

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PROGENICS PHARMACEUTICALS, INC.,
Petitioner,

v.

MAX-PLANCK-GESELLSCHAFT ZUR FOERDERUNG DER
WISSENSCHAFTEN E.V.
AND
UNIVERSITAT ZU KOLN,
Patent Owners.

PGR2019-00052
Patent 10,112,974 B2

Before GEORGIANNA W. BRADEN, J. JOHN LEE, and
MICHAEL A. VALEK, *Administrative Patent Judges*.

VALEK, *Administrative Patent Judge*.

JUDGMENT
Final Written Decision
Determining No Challenged Claims Unpatentable
35 U.S.C. § 328(a)

I. INTRODUCTION

This Final Written Decision is issued pursuant to 35 U.S.C. § 328(a) and 37 C.F.R. § 42.73. Progenics Pharmaceuticals, Inc., (“Petitioner”) bears the burden of providing the unpatentability of the challenged claims by a preponderance of the evidence. 35 U.S.C. § 326(e) (2018). For the reasons explained below, we determine Petitioner has failed to establish by a preponderance of the evidence that claims 6, 8, and 10–12 of U.S. Patent No. 10,112,974 B2 (Ex. 1001, “the ’974 patent”) are unpatentable. Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V. and Universitat zu Koln (collectively “Patent Owner”) have disclaimed all of the other claims of the ’974 patent previously at issue in this proceeding.

A. *Procedural Background*

Petitioner filed a Petition seeking post-grant review of claims 1–15 and 31 of the ’974 patent. Paper 2 (“Pet.”). Patent Owner did not file a preliminary response. Upon consideration of the information presented in the Petition, we determined Petitioner had shown it was more likely than not that claims 1–5, 7, 9, 13, 15, and 31 were unpatentable for one or more of the asserted grounds. Paper 7, 35 (“Institution Decision”). We also explained why we were not persuaded that Petitioner had met its burden with respect to the other challenged claims. *Id.* Nevertheless, following *SAS Institute Inc. v. Iancu*, 138 S. Ct. 1348 (2018) and USPTO guidance, we instituted review of all claims challenged under all grounds in the Petition. *Id.*

After institution, Patent Owner notified the Board that it intended to file a statutory disclaimer of claims 1–5, 7, 9, 13, 15, and 31 and was waiving its opportunity to file a response and motion to amend. Paper 9, 2. Patent Owner further indicated that it would “not request adverse judgment

as to Petitioner’s grounds for claims 6, 8, 10–12, and 14.” *Id.* Thus, we ordered that “the post grant review will continue as instituted, albeit without a response or other papers from Patent Owner.” *Id.*

On March 13, 2020, Patent Owner filed a statutory disclaimer disclaiming claims 1–5, 7, 9, 13–15, and 31. Ex. 2001. Claims 1–5, 7, 9, 13–15, and 31 are, therefore, no longer at issue in this proceeding. *See* 35 U.S.C. § 253 (2018) (disclaimer of claims considered effective as if part of original patent); 37 C.F.R. § 42.207(e) (“No post-grant review will be instituted on disclaimed claims.”). Claims 6, 8, and 10–12 remain at issue.

Both Petitioner and Patent Owner subsequently confirmed that they would not request oral argument and did not intend to file any other paper prior to entry of our Final Written Decision on the remaining claims. As such, the record is complete and consists of the Petition and accompanying exhibits Ex. 1001–1033, as well as Patent Owner’s statutory disclaimer (Ex. 2001).

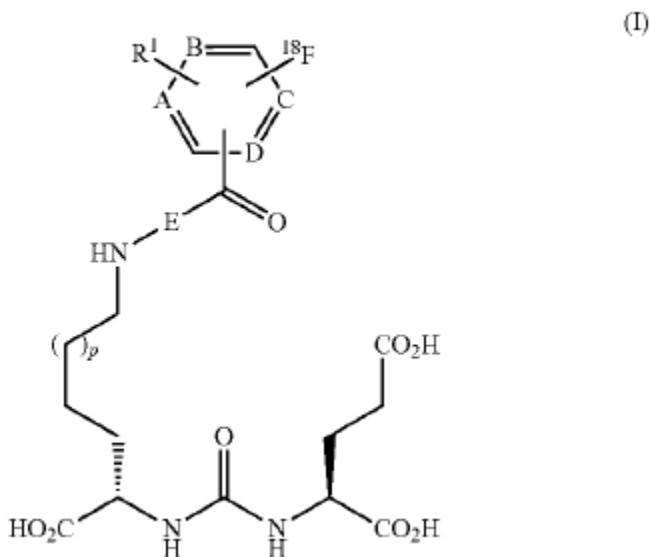
B. The ’974 Patent

The ’974 patent describes methods and chemical precursors for making “¹⁸F-labelled active esters via nucleophilic substitution of the corresponding onium precursors with ¹⁸F- . . .” Ex. 1001, Abstr. The Specification indicates that such compounds are “useful for positron emission tomography (PET) imaging, especially imaging prostate tumor.” *Id.* at 1:14–18. According to the Specification,

In recent years imaging of prostate carcinoma (PCa) with PET isotope labelled PSMA ligands has become of considerable importance in clinical diagnosis. This can mainly be attributed to the high expression of the extracellular localized prostate specific membrane antigen (PSMA) in PCa. Ligands bearing the syL-C(O)-Glu-binding motif exhibit high binding affinity to PSMA.

