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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte VIKTOR S. GOLDMAKHER

Appeal 2019-004443
Application 14/327,888
Technology Center 1600

BEFORE TINA E. HULSE, JOHN E. SCHNEIDER, and RYAN H. FLAX, *Administrative Patent Judges*.

Hulse, *Administrative Patent Judge*.

DECISION ON APPEAL

STATEMENT OF THE CASE

Pursuant to 35 U.S.C. § 134(a), Appellant[1] appeals from the Examiner's decision to reject claims 8, 9, 13–15, and 29–32. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm-in-part.

[1] We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies the real party-in-interest as Biotest AG, Germany and ImmunoGen Inc. USA. Appeal Br. 3.

CLAIMED SUBJECT MATTER

The claimed invention relates to immunoconjugates comprising one or more CD138 (or syndecan-1) targeting agent and highly potent effector molecules that are attached to the targeting agent. Spec. 1. CD138 is a membrane protein that is highly expressed on the majority of multiple myeloma cells and other carcinoma cells such as ovarian, kidney, gall bladder, breast, prostate, lung, and colon cells. *Id.* at 15. The effector molecule is activated by cleavage or dissociation from the targeting agent portion of the immunoconjugate in, at, or near the target cells, tissues, or organs. *Id.* at 1.

Claims 8, 9, 13–15, and 29–32 are on appeal.

Claim 13, the only independent claim on appeal, is illustrative and is reproduced below:

> 13. A method for inhibiting, delaying and/or preventing the growth of a tumor and/or spread of malignant tumor cells expressing CD138 in a patient in need thereof, comprising
>
> (a) administering to said patient one or more cancer drugs and/or radiation in an amount effective to reduce tumor load; and
>
> (b) administering to said patient at least one immunoconjugate in a growth of a tumor and/or spreading of tumor cells inhibiting, delaying or preventing amount,
>
> wherein said immunoconjugate comprises an anti-CD 138 targeting antibody binding CD 138 and an effector molecule that is a cytotoxic drug having a molecular weight of less than 2 kDa, wherein the effector molecule is released to inhibit, delay and/or prevent the growth of the tumor and/or spread of the malignant tumor cells expressing CD138.

Appeal Br. 17 (Claim Appendix).

REJECTIONS

Claims 8, 9, 13–15, and 29–32 stand rejected for nonstatutory obviousness-type double patenting ("ODP") over the following patents' claims in view of Hanna:[2]

- claims 1–18 of U.S. Patent No. 9,011,864 B2[3] ("the '864 patent");
- claims 1–47 of U.S. Patent No. 9,289,509 B2[4] ("the '509 patent");
- claims 1–10 of U.S. Patent No. 9,446,146 B2[5] ("the '146 patent");
- claims 1–9, 11–44, and 46–51 of U.S. Patent App. 13/708,014, now U.S. Patent No. 10,117,932 B2[6] ("the '932 patent").

Claims 8, 9, and 13–15 stand rejected for ODP over claims 1–18 of U.S. Patent No. 9,387,261 B2[7] ("the '261 patent").

Claims 8, 9, 13–15, 29, and 32 stand rejected under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Supiot[8] in view of Hanna.

DISCUSSION

I. Obviousness-Type Double Patenting Rejections

The Examiner rejected each of the appealed claims under the judicially created doctrine of ODP. To evaluate an ODP rejection, we

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[2] Nabil Hanna, US 2002/0193569 A1, published Dec. 19, 2002.
[3] Schulz et al., US 9,011,864 B2, issued Apr. 21, 2015.
[4] Osterroth et al., US 9,289,509 B2, issued Mar. 22, 2016.
[5] Daelken et al., US 9,446,146 B2, issued Sept. 20, 2016.
[6] Schulz et al., US 10,117,932 B2, issued Nov. 6, 2018.
[7] Kraus et al., US 9,387,261 B2, issued July 12, 2016.
[8] Supiot et al., *Comparison of the Biologic Effects of MA5 and B-B4 Monoclonal Antibody Labeled with Iodine-131 and Bismuth-213 on Multiple Myeloma*, 94 CANCER 1202–09 (2002).

must determine "whether the claimed invention in the application for the second patent would have been obvious from the subject matter of the claims in the first patent, in light of the prior art." *In re Longi*, 759 F.2d 887, 893 (Fed. Cir. 1985).

