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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte DEVIN WILEY, ANDREW CLARK, and MARK E. DAVIS

Appeal 2019-005787
Application 14/120,309
Technology Center 1600

Before DEBORAH KATZ, JOHN G. NEW, and RYAN H. FLAX, *Administrative Patent Judges*.

FLAX, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134(a) involving claims to a method of delivering enhanced levels of a therapeutic agent to a brain parenchyma of a subject having a neurological brain disorder. Appellant appeals the Examiner's rejection of claims 1–8, 18–23, 28–36, 38–41, 46–49, 52–54, and 56–60 under 35 U.S.C. § 103(a) and for obviousness-type double patenting.[1] We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.[2]

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[1] "Appellant" herein refers to the "applicant" as defined by 37 C.F.R. § 1.42. Appellant identifies "California Institute of Technology," as the real party-in-interest. Appeal Br. 1.

[2] A hearing was conducted on May 6, 2020. The transcript ("Hr'g Tr.") of the hearing is a part of the record on appeal.

RELATED MATTERS

Appellant indicates that there are no related appeals, interferences, or trials with respect to the appealed claims. Appeal Br. 1.

STATEMENT OF THE CASE

The application includes one independent claim, claim 1, which is reproduced below:

> 1. A method of delivering enhanced levels of a therapeutic agent to a brain parenchyma of a subject having a neurological brain disorder, the method comprising:
>
> systemically administering nanoparticles to the subject having the neurological brain disorder and in need of delivery of an enhanced level of the therapeutic agent across a blood-brain barrier to the subject's brain parenchyma, each nanoparticle comprising a nanoparticle core having a surface comprising a cationic mucic acid polymer (cMAP), a poly(lactic-co-glycolic acid) (PLGA), chitosan, polyethyleneimine, iron oxide, or gold; wherein
>
> the nanoparticle further comprises (a) the therapeutic agent and (b) a targeting agent, the targeting agent comprising a targeting ligand attached to the surface of the nanoparticle core by a linker;
>
> the targeting ligand having an affinity for binding to a receptor expressed by endothelial cells of the blood-brain barrier; and
>
> the linker comprising a polyethylene glycol (PEG) polymer moiety that is conjugated to the surface of the nanoparticle core by a pH sensitive linkage selected from the group consisting of diamino ketal, orthoester, nitrophenyl boronic ester, acetal, ketal, imine, and hydrazone or an enzymatically cleavable disulfide or polypeptide bond; and
>
> wherein

> each nanoparticle has a size in a range of from about 40 nm to 100 nm and a zeta potential in a range of from about- 0.5 mV to -10.0 mV; and wherein
>
> the therapeutic agent is effective against a neurological disorder; and
>
> the enhanced level of the therapeutic agent delivered by the nanoparticles to the brain parenchyma is an amount that is greater than is delivered using otherwise equivalent nanoparticles that do not contain the cleavable linker under the same conditions.

Appeal Br. 21 (Claims Appendix).

The Specification states that "[c]hronic diseases of the central nervous system (CNS) are a major cause of morbidity and mortality in the developed world," and lists conditions such as Alzheimer's disease, Huntington's disease, Parkinson's disease, and multiple sclerosis. Spec. ¶ 3. The Specification further states that "[a] major reason for the lack of progress in treating these diseases is due to the presence of the blood-brain barrier (BBB). The BBB is a physical barrier between the CNS parenchyma and vasculature that plays a critical role in maintaining homeostasis within the CNS." *Id.* ¶ 4.

In view of this issue, the Specification provides Figure 2, reproduced below, which illustrates how the components of the claimed invention, noted above, allow the crossing of the BBB for a drug-delivering nanoparticle:

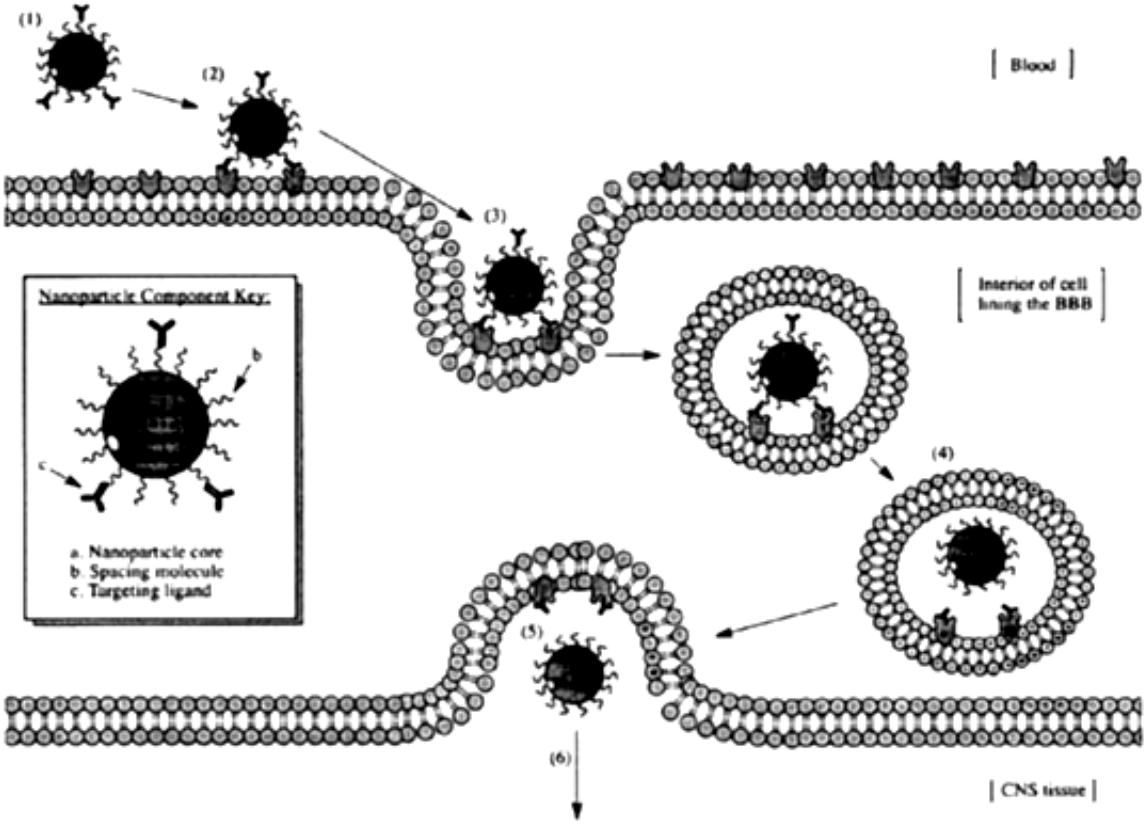

Fig. 2

Spec., Fig. 2. Figure 2, above, shows:

Transit of targeted nanoparticle through the blood-brain barrier (BBB) facilitated by targeting molecules falling off the nanoparticle. (1) Targeted nanoparticle in the blood reaches the BBB luminal surface. (2) Nanoparticle ligand [e.g., transferrin] binds to its receptor on the blood side of the BBB. (3) Internalization of the receptor-nanoparticle complex. (4) Chemical and/or physical changes experienced by the nanoparticle as it crosses the BBB cause detachment of the ligand from the rest of the nanoparticle. (5) The untargeted nanoparticle reaches the brain side of the BBB. (6) The nanoparticle diffuses into the CNS. Components of the nanoparticle are identified in the inset key on the left of the figure. Terms in the brackets on

> the right side of the figure indicate relative compartments involved in this sequence.

Id. ¶ 13 (addition identifies specifically claimed components providing the described functionality); *see also id.* ¶¶ 37–38, 52–53 (describing the claimed targeting ligand and transferrin as a suitable protein for such purpose).

The following rejections by the Examiner are appealed:

Claims 1–8, 18–23, 28–36, 38, 40, 41, 46–49, 53, 54, 56, 57, and 59 stand rejected under 35 U.S.C. § 103 over Davis '556[3] and Lam.[4] Final Action 4.

Claims 1–8, 18–23, 28–36, 38–41, 46–49, 52–54, and 56–60 stand rejected under 35 U.S.C. § 103 over Davis '556, Lam, and Pratt.[5] *Id.* at 6–7. As apparent from a comparison of the rejections, this rejection adds claims 39, 52, 58, and 60.

Claims 1–8, 18–23, 28–36, 38–41, 46–49, 51–54, and 56–60 stand rejected on the ground of non-statutory, obviousness-type double patenting over claims 1–30 of Davis '097.[6] *Id.* at 9.

DISCUSSION

I. LEGAL STANDARDS

Arguments made by Appellant in the Appeal Brief and properly presented in the Reply Brief have been considered; arguments not so-presented are waived. *See* 37 C.F.R. § 41.37(c)(1)(iv) (2017); *see also Ex*

[3] US 2010/0040556 A1 (published Feb. 8, 2010) ("Davis '556").
[4] WO 2012/158622 A2 (published Nov. 22, 2012) ("Lam").
[5] US 8,367,116 B2 (issued Feb. 5, 2013) ("Pratt").
[6] US 9,132,097 B2 (issued Sept. 15, 2015) ("Davis '097").

parte Borden, 93 USPQ2d 1473, 1474 (BPAI 2010) (informative) ("Any bases for asserting error, whether factual or legal, that are not raised in the principal brief are waived.").