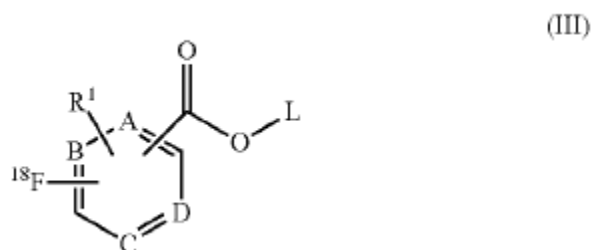
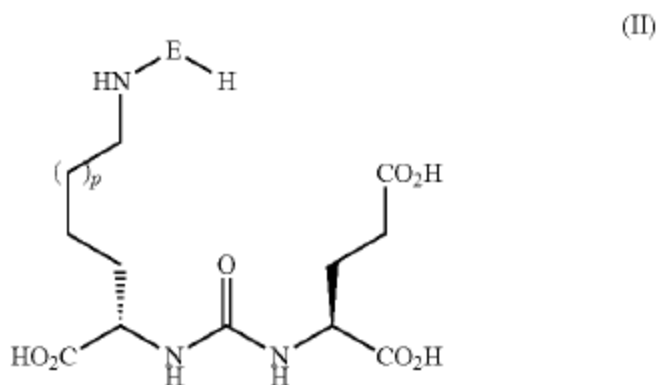
Id. at 5:60–66.

The ^{18}F -labelled compounds taught in the Specification exhibit a “syL-C(O)-Glu” or glutamate-urea-lysine (“GUL”) motif and correspond to general formula (I), which is reproduced below.

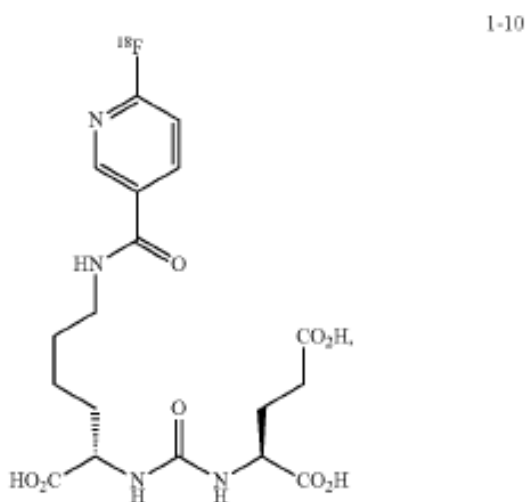


Id. at 7:40–55.¹ The compounds in formula (II) and formula (III), shown below, are described in the Specification as precursors used to make compounds of formula (I) according to the methods therein.

¹ The Specification’s descriptions for the variables depicted in formulas (I), (II), and (III) are not reproduced here for sake of brevity.



The Specification provides numerous examples of compounds corresponding to general formula (I) that may be made with the disclosed methods. *See generally id.* at 26:11–28:10; 45:45–59:60 (listing compounds). One of these examples, “[¹⁸F]DCFPyL” or compound 1-10 in the Specification, is shown below.

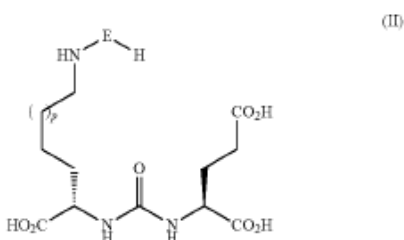


The Specification acknowledges that a method for making [^{18}F]DCFPyL was known in the prior art, but describes certain “disadvantages” to that method. *See id.* 5:66–7:20 (citing “Pomper et al. (WO2010/01493; *Clin. Cancer Res.* 2011, 17, 7645-7653) (“Pomper”)”). According to the Specification, the methods described therein involve the use of compounds corresponding to formula (II) and formula (III) as precursors and provide advantages over the prior art method in Pomper. *See id.* at 62:54–64:8 (describing “Scheme 6: The novel method for the preparation of [^{18}F]DCFPyL 1–10” and comparing it to “the published radiosynthesis of [^{18}F]DCFPyL 1–10 by Pomper et al.”).

