sup. Ct. transcript from oral argument, April 15, 2013 at 8. Despite this and further colloquy regarding the product from the Amazon, the Court clearly limited its decision to DNA. Accordingly, to the extent the Guidance is applied to purified natural products that are not DNA, and the Examiner has relied on the Guidance, there is no basis in *Myriad*, upon which the Guidance states it relies, to support a rejection of such claims.

As the cases concerning purified natural products above exemplify, discovering new therapeutic compounds, patenting them, developing them as therapeutics and modifying them to arrive at new ones is the paradigm that has fueled the pharmaceutical industry for over hundred years. Applicants emphasize that the holding in *Myriad* has no bearing on the patentability of purified non-DNA natural products wherein these purified compositions have markedly distinct characteristics from the natural material from which they were derived and wherein the step of isolation confers a new utility to the purified material.

The factors created by the USPTO, presented in the Guidance and used to reject the present claims require that a claim recite elements or steps that are in addition to the judicial exceptions and "that add significantly more to the judicial exception." Further, the Guidance has inappropriately set the threshold for patentability to the presence of "a marked difference in *structure*" from the naturally occurring products. The Guidance claims that "*Myriad* is a reminder that claims reciting or involving natural products should be examined for a marked difference under *Chakrabarty*." However, *Chakrabarty*'s standard is "markedly different *characteristics* from any found in nature and one having the potential for *significant utility*." Emphasis added.

Chakrabarty, at 310. The Guidance further states that *Myriad* has "clarified that not every change to a product will result in a marked difference, and that the mere recitation of particular words (e.g., "isolated") in the claims does not automatically confer eligibility." However, as explained above, by reciting that the claimed compounds are "purified," Applicants do confer a significantly different characteristic on the compounds as claimed compared to their characteristics in their natural environment of the marine sponge and that difference results in a significant utility not found in the natural source – treatment of cancer.

The USPTO issued its Guidance under the premise that *Myriad* has changed the law regarding the patentability of purified natural products. However, as explained above, neither *Myriad*, nor its reliance on *Chakrabarty*, change the long held legal standard that entitles patent protection to those inventors who produce new compositions isolated from nature that possess different characteristics and substantial utility, as discussed above. Such protection provides the necessary "incentives that lead to creation, invention, and discovery" (*Mayo Collaborative Services, v. Prometheus Laboratories, Inc., 566 U.S.___*, , Slip Op. at 23) of new therapeutics that continue to improve the health of countless people throughout the world. In addition, the Supreme Court's explanation in *Chakrabarty* of the definition of "manufacture" as used in section 101 citing to *American Fruit Growers, Inc. v. Brogdex Co., 283 U.S.1, 11 (1931)* as "the production of articles for use from raw or prepared materials by giving to these materials new forms, qualities, properties, or combinations, whether by hand-labor or by machinery" provides strong basis to support the patent eligibility of purified natural products. Such purified products, as Applicants' claimed products, are purified from a raw material, the marine sponge; are given a new form by being separated from the marine organism and other chemical compounds and being in a suitable buffer or other form; and have new qualities and properties resulting in a new utility, treating cancer, which is unrelated to its activity in nature as it resides in the sponge.

Even within the USPTO's newly issued guidelines, the claimed purified compounds and purified compositions differ from the substance from which they were purified not only in degree, but more importantly in kind. Specifically, the application discloses a new specific, substantial, and credible utility under 35 U.S.C. §101 for the claimed purified compounds and purified compositions. In particular, the application describes that the claimed compounds and compositions are therapeutically useful for treating cancer (see, the Specification at ¶¶ [0020]-[0022] and [0062]-[0064]). The specification establishes that purified Pipecolidepsins A, B and

C exhibit cytotoxic activity in *in vitro* assays of cell lines derived from human lung carcinoma (A549 CCL-185), human colon colorectal adenocarcinoma ((NSCLC) HT29 HTB-38) and human breast adenocarcinoma (MDA-MB-231 HTB-26). These assays indicate that purified Pipecolidepsin A, B and C are highly active compounds that effect i) 50% cell growth inhibition (GI_{50}), ii) total cell growth inhibitions (TCI) and iii) 50% net cell killing at low concentrations compared to control cultures. In contrast, the naturally occurring marine sponge from which the inventive compounds and compositions were originally extracted, *Homophymia lamellose*, is not known to have any utility in the treatment of human disease.