A. Whether Requiring a Terminal Disclaimer in an Earlier-Filed Generic Application Is Against Public Policy

As an initial matter, Appellant argues that requiring a terminal disclaimer in an earlier-filed generic application is against public policy. Appeal Br. 6–8. Specifically, Appellant asserts that ODP serves to prevent the improper extension of patent term and to prevent possible harassment by multiple assignees. *Id.* at 7. Because the asserted patents each have a later effective filing date than the instant application, Appellant notes that the extension of patent term is not an issue here. *Id.* Thus, Appellant argues that a terminal disclaimer would solely serve the purpose of preventing possible harassment by multiple assignees. *Id.*

According to Appellant, however, the present application is distinguishable from the scenario in *In re Van Ornum*, 686 F.2d 937 (CCPA 1982), which established that terminal disclaimers should contain a provision stating "any patent granted on an application in which the terminal disclaimer is filed will be enforceable only for and during the period that it and the patent over which the terminal disclaimer was filed are commonly owned." Appeal Br. 7. Appellant attempts to distinguish *Van Ornum* because the rejected application that contained a claim generic to the claims of the earlier-issued species patents was filed after the species applications had been filed. *Id.* The present application, however, was filed before the

species applications that led to the patents over which the claims are rejected.

Appellant also argues that requiring the owner of an earlier generic application to file a terminal disclaimer while "allowing others to build on the knowledge and obtain patents on species would argue against the early and full disclosure of an invention in a patent application, one of the very goals for which the U.S. patent system was set up." *Id.* at 8.

We are not persuaded by Appellant's policy argument. Appellant does not explain how its argument resolves the potential multiple assignee issue that terminal disclaimers are also meant to address. The relative filing dates of the generic application versus the species application have no bearing on the multiple assignee issue. Moreover, Appellant does not point to anything in the *Van Ornum* decision—nor do we discern anything in that decision—that turns on the relative filing dates of the generic application and the species patents. Accordingly, we reject Appellant's policy argument that it should not be required to file a terminal disclaimer for its earlier-filed generic application.

B. ODP Rejections over the '864 Patent, the '509 Patent, and the '932 Patent in View of Hanna

Appellant filed a Terminal Disclaimer over the '932 patent, the '864 patent, and the '509 patent. Electronic Terminal Disclaimer (filed Nov. 21, 2018). Thus, Appellant states that, although it disagrees with the Examiner, Appellant has obviated the ODP rejection over those patents by submitting the terminal disclaimer. Appeal Br. 9, 12–13. The Examiner withdrew the rejections over the '864 and '509 patents in light of the Terminal Disclaimer. Ans. 8. Although the Examiner did not expressly withdraw the ODP

rejection over the ’932 patent, the Examiner acknowledged the terminal disclaimer and stated Appellant’s argument is moot. *Id.* at 14.

We, therefore, conclude that the ODP rejections over the ’864 patent, the ’509 patent, and the ’932 patent are moot in view of the Terminal Disclaimer.

C. ODP Rejection over the ’146 Patent in View of Hanna

The Examiner rejected claims 8, 9, 13–15, and 29–32 over the ’146 patent in view of Hanna. The Examiner stated the conflicting claims are not identical, but they are not patentably distinct because the copending application claims the same method, using the same material, for treating the same diseases. Ans. 3. The Examiner stated the claims of the ’146 patent are “drawn to a method for destroying CD138 expressing [multiple myeloma] cells and diminishing adhesion of stroma cell comprising administering CD138 antibody and an effector molecule conjugate, wherein the antibody comprising 6 CDRs and effector molecule is maytansinoid, DM1, DM3, and DM4.” *Id.* at 4. The Examiner relied on Hanna for its teaching of combinational therapy comprising administering an immunoconjugate and an anti-cancer agent. *Id.* The Examiner stated that a person of ordinary skill in the art would have been motivated with a reasonable expectation of success to use the combination therapy to increase the efficacy of treatment and to arrive at the current invention without unexpected result. *Id.*