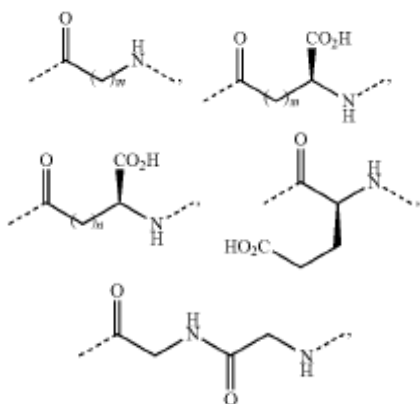
C. Illustrative Claim

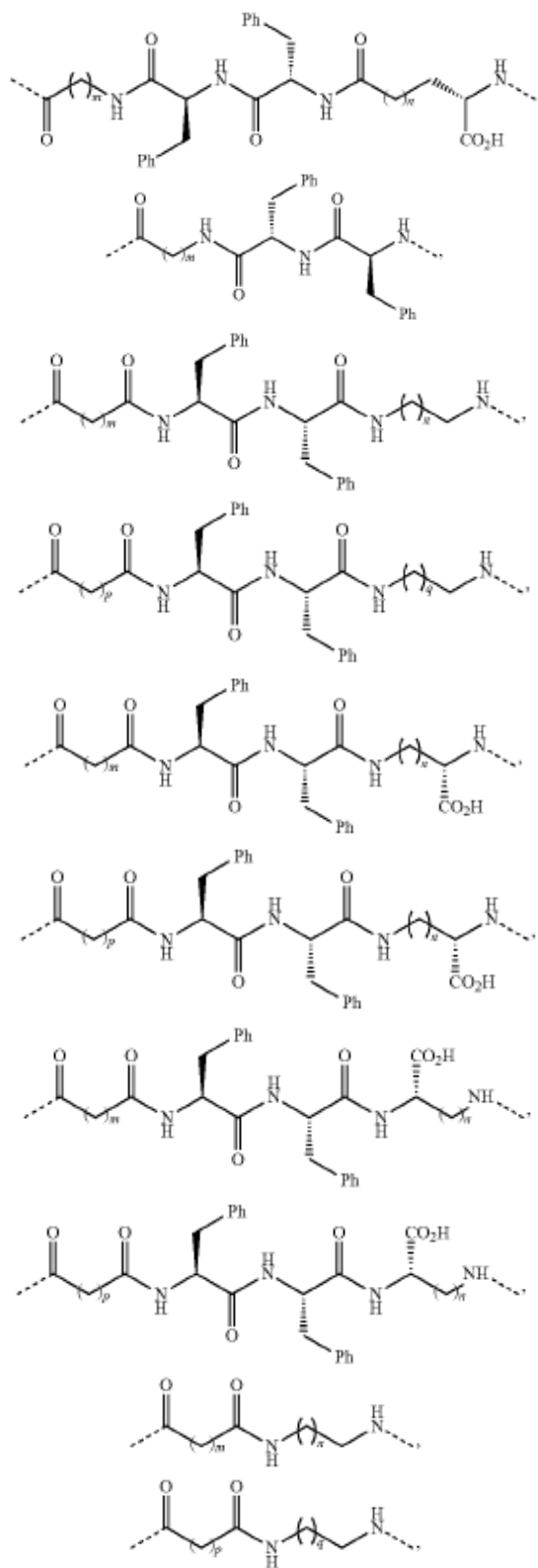
Claims 6, 8, and 10–12 depend from claim 1 and, therefore, incorporate the limitations of claim 1 as recited below:

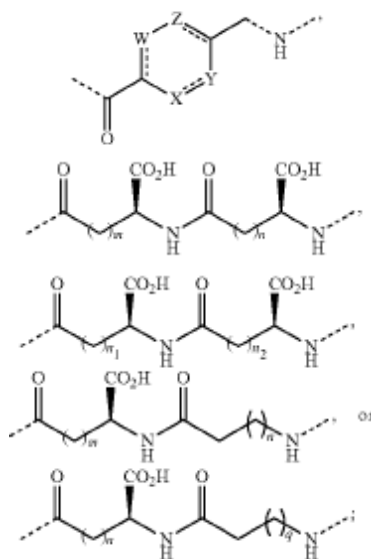
1. A compound of formula (II)



wherein, E represents a covalent bond or







wherein

- n is an integer selected from 0 to 10;
- n₁ is an integer selected from 0 to 10;
- n₂ is an integer selected from 0 to 10;
- m is an integer selected from 1 to 18;
- p is an integer selected from 0 to 10;
- q is an integer selected from 1 to 18;
- X, Y, W, and Z represent independently of each other
 —CH₂—, —CH—, —NH— or —N—;
- == represents a single or double bond;
- and diastereomers, enantiomers, hydrates, and salts thereof.

Ex. 1001, 101:25–103:25. Each of claims 6, 8, and 10–12 recite an additional limitation narrowing the range of integers for certain variables recited in claim 1. *See id.* at 108:38–55. The text of these claims, as they appear in the '974 patent, is reproduced below.

6. The compound according to claim 1, wherein either of n or n₁ or n₂ is an integer selected from 1 or 2.
8. The compound according to claim 1, wherein either of m is an integer selected from 1 to 4.

10. The compound according to claim 1, wherein either of p is an integer selected from 0, 2 to 4.

11. The compound according to claim 1, wherein either of q is an integer selected from 1 to 10.

12. The compound according to claim 1, wherein either of q is an integer selected from 1 to 3.

Id.

D. The Asserted Grounds of Unpatentability

Petitioner asserted the following grounds in the Petition (Pet. 29–30):

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1, 3–15, 31	112(b)	Indefiniteness
2	112(b)	Indefiniteness
3, 4, 15	112(d)	
1–4, 9, 13, 15	102	'192 publication ²
1–5, 7, 9, 11, 12, 15	102	Shallal ³
1–4, 9, 13, 15	102	'529 publication ⁴
5–8, 10–12, 14	103	'529 publication
31	103	'933 publication ⁵

² WO2008/058192 A2, published May 15, 2008 (“’192 publication”) (Ex. 1004).

³ Hassan M. Shallal et al., *Heterobivalent Agents Targeting PSMA and Integrin- $\alpha_v\beta_3$* , *Bioconjugate Chem.*, Vol. 25, 393–405 (2014) (“Shallal”) (Ex. 1005).

⁴ WO2009/002529 A2, published Dec. 31, 2008 (“’529 publication”) (Ex. 1006).

⁵ WO2010/014933 A2, published Feb. 4, 2010 (“’933 publication”) (Ex. 1007).

1–12, 14, 15	112(a)	Enablement
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Because claim 1–5, 7, 9, 13–15, and 31 have been disclaimed, Petitioner’s asserted grounds of unpatentability as applied to those claims are now moot. The following grounds remain at issue in this proceeding:

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
6, 8, 10–12	112(b)	Indefiniteness
11, 12	102	Shallal
6, 8, 10–12	103	’529 publication
6, 8, 10–12	112(a)	Enablement

Patent Owner has chosen to waive its response to Petitioner’s arguments and evidence concerning these grounds. Nevertheless, the burden of proof for each of the alleged grounds of unpatentability remains on Petitioner.