The claimed purified compounds, as a whole, are markedly different than the composition found in nature having a new and distinct utility of treating cancer. As such, the patentability of the claimed subject matter is consistent with Supreme Court precedent. Applicants' claims constitute a new and useful composition of matter and methods of use thereof within the meaning of § 101. Accordingly, Applicants respectfully request withdrawal of this ground of rejection.

Claims 27, and 34-36 Pharmaceutical Compositions

The claimed pharmaceutical compositions are patent eligible subject matter for at least the reasons that the purified compounds in the pharmaceutical compositions represent chemical compositions that are not 'naturally occurring,' as discussed above.

In addition to depending from purified compound claim 26, claims 27, 34-36 and 44-47 have the additional meaningful element that the claims are directed to a pharmaceutical composition which includes "a pharmaceutically acceptable carrier or diluent." The claimed pharmaceutical compositions include a further distinction from the product of nature from which they were originally derived in that these compositions which comprise the purified compound in a pharmaceutically acceptable carrier or diluent are suitable for pharmaceutical use, e.g., human administration. In particular, the specification contemplates administration of the claimed pharmaceutical compositions by intravenous infusion, or orally or topically. Applicants further submit that a person of ordinary skill in the art would readily appreciate that Pipecolidepsins A, B and C, as found in their natural state within the marine organism would not be suitable for use in the claimed pharmaceutical compositions, in particular with respect to oral administration and intravenous infusion.

Also, in order to achieve a typical therapeutic concentration of Pipecolidepsin A, for example, the active concentration corresponding to an LC_{50} for human breast carcinoma, i.e., 1.75 E -6 M (see, the Specification at Table 4), assuming that an average 155 lb person has a total water volume of 42 L, 113 mg of Pipecolidepsin A would be required to be administered, assuming that Pipecolidepsin A is distributed throughout the body water. Considering that an 82 gram specimen affords 2 mg pure Pipecolidepsin A having a MW of 1541.9, (see Specification at Example 1, ¶¶ [0066]-[0069]), a therapeutic dose would require administering 57 sponges or 4.7 kilograms of sponge either orally or via intravenous infusion. Clearly, by purifying the claimed compounds and providing them to be concentrated into pharmaceutical compositions in a pharmaceutically acceptable carrier or diluent, one is able to administer reasonable dosage forms. Moreover, even if the pharmaceutically acceptable diluent is a well known diluent such as phosphate buffered saline, the presence of the newly discovered compounds in such a new and unnatural environment imparts an entirely new utility making this element more than just "nominally, insignificantly, or tangentially related to the judicial exception(s)."

Claims 30, and 37-39 Methods of Treatment

The claimed methods of treatment are patent eligible subject matter for at least the reasons that the purified compounds represent chemical compositions that are not 'naturally occurring,' as discussed above. In addition, as method of treatment claims, claims 30, 38, 39 and 48-51 also recite additional elements that add a new feature to the judicial exception. Only after discovering the new compounds, purifying them and testing them for biological activity were Applicants able to claim methods of using the purified compounds to treat the specific forms of cancer being claimed, lung, colon and breast. The recitation of the method using newly discovered compounds to treat specific forms of cancer adds meaningful elements to the claims, making the subject matter claimed significantly different from the compounds found in the marine sponge. At least factors b, c, d and f of the Guidance supporting patent eligibility are met.