Appellant argues the claims are patentably distinct because the ’146 patent claims require a first administration of the immunoconjugate followed by at least a 12-hour delay to administer the cytotoxic agent. Appeal Br. 11. During that 12-hour delay, the multiple myeloma cells are destroyed and are

prevented from adhering to bone marrow stromal cells to overcome cell adhesion mediated drug resistance (CAM-DR). *Id.* Because CAM-DR is a prerequisite for the cytotoxic drug to be administered, according to Appellant, the claims of the '146 patent are directed to a different patient population than the application claims. *Id.* That is, in the application claims, there is no need for alleviation of CAM-DR by the immunoconjugate before administering the cancer drug. *Id.* As such, Appellant argues one skilled in the art would not have been motivated to use the combination therapy to increase the efficacy of treatment to arrive at the current invention. *Id.*

In response, the Examiner states Appellant's arguments are unpersuasive because both claims are drawn to a method of treating the same disease with a same material (CD138 immunoconjugate) in combination with a cytotoxic drug. Ans. 11. The Examiner notes that "Appellant already admitted the patented invention is a species (improvement) of the invention claimed in this [earlier-filed] application." *Id.* Thus, because the claims of the '146 patent are to a species of the generic application claims, the Examiner states they anticipate the application claims. *Id.*

We find the Examiner to have the better position with respect to claims 8, 9, 13, 14, and 29–31. Claim 1 of the '146 patent recites a method for destroying multiple myeloma cells comprising administering an immunoconjugate comprising a chimeric CD138 antibody and a maytansinoid effector molecule, waiting for 12 hours to 6 days and then subsequently administering a further cytotoxic agent. Independent claim 13 of the instant application recites a method for inhibiting, delaying, and/or

preventing the growth of a tumor and/or spread of malignant tumor cells expressing CD138 by administering a cancer drug and an immunoconjugate with a cytotoxic effector molecular. Br. 17. Thus, we agree with the Examiner that claim 1 of the '146 patent is a species of claim 13 of the instant application.

As for the dependent claims of the instant application, dependent claims 8 and 9 include patients who suffer from multiple myeloma. *Id.* Dependent claim 14 requires administering the cancer drug and the immunoconjugate consecutively. *Id.* Dependent claim 29 recites binding to residues 90–95 of the core protein on human CD138. *Id.* Dependent claims 30–31 recite the effector molecule is a maytansinoid. *Id.* at 18. Thus, each limitation of dependent claims 8, 9, 14, and 29–31 of the instant application is taught by claim 1 of the '146 patent.

Accordingly, viewing the claims as a whole, we agree with the Examiner that claim 1 of the '146 patent is a species to the generic application claims 8, 9, 13, 14, and 29–31 of the instant application and, therefore, anticipates the claims. Thus, we affirm the ODP rejection over the '146 patent in view of Hanna as to claims 8, 9, 13, 14, and 29–31. *In re Goodman*, 11 F.3d 1046, 1053 (Fed. Cir. 1993) ("[W]ithout a terminal disclaimer, the species claims preclude issuance of the generic application.").

We do not agree, however, that any of the claims of the '146 patent are species to dependent claim 15, which requires administering the cancer drug and the immunoconjugate in a single administration step. As Appellant notes, the '146 patent claims require administering the cancer drug and the immunoconjugate sequentially with at least 12 hours in between treatments.

Appeal Br. 11. Moreover, the '146 patent claims require treating multiple myeloma cells, which are not "solid tumor cells" as required by dependent claim 32 of the application. The Examiner is silent as to these distinctions and, therefore, has not sufficiently explained how the '146 patent claims render obvious claims 15 or 32 of the instant application. Accordingly, we reverse the ODP rejection as to those claims.