35 U.S.C. § 326(e) (2018); *see Dynamic Drinkware, LLC v. Nat’l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015).

II.ANALYSIS

A. *Claim Construction*

In a post-grant review, the claims are construed “using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b).” 37 C.F.R. § 42.200(b)(2019). Therefore, we construe the challenged claims under the framework set forth in *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–19 (Fed. Cir. 2005) (en banc). Under this framework, claim terms are given their ordinary and customary meaning, as would be understood by a person of ordinary skill in the art at

the time of the invention, in light of the language of the claims, the specification, and the prosecution history of record. *Id.*

1. Variable “p” (claims 1–15, 31)

Petitioner asserts that the challenged claims are unpatentable under 35 U.S.C. § 112(b) because the variable “p” as recited in claim 1 is indefinite. *See* Pet. 30–35. To the extent Petitioner’s argument raises a claim construction issue, we address that issue in our analysis of Petitioner’s indefiniteness ground.

2. Remaining Claim Terms

Petitioner does not seek a construction for any other term and contends that these “claim terms should be given their ordinary and customary meaning.” Pet. 28–29. We agree that it is unnecessary to expressly construe any of the remaining claim terms to resolve the asserted grounds of unpatentability. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (explaining that it is only necessary to “construe terms ‘that are in controversy, and only to the extent necessary to resolve the controversy’” (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999))).

B. *Level of Ordinary Skill in the Art*

Petitioner describes a person with ordinary skill in the art as having “a Ph.D. degree and training in organic chemistry, medicinal chemistry, radiopharmaceutical chemistry, or a related field with at least two years of post-doctoral experience.” Pet. 18–19.

Petitioner’s description of the level of ordinary skill in the art is sufficiently supported by the record. Moreover, we note that the applied prior art reflects the appropriate level of skill at the time of the claimed invention, which is consistent with Petitioner’s description. *See Okajima v.*

Bourdeau, 261 F.3d 1350, 1355 (Fed. Cir. 2001). Thus, we adopt Petitioner’s description of a person of ordinary skill.

C. *Indefiniteness (claims 6, 8, and 10–12)*

Petitioner asserts that claims 6, 8, and 10–12 are indefinite because “[v]ariable p . . . appears at multiple locations on compounds of formula (II)” as recited in independent claim 1 and it is unclear whether: (1) “p is the same at each instance it appears in formula (II),” or (2) “p is independently selected each time it appears in formula (II).” Pet. 31. Petitioner urges that it “is not evident from the face of the claims” which of these two interpretations applies and that nothing in the intrinsic record of the ’974 patent “resolve[s] the ambiguity in the claim language.” *Id.* at 33. Thus, Petitioner argues claims 6, 8, and 10–12 by virtue of their dependency of claim 1 are indefinite under both the “reasonable certainty” standard set forth in *Nautilus Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 901 (2014), and the “amenable to two or more plausible claim constructions” analysis employed in *Ex parte Miyazaki*, 89 USPQ 2d 1207, 1211 (BPAI 2008) (precedential). *Id.*

We are not persuaded that the variable “p” in claim 1 is reasonably susceptible to Petitioner’s second interpretation. *Phillips* makes clear that the surrounding claim language should be considered in determining the proper construction of a claim term. *See Phillips*, 415 F.3d at 1314. Here, both the context provided by the surrounding claim language and well-established claim construction principles support interpreting “p” to be the same integer each time it appears in the claim.

Claim 1 recites express definitions for the variables in the recited formula. *See Ex. 1001*, 103:15–25. According to that claim language, “p is an integer selected from 0 to 10.” *Id.* But p is not the only variable given

that definition. Claim 1 also defines “n,” “n₁,” and “n₂” as “an integer selected from 0 to 10.” *Id.* If p were “independently selected each time it appears,” according to Petitioner’s second interpretation, the same variable “p” could be used throughout the recited formula. Pet. 31. Thus, the fact that claim 1 recites four different variables (i.e., p, n, n₁, and n₂) with the same definition cuts against interpreting p to be independently selected each time it appears in the recited formula because such an interpretation would render the other identically-defined variables redundant. *See, e.g., Akzo Nobel Coatings, Inc. v. Dow Chem. Co.*, 811 F.3d 1334, 1340 (Fed. Cir. 2016) (quoting *Power Mosfet Techs., L.L.C. v. Siemens AG*, 378 F3d 1396, 1410 (Fed. Cir. 2004) (“Interpretations that render some portion of the claim language superfluous are disfavored.”)).

In addition, claim 1 defines other variables in the recited formula as follows: “wherein . . . X, Y, W, and Z represent *independently* of each other” Ex. 1001, 103:15–22 (emphasis added). The fact that claim 1 expressly recites the term “independently” to define the selection of some of the variables in the recited formula, but not “p,” evidences that independent selection is not within the plain meaning of “p” and must be separately recited. *See, e.g., Phillips*, 415 F.3d at 1314 (explaining, by way of example, that the claim’s reference to “‘steel baffles’ . . . strongly implies that the term ‘baffles’ does not inherently mean objects made of steel.”).