Applicants disagree with the Examiner's contention that none of factors b, c, d and e are satisfied. Applicants agree that factor f is satisfied. Regarding factor b, the Examiner contends that, even though Applicants claims state methods for treating lung, colon and breast cancer, such elements do "not meaningfully limit the scope of the claims of a particular application of

Pipecolidepsins A, B and C because the composition does not markedly differ from the composition found in nature. The methods do not recite a specific dose, regime, administration route, carrier or formulation. As a result, others are substantially foreclosed from using Pipecolidepsins A, B and C to treat lung, colon and breast cancer." The Examiner's rejection is not supported by the law and is at odds with the fundamental basis for why patents are granted. Applicants have searched the oceans and discovered that a marine sponge has compounds that, when purified from their natural source and formulated in a pharmaceutically acceptable carrier or diluent, are useful for treating specific forms of cancer. Applicants' method claims do not by themselves foreclose others from using the compounds for a myriad of other purposes whether those purposes are medicinal or not. Methods of using the compounds for cardiovascular, neurologic or other cancers not specifically recited are not foreclosed by Applicants' method claims. Applicants point out that in their Amendment and Remarks filed on June 11, 2013, Applicants had amended their claims from methods of treating cancer generally, to the three types that are now specifically recited. Thus, the method claims contain additional meaningful limitations related to the discoveries made by Applicants satisfying element b.

Regarding Factor c, the Examiner improperly requires that the claims be limited to a specific dose, regime or administration. A "therapeutically effective amount" is a meaningful claim element that has a long and accepted use in pharmaceutical claims. As the calculations shown above clearly demonstrate, being able to administer meaningful therapeutically effective amounts of the claimed compounds to one in need thereof rather than the kilogram quantities of marine sponge that would need to be administered to such a person, which would not even be possible in the form of the sponges, is a significant addition to the judicial exception therefore satisfying Factor c.

Regarding Factor d, Applicants assert that this factor is satisfied for the same reasons discussed above regarding factors b and c. By including the specific elements of treating specific forms of cancer with a therapeutically effective dose, Applicants have provided significant elements to the claim to make it significantly different from the judicial exception.

The Examiner's recognition that factor f is satisfied should be sufficient to support patentability of the claims as Applicants have provided new compounds not known to exist before which provide new methods for treating serious, often fatal, diseases. Applicants

distinguish the pending method claims from those at issue in the *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, S.Ct. 440, 92 L.Ed. 588 wherein the isolated bacteria was determined to have "the same effect it as always had" and continued to "serve the ends nature originally provided and act quite independently of any effort of the patentee." Instead, Applicant's claimed purified products and methods of using the purified compounds are for an entirely different use than they serve in the natural source from which Applicants' materials were first obtained. In particular, unlike *Funk Bros.* where bacteria were put back into the environment from which they came so that they could function as they naturally, do, Applicants do not put the compounds back into their normal habitat at all and, in fact, use them for a function having nothing to do with their marine environment. Instead, Applicants' have devoted considerable effort to discover and purify the claimed compounds so that they can be used in pharmaceutical compositions for treating people with cancer, a utility also discovered by Applicants that is far from whatever the compounds do in their natural environment in the marine sponge in the ocean. Applicants point out that the Examiner has acknowledged that "it was not well known to use Pipecolidepsins A, B and C or the organism from which they are isolated/purified to treat lung, colon or breast cancer." Office Action, page 6.

In summary, the amended claims are directed to patent eligible subject matter. For at least the reasons discussed above, Applicants respectfully request reconsideration and withdrawal of the rejection under U.S.C. § 101 of claims 26, 27, and 30-39.

Rejection under 35 U.S.C. § 102

Claims 26, and 31-33 are rejected under pre AIA 35 U.S.C. § 102(b) as being anticipated by Vacelet & Vasseur, 1971. Applicants respectfully traverse this rejection.

The Examiner states that instant claims 26, and 31-33 are drawn to compounds of Pipecolidepsins A, B and C and do not require that the compounds be isolated or separated from the sponge in which they occur naturally. The Examiner therefor believes that Vacelet & Vasseur inherently disclose Pipecolidepsins A, B and C and anticipate the instant claims.