D. ODP Rejection over the '261 Patent in View of Hanna

The Examiner rejected claims 8, 9, and 13–15 under ODP over the '261 patent claims in view of Hanna. According to the Examiner, the products recited in both claim sets are identical and the specification of the '261 patent indicates that the utility of the products includes methods of inhibiting the growth of CD138 expressing tumors for treating cancer. Ans. 5 (citing '261 patent, cols. 1–6, Figs. 8–12). The Examiner states the '261 patent specification also teaches the utility of the claimed product is to treat CD138 expressing cancer in combination with other anticancer therapy and cytotoxic agents. *Id.* (citing '261 patent, col. 27, line 25+); *see* '261 patent, col. 27, ll. 22–36 (describing cytotoxic agents that can be co-administered with the immunoconjugate of the invention). As such, the Examiner concludes the patented product claims and the claimed methods in the application are obvious alternatives that are not patentably distinct. *Id.* Moreover, the Examiner found that an ordinary artisan would have been motivated to arrive at the claimed invention by using the immunoconjugate of the '261 patent in combination with radiation or other anti-cancer drug taught by Hanna. *Id.*

Appellant argues that the Examiner erred because neither the claims of the '261 patent nor Hanna mention the "same diseases" as the application

claims. Appeal Br. 12. According to Appellant, "the Office's argument essentially assumes that any treatment method become[s] obvious when the substance that is used for the treatment is known." *Id.* Appellant argues the specification can only be used for claim construction and only the disclosure of the invention claimed may be examined for that purpose. *Id.*

We are not persuaded by Appellant's argument. The Federal Circuit has repeatedly held that a "claim to a method of using a composition is not patentably distinct from an earlier claim to the identical composition in a patent disclosing the identical use." *Geneva Pharms., Inc. v. GlaxoSmithKline*, 349 F.3d 1373, 1385–86 (Fed. Cir. 2003); *see also Pfizer, Inc. v. Teva Pharms. USA, Inc.*, 518 F.3d 1353, 1363 (Fed. Cir. 2008) (finding patent that "merely claims a particular use described in the [earlier] patent of the claimed compositions of the [earlier] patent" not patentably distinct over the earlier patent).

As the Examiner notes, the '261 patent teaches that an example of the utility of the claimed product includes treating solid tumors using chemotherapy or radiation followed by administration of the immunoconjugate. Ans. 13 (citing '261 patent, 29:1–19); *see also id.* at 5 (citing '261 patent, 27:25–35). The Examiner also notes the '261 patent teaches a method of using the claimed product. *Id.* at 14. Specifically, the '261 patent confirms:

> The present invention is also directed at a method for inhibiting, delaying and/or preventing the growth of a tumor and/or spread of malignant tumor cells in a patient in need thereof, comprising
>
> (a) administering to said patient one or more cytotoxic agents and/or radiation in an amount effective to reduce tumor load; and

> (b) administering to said patient at least one of the immunoconjugates specified herein in a growth of a tumor and/or spreading of tumor cells inhibiting, delaying or preventing amount,
>
> wherein said immunoconjugate inhibits, delays or prevents the growth and/or spread of tumor cells comprising CD138 expressing cells.

'261 patent, 3:43–56. Thus, the '261 patent teaches a method substantially similar to the method of claim 13 of the instant application.

Accordingly, we find Appellant's claims to methods of using the immunoconjugate are obvious alternatives that are not patentably distinct from the '261 patent's claim to the identical composition and its disclosure of the identical use claimed in the instant application. *See Geneva Pharms.*, 349 F.3d at 1385–86. We, therefore, affirm the ODP rejection of claims 8, 9, and 13–15.

II. Obviousness of Claims 8, 9, 13–15, 29, and 32 over Supiot and Hanna

The Examiner rejected claims 8, 9, 13–15, 29, and 32 as unpatentable under pre-AIA 35 U.S.C. § 103 over Supiot and Hanna. The Examiner states that Supiot teaches a method of inhibiting CD138-expressing multiple myeloma cell growth comprising administering an immunoconjugate comprising anti-CD138 B-B4 conjugated with radionucleotides, Iodine-131 (I^{131}) or Bismuth-213. Ans. 7. The Examiner states Supiot does not teach combination therapy with another anti-cancer agent. *Id.* Hanna, however, teaches a method of treating a tumor using an immunoconjugate in combination with different cancer treatment modalities such as radiotherapy, immunotherapy, and/or chemotherapy. *Id.* The Examiner states it would have been obvious to an ordinary artisan to combine the immunotherapy of

anti-CD138 with a common anticancer therapy to treat a patient having CD138+ multiple myeloma to increase the efficacy of CD138+ multiple myeloma treatment because Supiot shows the antibody-I^{131} conjugate has specific cytotoxicity towards antigen-expressing cells. *Id.* at 8.