In addition, as a matter of general claim construction principles, there is a “presumption that the same terms appearing in different portions of the claims should be given the same meaning unless it is clear from the specification and prosecution history that the terms have different meanings at different portions of the claims.” *Paragon Sol., LLC v. Timex Corp.*, 566 F.3d 1075, 1087 (Fed. Cir. 2009) (quoting *PODS, Inc. v. Porta Stor, Inc.*,

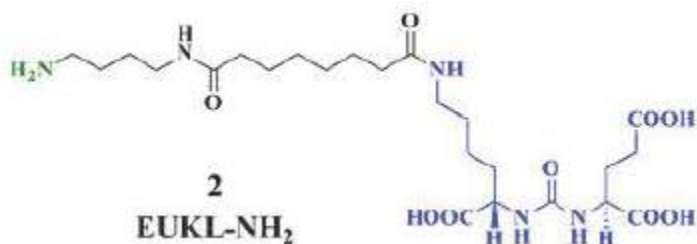
484 F.3d 1359, 1366 (Fed. Cir. 2007)). Petitioner’s first interpretation is consistent with this presumption because it interprets “p” to be the same integer at each instance of “p” in recited formula. On the other hand, Petitioner’s second interpretation runs contrary to the presumption because, as Petitioner points out, that interpretation allows “p” to have different meanings at each instance of “p” in the recited formula. See Pet. 32–33 (giving an example where “p is 1 on the lysine-like moiety” and p is “6 on the linker”). Petitioner acknowledges that “nothing within the specification provides context” for selecting one interpretation over the other and Patent Owner “did not comment on the interpretation of p during prosecution.” *Id.* at 33. Thus, there is nothing in the Specification or prosecution history that provides the clear evidence typically necessary to depart from the presumption that “p” has the same meaning each time it appears in Patent Owner’s claims. Moreover, as explained above, the surrounding claim language affirmatively supports that “p” should be construed to be the same integer throughout claim 1.

For these reasons, we construe “p” to be limited to the same integer selected from 0 to 10 at each instance within the formula recited in claim 1 (and by dependency claims 6, 8, and 10–12). We do not agree that variable “p” is reasonably amenable to Petitioner’s second interpretation. Thus, we do not agree with Petitioner that claims 6, 8, and 10–12 are indefinite according to the analysis in *Miyazaki*. For similar reasons, we also are unmoved by Petitioner’s argument that these claims fail to meet the “reasonable certainty” standard in *Nautilus*. Accordingly, we determine Petitioner has failed to show that claims 6, 8, and 10–12 are indefinite by a preponderance of the evidence.

D. Anticipation by Shallal (claims 11 and 12)

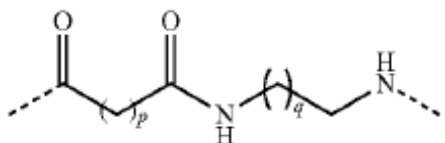
Petitioner contends that Shallal was published on January 11, 2014, and is, therefore, prior art to the '974 patent under 35 U.S.C. § 102(a)(1). Pet. 13–14. Petitioner asserts that claims 11 and 12 are anticipated by the disclosure of the compound “EUKL-NH₂” in Shallal. *See id.* 45–54.

Shallal discloses the synthesis of a “PSMA Targeting Agent” in the synthetic pathway shown in scheme 1. Ex. 1005, 397. EUKL-NH₂ is disclosed as an intermediate in that pathway with the chemical structure shown below.



Id.; *see also id.* at 394 (explaining that EUKL-NH₂ “was obtained from the corresponding protected NHS ester 1”).

Claims 11 and 12 depend from claim 1 and further limit “q” to an integer selected from “1 to 10” and “1 to 3” respectively. Ex. 1001, 108:50–54. Petitioner contends EUKL-NH₂ discloses these limitations because it corresponds to the formula recited in claim 1, wherein E has the structure shown below. Pet. 47–48.



According to Petitioner, EUKL-NH₂ is structurally identical to the formula recited in claim 1 where the p in the formula (II) backbone is 1, the p in the E group above is 6, and q is 3. *Id.* at 48.

We do not agree with Petitioner. Petitioner's argument relies upon an interpretation of the variable "p" that allows "p" to be independently selected each time it appears in the recited formula. As explained in our analysis of the indefiniteness ground, Petitioner's interpretation is not supported by the intrinsic record and runs contrary to established claim construction principles. Instead, we construe "p" such that it must be the same integer throughout the recited formula.

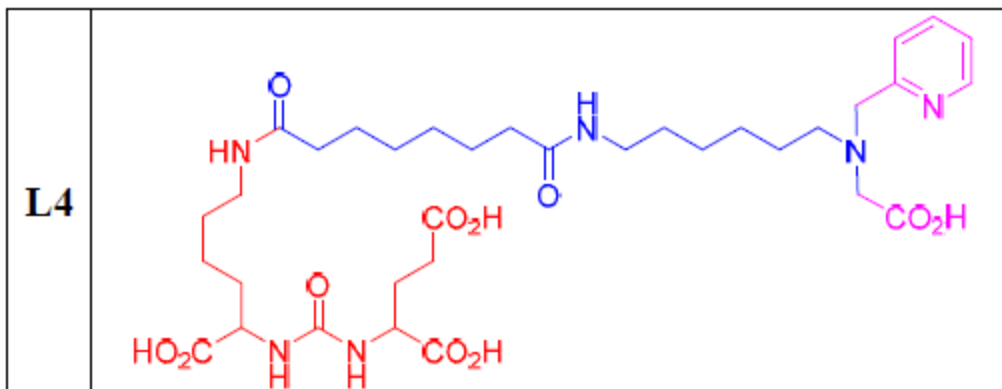
Under that construction EUKL-NH₂ does not anticipate claims 11 and 12 because EUKL-NH₂ does not disclose the recited composition wherein the "p" in the formula (II) backbone and the "p" in the selected E group are the same integer. Accordingly, Petitioner has not shown by a preponderance of the evidence that claims 11 and 12 are anticipated by Shallal.⁶

E. Obvious over the '529 Publication (claims 6, 8, 10–12)

Petitioner contends that the '529 publication, which was published on December 31, 2008, is prior art to the '974 patent under 35 U.S.C. § 102(a)(1). Pet. 14. Petitioner asserts that claims 6, 8, and 10–12 would have been obvious over the '529 publication. *See Id.* at 59–77.