As discussed above, the claims 26, and 31-33 are amended herein without prejudice and recite wherein the claimed compounds are "purified." Vacelet & Vasseur do not suggest or

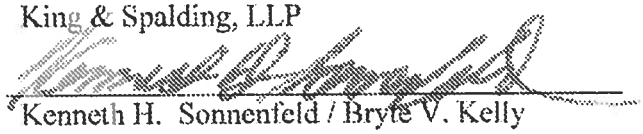
disclose extracting and purifying the specific Pipecolidepsins A, B and C compounds from the marine sponges. Thus the pending claims are novel over the cited art. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 26, and 31-33 for lack of novelty.

Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejections and allowance of this application.

AUTHORIZATION

The Commissioner is hereby authorized to credit any overpayment or charge any additional fees which may be required to Deposit Account No. 50-3732, Order No. 13566.105066.

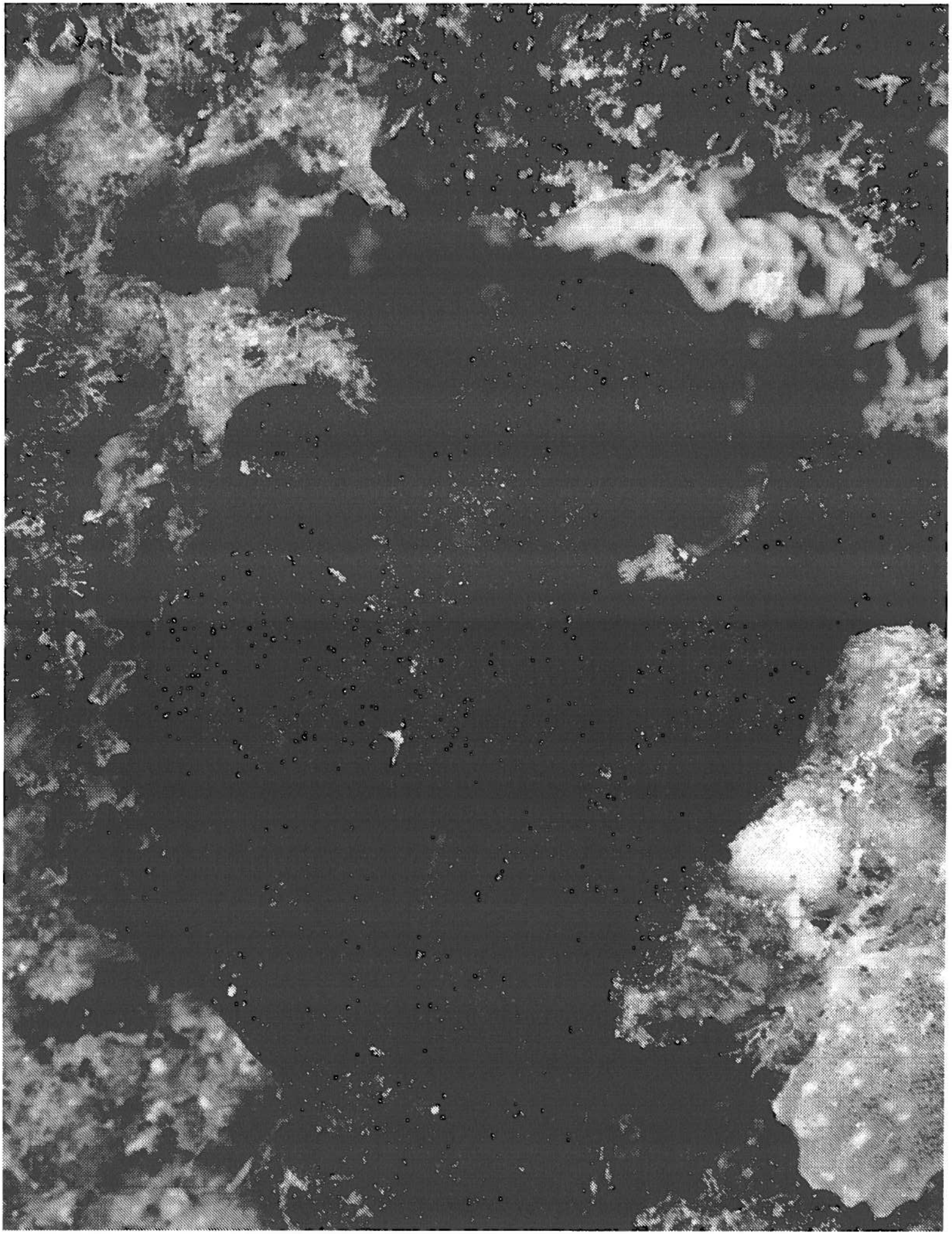
Respectfully submitted,
King & Spalding, LLP