Appellant argues the claimed method requires that the effector molecule is "released to inhibit, delay and/or prevent the growth of the tumor and/or spread of the malignant tumor cells expressing CD138." Appeal Br. 15 (emphasis omitted). Appellant argues Supiot's immunoconjugate acts by bringing the radionucleotide and the radiation associated with it to the tumor site. *Id.* Appellant argues that a person of ordinary skill in the art would not expect "release" of the radionucleotide because the immunoconjugate is not internalized. *Id.* According to Appellant, releasing the radionucleotide of Supiot would result in unwanted radiation away from the tumor site and the tumor cells may escape treatment. *Id.*

We agree with Appellant that Supiot does not teach "wherein the effector molecule is released to inhibit, delay, and/or prevent the growth of the tumor," as required by claim 13. Assuming the Iodine-131 or Bismuth-213 of Supiot's immunoconjugate is an "effector molecule" as required by the claim,[9] we agree with Appellant that Supiot does not teach "releasing" the radionucleotides from the immunoconjugate. The Specification states

[9] Appellant disputes whether Supiot's radionucleotides constitute a "cytotoxic drug," as required for the effector molecule of claim 13. Appeal Br. 14. We need not reach this issue for purposes of this Decision because, even if we assume the Examiner is correct, we reverse the Examiner's obviousness rejection for the reasons stated above.

that effector molecules "are attached to the targeting agent" and "activated by cleavage/dissociation from the targeting agent portion of the immunoconjugate in, at or near the target cells, tissues or organs." Spec. 1:16–19; *see also id.* at 6:28–30 ("The effector molecule or molecules may be released from the immunoconjugate by cleavage/dissociation in, at or close to the target cell, tissue or organ.").

We are persuaded that a person of ordinary skill in the art would not have understood Supiot to teach releasing the radionucleotides from the immunoconjugate, as doing so would release radioactive elements into the body, which could be harmful to the patient. Moreover, we agree that releasing the radionucleotides may adversely affect the radiation treatment because it would separate the radiation from the target cells.

The Examiner responds to Appellant's argument, stating that although Supiot does not teach internalizing the immunoconjugate into the body, the claims do not require the CD138 antibody to be internalized. Ans. 16. The Examiner, however, misses the point. The claims require the effector molecule to be released. Because the immunoconjugate of Supiot is not internalized, the radionucleotide effector molecule remains outside the cell. If it were cleaved or dissociated (i.e., released) from the immunoconjugate, as required by the claims, it would result in the radionucleotide being released into the patient's body. Thus, we are persuaded that a person of ordinary skill in the art would not have had a reason to use Supiot's immunoconjugate in a system that released the effector molecule to inhibit, delay, and/or prevent the growth of a tumor and/or the spread of malignant tumor cells.

Accordingly, we find Supiot does not teach or suggest an effector molecule that is "released," as required by claims 8, 9, 13–15, 29, and 32. We, therefore, reverse the obviousness rejection over those claims in view of Supiot and Hanna.

CONCLUSION

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
8, 9, 13–15, 29–32	103(a)	Obviousness-Type Double Patenting over the '864 patent		
8, 9, 13–15, 29–32	103(a)	Obviousness-Type Double Patenting over the '509 patent		
8, 9, 13–15, 29–32	103(a)	Obviousness-Type Double Patenting over the '146 patent	8, 9, 13, 14, 29–31	15, 32
8, 9, 13–15, 29–32	103(a)	Obviousness-Type Double Patenting over the '932 patent		
8, 9, 13–15	103(a)	Obviousness-Type Double Patenting over the '261 patent	8, 9, 13–15	
8, 9, 13–15, 29, 32	103(a)	§ 103 over Supiot and Hanna		8, 9, 13–15, 29, 32
Overall Outcome			8, 9, 13–15, 29–31	32

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a). *See* 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED-IN-PART