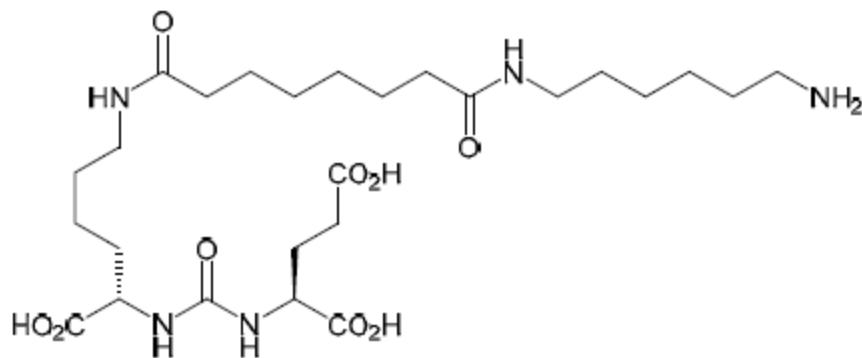
Petitioner's obviousness theory for claims 6 and 10–12 is premised on the '529 publication's disclosure of compound L4. *Id.* The structure of compound L4, as depicted in the Petition, is shown below.

⁶ The only ground of unpatentability that Petitioner advances based on Shallal is anticipation under 35 U.S.C. § 102. *See* Pet. 45–51. We have not been asked to consider whether any of the claims of the '974 patent would have been obvious over EUKL-NH₂ or any other teaching in Shallal.



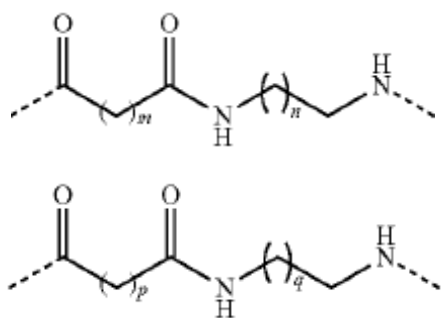
Id. at 62. According to Petitioner, such conjugates have a “modular Block A- Block B-Block C structure comprising a “GUL [Block A]” shown in red in the figure above, “a linker [Block B]” shown in blue, and a “radiolabel/chelator [Block C]” shown in pink. *Id.* at 61. Using Petitioner’s terminology, compounds of formula (II) of the ’974 patent are Block A-Block B intermediates.

Petitioner acknowledges that “the ’529 publication discloses producing L4 by coupling the GUL (Block A) to a linker-chelator intermediate (Block B-Block C).” *Id.* at 63 (citing Ex. 1006, 33 (scheme 2)). Thus, the ’529 publication does not teach the synthesis of L4 through a pathway involving a Block A-Block B intermediate like that in formula (II). But according to Petitioner, “a person of ordinary skill in the art would have recognized that L4 could also be prepared, e.g., using a GUL-linker intermediate (Block A-Block B).” *Id.* Petitioner contends this “example intermediate” would comprise a GUL moiety wherein the nitrogen in the lysine amine forms an amide with the carbonyl of a linker group composed of a six carbon alkyl chain joined by a secondary amide to another six carbon alkyl chain terminating in a primary amine as shown in the structure below (reproduced from the Petition).



Example Intermediate of L4

Id. According to Petitioner this “example intermediate” of L4 is similar to the formula of claims 6 and 10–12, where the linker group E is one of the two structures shown below and, therefore, has a structure similar to that described above. *See id.* at 68–69, 75–77.



Claims 6 and 10–12 differ from Petitioner’s “example intermediate” of L4 with respect to the length of the linker group adjacent to the terminal amine. Petitioner asserts that it would have been obvious to modify the linker of this “example intermediate” by changing the number of carbons in the linker to arrive at the compounds in claims 6 and 10–12 because the linkers in those claims are all within the “range of lysine-linker lengths taught by the ’529 publication (i.e., of between 7.7 and 33 Å).” *Id.* at 68 (citing Ex. 1006, 31:11–16, 38:29–39:2).

We do not agree with Petitioner’s argument that claims 6 and 10–12 would have been obvious over the ’529 publication. A patent claim is