Dated: June 9, 2014 By: 

Kenneth H. Sonnenfeld / Bryte V. Kelly
Reg. No. 33,285 / Reg. No. 63,660

Customer Number 65989
Correspondence Address:
King & Spalding
1185 Avenue of the Americas
New York, NY 10036-4003
(212) 556-2100 Telephone
(212) 556-2222 Facsimile

Exhibit 1



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/133,359	06/07/2011	Laura Coello Molinero	13566-105066	2441

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KING & SPALDING
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036-4003

EXAMINER	
BRADLEY, CHRISTINA	
ART UNIT	PAPER NUMBER
1675	

NOTIFICATION DATE	DELIVERY MODE
06/20/2014	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

usptomailnyc@kslaw.com

Office Action Summary	Application No. 13/133,359	Applicant(s) COELLO MOLINERO ET AL.	
	Examiner CHRISTINA BRADLEY	Art Unit 1675	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *June 9, 2014*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) *26,27 and 30-51* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *26, 27, and 30-51* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

4) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 26, 27, and 30-51 are pending. Claims 26, 27, and 30-39 were amended and claims 40-51 were added in the response filed June 9, 2014.

The rejection of claims 26, and 31-33 under pre-AIA 35 U.S.C. 102(b) as being anticipated by Vacelet & Vasseur is withdrawn in view of the amendment filed June 9, 2014.

Interview Summary

In a telephone conversation with Kenneth Sonnenfeld on June 16, 2014, the Examiner informed Applicant that the 102 rejection would be withdrawn and that the 101 rejection would be maintained in response to the amendment filed June 9, 2014. The Examiner stated that the 101 rejection is consistent with the USPTO's guidance on patent eligibility, and advised Applicant to appeal the rejection rather than file an RCE.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 26, 27, and 30-51 are rejected under 35 U.S.C. 101 because the claimed invention is not directed to patent eligible subject matter. Based upon an analysis with respect to the claim as a whole, claim(s) 26, 27, and 30-51 do not recite something significantly different than a judicial exception. The rationale for this determination is explained below and is based on the analysis presented in the USPTO's "Guidance For Determining Subject Matter Eligibility Of Claims Reciting Or Involving Laws of Nature, Natural Phenomena, & Natural Products" dated March 4, 2014 (hereafter "Guidance", refer to the flow chart in Section I of the Guidance).

Claims 26, 31-33, and 40-43

Question 1: The instant claims are directed to a statutory patent-eligible subject matter category, composition of matter.

Question 2: The claims involve a judicial exception, natural products. The instant claims recite Pipecolidepsins A, B and C. As evidenced by the instant specification on p. 18, lines 7-11, these compounds are naturally-occurring:

Pipecolidepsins A, B and C were isolated from a sponge of the order Lithistida, family Neopeltidae, genus Homophymia, species Homophymia lamellosa Vacelet & Vasseur, 1971. This sponge was collected by hand using SCUBA diving in Saint Marie Island, Madagascar (17° 07. 436'S / 49° 47. 525' E) at depths ranging between 3 and 7 m.

Question 3: To determine if the claim as a whole recites something significantly different than the judicial exception, the following factors are considered.

With respect to factors weighing toward eligibility:

• Factor a) is not satisfied, because there is no structural difference between the Pipecolidepsins A, B and C claimed and the Pipecolidepsins A, B and C found in nature.

The word "purified" does not render the claim markedly different from what exists in nature. *Myriad* clarified that not every change to a product will result in a marked difference, and that the mere recitation of particular words (e.g., "isolated") in the claims does not automatically confer eligibility. *Id.* at 2119. *See also Mayo*, 132 S. Ct. at 1294 (eligibility does not "depend simply on the draftsman's art").