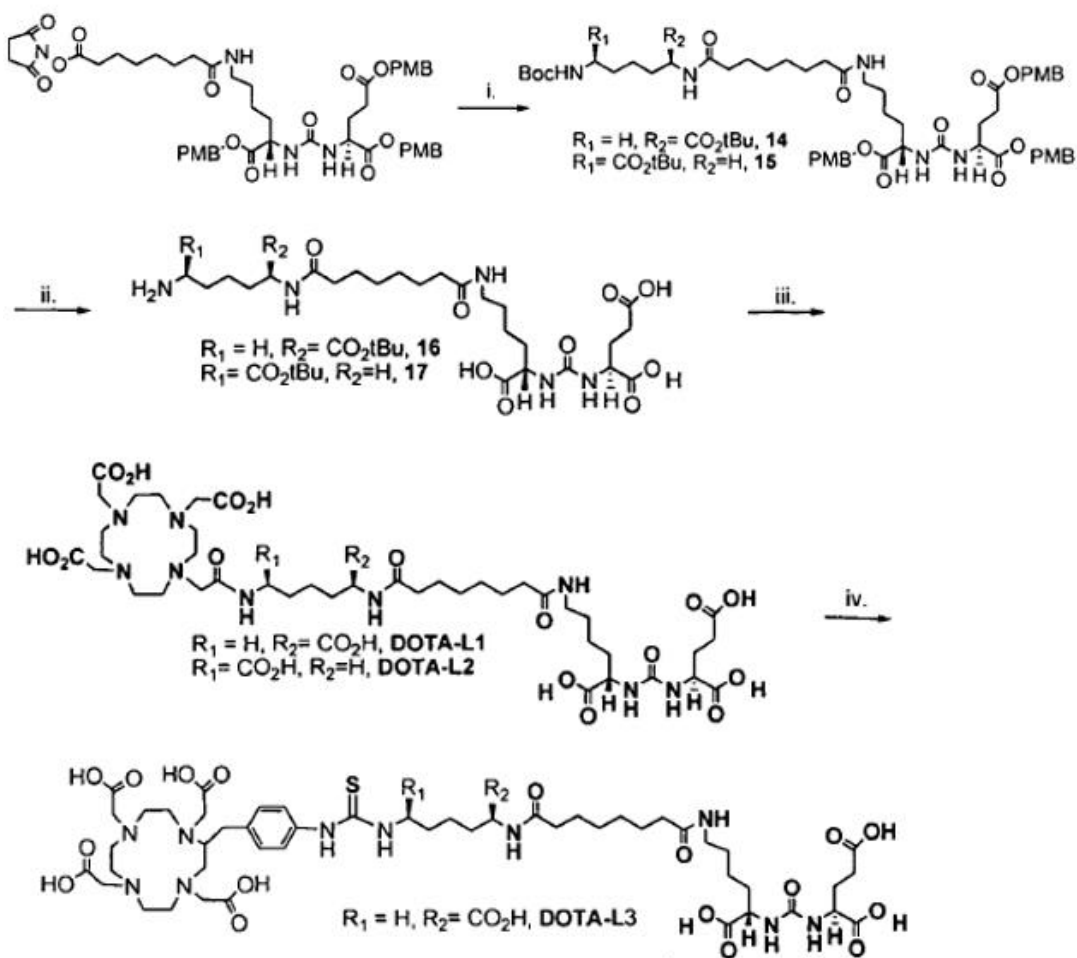
unpatentable under 35 U.S.C. § 103 if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, “would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). Here, there are two modifications that would have had to be made to teachings in the ’529 publications teachings to arrive at a compound within the scope of claims 6 and 10–12. First, one of skill in the art would have had to use a different synthetic scheme than the one taught in the ’529 publication so as to arrive at Petitioner’s “example intermediate of L4.” Second, one would have needed to vary the length of the linker so that the variables “m,” “n,” “p,” and “q” in the E group were within the range of integers recited in those claims.

Regarding the first difference, Petitioner has not explained sufficiently why one of ordinary skill in the art would have been motivated to depart from the synthetic scheme taught in the ’529 publication and instead adopt a different scheme involving the preparation of Petitioner’s “example intermediate.” Petitioner relies on the testimony of its expert, Dr. Stephen G. DiMagno, that “[d]espite the fact that the ’529 publication reports preparing L4 by coupling GUL (Block A) to a linker-chelator intermediate (Block B-Block C), a person of ordinary skill in the art would also recognize that L4 could easily be prepared using” a Block A-Block B intermediate, i.e., the “Example Intermediate of L4.” Ex. 1002 ¶ 70. But evidence that L4 could have been prepared according to an alternative pathway involving Petitioner’s “example intermediate” does not demonstrate that it would have been obvious to make such a modification to the teachings in the ’529 publication. “In cases involving new chemical compounds, it remains

necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound.” *Sanofi-Aventis U.S., LLC v. Dr. Reddy’s Labs., Inc.*, 933 F.3d 1367, 1375 (Fed. Cir. 2019) (quoting *Takeda Chem. Indus. Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007)). Here, neither Petitioner, nor its expert, have sufficiently identified a reason why one of skill in the art would have modified the synthetic pathway taught for making L4 in the ’529 publication (i.e., scheme 2) so as to arrive at Petitioner’s “example intermediate.”

We also do not agree with Petitioner’s reliance on scheme 7 of the ’529 publication. The ’529 publication teaches that scheme 7 (reproduced below) is the synthetic pathway used for “Synthesis of DOTA analogs.”

Scheme 7



Ex. 1006, 35–36. According to Petitioner, scheme 7 depicts a reaction involving the coupling of a Block A-Block B intermediate (16, 17) to a Block C chelator. See Pet. 61–62. But again, the Petition fails to identify a reason why one of skill in the art would have modified the teachings in the '529 publication so as to use such a reaction to make L4. Indeed, the '529 publication teaches the pathway and intermediates shown in scheme 7 to make “DOTA analogs,” not L4. Ex. 1006, 35. The synthesis of L4 is described in a separate section of the '529 publication titled “Synthesis of Urea-linked Chelators” that describes the synthesis of compounds L1–L7 according to different synthetic schemes. *Id.* at 31–33. Petitioner has not

identified anything in the '529 publication that suggests scheme 7 should be used to make L4 or any other non-DOTA compound.

For these reasons, Petitioner has not shown its “example intermediate of L4” would have been an obvious modification of the teachings in the '529 publication. Since Petitioner’s obviousness argument for claims 6 and 10–12 is premised on first modifying the synthetic pathway taught in the '529 publication so as to make this “example intermediate” before making further modifications to change the length of the linker, Petitioner has not shown by a preponderance of the evidence that the compositions recited in claims 6 and 10–12 would have been obvious over the '529 publication.

Petitioner’s obviousness theory for claim 8 is similar to that for the other claims, but premised upon an “example intermediate” for a different compound, i.e., compound L7, of the '529 publication. See Pet. 74–75. The '529 publication teaches that L7 is prepared according to the same reaction scheme as L4. Ex. 1006, 33 (scheme 2). This scheme does not involve formation of a Block A-Block B intermediate like that in formula (II) of the '974 patent. Accordingly, Petitioner’s obviousness argument for claim 8 is likewise premised on modifying the synthetic pathway taught in the prior art to produce an “example intermediate” that is not explicitly taught in the '529 publication. As explained above, Petitioner has not sufficiently identified a reason why one of skill in the art would have been motivated to make such a modification. Thus, we determine Petitioner has not shown by a preponderance of the evidence that claim 8 would have been obvious over the '529 publication.

F. Enablement (claims 6, 8, and 10–12)

Petitioner asserts that claims 6, 8, and 10–12 are unpatentable for lack of enablement under 35 U.S.C. § 112(a). See Pet. 84–93 (analyzing factors

articulated in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988)). Petitioner argues that the Specification exemplifies preparation of “only 5 compounds of formula (II) (compounds 2b, 2d, 2k, 2p, and 2n).” *Id.* at 88. Thus, according to Petitioner, many of the “E values” recited in claim 1 (and by dependency claims 6, 8, and 10–12) are not exemplified, nor does the Specification otherwise “provide the requisite description of how to prepare the full scope of the claimed linker moieties.” *Id.* at 89–92. In sum, Petitioner argues,

because the ’974 patent fails to provide any illustration as to how to prepare the claimed compounds, including the recited linker moieties highlighted above (i.e., benzyl-substituted linker moieties), and because there is no known correlation between these compounds and the exemplified compounds, claims 1–12, 14, and 15 (i.e., claims related to formula (II) that encompass these E values) are unpatentable for lack of enablement.

Id. at 93.

We do not agree with Petitioner’s lack of enablement argument. As Petitioner acknowledges, the Specification provides working examples for a number of the recited E groups and teaches a general method “using urea-glutamate based compounds . . . as building blocks” to make such compounds. *See Id.* at 88–91 (citing Ex. 1001, 21:3–21 and Examples 13–18). Petitioner has not, however, presented persuasive evidence or argument to explain why one of ordinary skill in the art could not or would not readily adapt these techniques to make compounds embodying the full scope of recited E groups.

The Specification provides a number of teachings regarding the synthesis of formula (II) compounds that are not addressed in Petitioner’s enablement analysis. For example, the Specification explains, “[t]ypically, the synthesis of the compounds is started by the preparation of urea

pharmacophore units . . . as described by Maresca et al. (J. Med. Chem., 2009, 52 (2), pp 347–357).” Ex. 1001, 20:66–21:3. But the Petition does not address whether such prior art synthetic techniques could be used to make the claimed compounds. Moreover, the Specification teaches that formula (II) compounds “may be readily prepared by reactions between amines and activated carboxylic acids or active esters” and provides specific examples of reagents for these techniques. *See id.* at 21:4–13. In addition, the Specification teaches that “protecting groups” may be used to allow “amines, carboxylic acids, and amino acids” to be used as “building blocks” to make such compounds. *Id.* at 21:15–21.

Petitioner does not sufficiently account for these teachings in its *Wands* factor analysis. *See* Pet. 88–92. For instance, the Specification states that “amino acids” can be used as “building blocks” for formula (II) compounds and cites Examples 15–18 as evidence of such. Ex. 1001, 21:15–21. Example 16 uses a reagent comprising two glycine residues with a protected amine to make compound 2p. *See id.* at 77:50–79:31.

Petitioner’s analysis does not address whether undue experimentation would be required to apply the same methodology with different amino acids, e.g., phenylalanine, to produce formula (II) compounds with E groups comprising the recited benzyl-substituted linker moieties. Nor does the Petition present evidence in support of Petitioner’s argument that one of skill “would need to perform a high volume of complex and time-consuming experimentation to make compounds across the scope of the claims.” *See* Pet. 92. Indeed, Petitioner’s *Wands* factor analysis is not supported by expert testimony, or any other evidence, beyond the ’974 patent itself. Accordingly, based on the entirety of the record, we do not agree that the “examples together with the other parts of the specification are not enabling.” *See Alcon Research Ltd. v.*

Barr Labs., Inc., 745 F.3d 1180, 1190 (Fed. Cir. 2014) (quoting *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1577 (Fed. Cir. 1984)).

For these reasons, we determine Petitioner has failed to show by a preponderance of the evidence that claims 6, 8, and 10–12 are not enabled.

III. CONCLUSION

As summarized in the table below, we determine Petitioner has not shown by a preponderance of the evidence that the claims remaining in this proceeding after Patent Owner’s statutory disclaimer (Ex. 2001) are unpatentable.

Claims	35 U.S.C. §	Reference(s)/Basis	Claims Shown Unpatentable	Claims Not Shown Unpatentable
6, 8, 10–12	112(b)	Indefiniteness		6, 8, 10–12
11, 12	102	Shallal		11, 12
6, 8, 10–12	103	’529 publication		6, 8, 10–12
6, 8, 10–12	112(a)	Enablement		6, 8, 10–12
Overall Outcome				6, 8, 10–12

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that Petitioner has not shown that claims 6, 8, and 10–12 of U.S. Patent No. 10,112,974 B2 are unpatentable; and

FURTHER ORDERED that, because this is a Final Written Decision, parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

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Patent 10,112,974 B2

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