• Factors b) through f) are not relevant, because the claims do not include any elements in addition to the natural product.

With respect to factors weighing against eligibility:

• Factor g) is satisfied. The claim is a product claim reciting Pipecolidepsins A, B and C and is not markedly different from naturally occurring Pipecolidepsins A, B and C.

• Factors h) through l) are not relevant, because the claim does not include any elements in addition to the natural product, i.e., there is nothing in the claim other than the natural product.

In sum, when the relevant factors are analyzed, they weigh against significantly different. Accordingly, the claim does not qualify as eligible subject matter.

Response to Arguments

Applicant's arguments filed June 9, 2014 have been fully considered but they are not persuasive.

Applicant argues on pages 9-10 of the response that the claim is drawn to a new aggregate structure resulting from purification steps which separate the Pipecolidepsins A, B and C from the marine sponge in which they are found in nature. Applicant argues that this new aggregate structure imparts a new utility of treating cancer on the purified product, and that for these reasons the claimed product is significantly different from the natural product.

It is noted that instant claims 26, 31-33, and 40-43 are analogous to claim 1 in Example B of the Guidance. Claim 1 of Example B is drawn to purified amazonic acid. The Example B applicant isolated and purified a cancer-fighting chemical from the leaves of the Amazonian cherry tree and discovered that a patient only needs one teaspoon of purified acid to get the same effects as 30 pounds of leaves. The Guidance considers the fact that the compound is removed from the natural environment of the leaves and concludes that purified amazonic acid is not patent eligible because there is no structural difference between the purified acid in the claim and the acid in the leaves. In contrast, claim 2 of Example B drawn to purified 5-methyl amazonic

acid is considered to be patent eligible because the 5-methyl group was added in the laboratory and is not found in the natural product.

The instantly claimed purified Pipecolidepsins A, B and C are analogous to the purified amazonic acid in Example B and are patent ineligible for the same reasons presented in Example B of the Guidance.

The additional arguments on pages 10-16 of the response pertain to the validity of the Guidance itself. Because this rejection is consistent with the Guidance, it is maintained.

Claims 27, 34-36 and 44-47

Question 1: The instant claims are directed to a statutory patent-eligible subject matter category, a composition of matter.

Question 2: The claims involve a judicial exception, natural products. The instant claims recite Pipecolidepsins A, B and C. As evidenced by the instant specification on p. 18, lines 7-11, these compounds are naturally-occurring:

Pipecolidepsins A, B and C were isolated from a sponge of the order Lithistida, family Neopeltidae, genus Homophymia, species Homophymia lamellosa Vacelet & Vasseur, 1971. This sponge was collected by hand using SCUBA diving in Saint Marie Island, Madagascar (17° 07. 436'S / 49° 47. 525' E) at depths ranging between 3 and 7 m.

Question 3: To determine if the claim as a whole recites something significantly different than the judicial exception, the following factors are considered.

With respect to factors weighing toward eligibility:

• Factor a) is not satisfied because there is no structural difference between the Pipecolidepsins A, B and C claimed and the Pipecolidepsins A, B and C found in nature. The specification does not provide a limiting definition for the term "pharmaceutical composition".

Although one of ordinary skill in the art would construe this term to mean a composition suitable for pharmaceutical use and possibly for human administration, this does not render the claim markedly different from what exists in nature. *Myriad* clarified that not every change to a product will result in a marked difference, and that the mere recitation of particular words (e.g., "isolated") in the claims does not automatically confer eligibility. *Id.* at 2119. *See also Mayo*, 132 S. Ct. at 1294 (eligibility does not "depend simply on the draftsman's art").

• Factor b) is not satisfied. The inclusion of Pipecolidepsins A, B and C in a pharmaceutical composition and the addition of a carrier or diluent does not meaningfully limit the scope of the claim. The claims do not recite a specific dose, regime, administration route, carrier or formulation. As a result, others are substantially foreclosed from using Pipecolidepsins A, B and C.

• Factor c) is not satisfied. The pharmaceutical composition is not significantly related to the judicial exception because it is not an element that impacts the Pipecolidepsins A, B and C in a particular way. The claims do not recite a specific dose, regime, administration route, carrier or formulation.

• Factor d) is not satisfied. The claims are not more than a general instruction to use Pipecolidepsins A, B and C.

• Factor e) is not satisfied. There is no machine or transformation recited in the claim.

• Factor f) is satisfied. It was not well-known, routine or conventional to use Pipecolidepsins A, B and C in a pharmaceutical composition.

With respect to factors weighing against eligibility:

• Factor g) is satisfied because there is no structural difference between the Pipecolidepsins A, B and C claimed and the Pipecolidepsins A, B and C found in nature..

• Factor h) is satisfied because the pharmaceutical composition is recited at a high level of generality. The claims do not require a specific dose, regime, administration route, carrier or formulation .

• Factor i) is satisfied. Pipecolidepsins A, B and C cannot be applied in other ways, e.g., other doses, regimes, administration routes, carriers or formulations.

• Factor j) is not satisfied. It was not well-known to use Pipecolidepsins A, B and C or the organism from which they are isolated to treat lung, colon or breast cancer.

• Factor k) is satisfied. The inclusion of the compounds in a pharmaceutical composition is merely appended to the judicial exception, and is not significantly related to the Pipecolidepsins A, B and C.

• Factor l) is satisfied. The inclusion of the compounds in a pharmaceutical composition is not more than a mere field of use because the claims do not require a specific dose, regime, administration route, carrier or formulation

In sum, when the relevant factors are analyzed, they weigh against significantly different. Accordingly, the claim does not qualify as eligible subject matter.

Response to Arguments

Applicant's arguments filed June 9, 2014 have been fully considered but they are not persuasive.

Applicant argues on pages 16-17 of the response that claims 27, 34-36 and 44-47 have the additional element of a "pharmaceutically acceptable carrier or diluent." Applicant notes that

Pipecolidepsins A, B and C, as found in their natural state within the marine organism, would not be suitable for oral or intravenous administration.

It is noted that broadest reasonable interpretation of the claim term "pharmaceutically acceptable carrier or diluent" includes water, another natural product. Therefore, the claims encompass a combination of natural products, purified Pipecolidepsins A, B and C and water. This scenario is considered in Example D of the Guidance which states a combination of natural products is patent ineligible if the composite elements are not markedly different from what exists in nature (see *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 131 (1948)). In the instant case, the dilution of purified Pipecolidepsins A, B and C in water would not change the chemical structure of either the Pipecolidepsins A, B and C or the water.

Applicant argues on page 17 that in order to achieve a typical therapeutic concentration of Pipecolidepsin A for human breast carcinoma, 113 mg of Pipecolidepsin A would have to be administered. This dose would require administering 57 sponges or 4.7 kilograms of sponge orally or via intravenous infusion daily. This argument is addressed in Example B of the Guidance. The fact that a teaspoon of purified amazonic acid was found to be therapeutically equivalent to 30 pounds of leaves was not sufficient to render the purified amazonic acid patent eligible.

Claims 30, 37-39, and 48-51

Question 1: The instant claims are directed to a statutory patent-eligible subject matter category, a process.

Question 2: The claims involve a judicial exception, natural products. The instant claims recite Pipecolidepsins A, B and C. As evidenced by the instant specification on p. 18, lines 7-11, these compounds are naturally-occurring:

> Pipecolidepsins A, B and C were isolated from a sponge of the order Lithistida, family Neopeltidae, genus Homophymia, species Homophymia lamellosa Vacelet & Vasseur, 1971. This sponge was collected by hand using SCUBA diving in Saint Marie Island, Madagascar (17° 07. 436'S / 49° 47. 525' E) at depths ranging between 3 and 7 m.

Question 3: To determine if the claim as a whole recites something significantly different than the judicial exception, the following factors are considered.

With respect to factors weighing toward eligibility:

• Factor a) is not relevant because the claim is a process claim, not a product claim.

• Factor b) is not satisfied. The step of administering Pipecolidepsins A, B and C to a particular patient (patient with lung, colon or breast cancer) does not meaningfully limit the scope of the claim to a particular application of Pipecolidepsins A, B and C because the composition does not markedly differ from the composition found in nature. The methods do not recite a specific dose, regime, administration route, carrier or formulation. As a result, others are substantially foreclosed from using Pipecolidepsins A, B and C to treat lung, colon and breast cancer.

• Factor c) is not satisfied. The administering step is not significantly related to the judicial exception because it is not a step in which Pipecolidepsins A, B and C are manipulated in a particular and significant way. The methods do not recite a specific dose, regime or administration nor do they require specific carrier or formulation.

• Factor d) is not satisfied. The administering step requires administration of Pipecolidepsins A, B and C to a patient with lung, colon or breast cancer but does not recite a

specific dose, regime, administration route, carrier or formulation. The methods are not more than a general instruction to use Pipecolidepsins A, B and C.

• Factor e) is not satisfied. There is no machine or transformation recited in the claim.

• Factor f) is satisfied. It was not well-known, routine or conventional to use Pipecolidepsins A, B and C to treat lung, colon or breast cancer.

With respect to factors weighing against eligibility:

• Factor g) is not applicable because the claim is not a product claim.

• Factor h) is satisfied because the administering step is recited at a high level of generality. The claims do not require a specific dose, regime, administration route, carrier or formulation

• Factor i) is satisfied. Pipecolidepsins A, B and C cannot be applied in other ways, e.g., other doses, regimes, administration routes, carriers or formulations.

• Factor j) is not satisfied. It was not well-known to use Pipecolidepsins A, B and C or the organism from which they are isolated to treat lung, colon or breast cancer.

• Factor k) is satisfied. The administering step is merely appended to the judicial exception, and is not significantly related to the Pipecolidepsins A, B and C.

• Factor l) is satisfied. Administering Pipecolidepsins A, B and C to specific patients is not more than a mere field of use because the claims do not require a specific dose, regime, administration route, carrier or formulation

In sum, when the relevant factors are analyzed, they weigh against significantly different. Accordingly, the claim does not qualify as eligible subject matter.

Response to Arguments

Applicant's arguments filed June 9, 2014 have been fully considered but they are not persuasive.

On pages 17-18 of the response, Applicant argues that factor b) is satisfied because the claims do not foreclose others from using the compounds for a myriad of other purposes such as for non-medicinal proposes or for treating conditions other than those recited in the claims. This argument is not persuasive because the claims prohibit others from using the natural product for treating lung, colon and breast cancer. Because the claim is not limited in dose or administration schedule, others would be foreclosed from using Pipecolidepsins A, B and C for all applications pertaining to the treatment of lung, colon and breast cancer. There is no evidence in the specification or on record that the claimed compounds could be used for other purposes.

On page 18 of the response, Applicant argues that factor c) is satisfied because a "therapeutically effective amount" is a meaningful claim element and that it is not possible to administer an effective amount of the claimed compounds by administering the marine sponge directly. This argument is not persuasive. The claim term "therapeutically effective amount" is meaningful and encompasses all dosages that are effective to treat lung, colon and breast cancer. Therefore, there are no doses excluded from the claims, a fact which forecloses others from using the claimed composition for this purpose.

On page 18 of the response, Applicant argues that factor d) is satisfied because the specific elements of treating specific forms of cancer with a therapeutically effective dose make the claim significantly different from the judicial exception. This argument is not persuasive because the claim is so broad as to include all dosages that are effective to treat the diseases.

On page 18 and 19, Applicant addresses factor f). The Examiner agrees that factor f) is satisfied but that when weighed with the other factors is insufficient to reach a conclusion of eligibility.

For these reasons, the rejection is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTINA BRADLEY whose telephone number is (571)272-9044. The examiner can normally be reached on Monday through Friday from 5:30 A.M. to 3:00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Alstrum-Acevedo can be reached on (571) 272-5548. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CHRISTINA BRADLEY/
Primary Examiner, Art Unit 1675

cmb