"The combination of familiar elements [or steps] according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). The test for obviousness is "whether the teachings of the prior art, taken as a whole, would have made obvious the claimed invention." *In re Gorman*, 933 F.2d 982, 986 (Fed. Cir. 1991). "What matters is the objective reach of the claim. If the claim extends to what is obvious, it is invalid under § 103." *KSR*, 550 U.S. at 419.

"[T]he law of obviousness-type double patenting looks to the law of obviousness generally. As . . . explained in *Amgen*, '[t]his part of the obviousness-type double patenting analysis is analogous to an obviousness analysis under 35 U.S.C. § 103.'" *AbbVie Inc. v. The Mathilda & Terrence Kennedy Inst. of Rheumatology Trust*, 764 F.3d 1366, 1378 (Fed. Cir. 2014) (second alteration in original) (citing *Amgen Inc. v. F. Hoffman-La Roche Ltd.*, 580 F.3d 1340, 1661 (Fed. Cir. 2009); *see also In re Braithwaite*, 379 F.2d 594, 600 n.4 (CCPA 1967) (A nonstatutory double patenting rejection is "analogous to the non-obviousness requirement of 35 U.S.C. 103," except that only the claims of, not the disclosure of, the reference patent underlying the double patenting rejection is considered prior art.).

With these standards in mind and in view of the Findings of Facts set forth above, we address the Examiner's rejections and Appellant's arguments there-over.

II. OBVIOUSNESS

We address both obviousness rejections together, because the same facts and arguments are determinative for each. Appellant likewise argues both obviousness rejections simultaneously and asserts a singular argument for both.

In the first obviousness rejection, the Examiner determined that the claimed method and particles used therein of, e.g., claim 1, were disclosed by the combination of Davis '556 and Lam, where Davis '556 teaches the nanoparticles of mucic acid polymer, with PEG and phenyl boronic acid linker, bound to a transferrin targeting agent, used to systemically administer therapeutic and imaging agents in the nanoparticles. Final Action 4–5 (citing Davis '556 ¶¶ 41, 63, 67–68, 72, 115, 119, 163, 176, 192, claims 1, 6, 8, 17, 24, Figs. 2, 5, 6, 14 15). The Examiner stated, "[t]he nanoparticle [of Davis '556] additionally comprised therapeutic agents and imaging agents, including Cu-64 (meeting claim 41), and were useful in treating mental disorders, considered to read on treating a neurological disorder of the brain as now recited in claim 1." *Id.* at 4. The Examiner cited Lam for teaching nitrophenyl boronic acid, as a part of nanoparticles, which the Examiner determined was predictably interchangeable with Davis '556's phenyl boronic acid as a linker component. *Id.* at 5–6 (citing Lam 47 (example 11)). In the second obviousness rejection directed most specifically to dependent claims 39, 52, 58, and 60, the Examiner adds Pratt to the aforementioned prior art combination for teaching the use of dopamine with nanoparticles as a therapeutic agent suitable to treat brain injury, cancer, and Alzheimer's disease. *Id.* at 6–7 (citing Pratt claims 1, 13, 22, 25, 27, 30).

Appellant's arguments focus only on whether Davis '556's discussion of treating mental disorders is sufficient to teach or suggest delivering drugs across the BBB. Appeal Br. 13–19. Appellant agues "Davis ['556] teaches a variety of nanoparticle compositions for drug delivery applications, but Davis ['556] nowhere discloses crossing the blood-brain barrier, or even mentions the brain, the brain parenchyma, or any neurological condition" and that Davis '556's disclosure of treating mental disorders would not render its claimed method, including crossing the BBB, obvious. *Id.* at 14, 16.

We are unpersuaded by Appellant's arguments. As the Examiner points out, "Davis ['556] teaches [its] nanoparticles were useful in treating mental disorders, considered to read on treating a neurological disorder of the brain." Answer 4; *see also* Davis '556 ¶ 172 ("Exemplary conditions include but are not limited to injuries, disabilities, disorders (including mental and physical disorders) . . ."). As the Examiner also points out, and Appellant concedes, Davis '556's disclosed administration of the therapeutic agent and its carrier nanoparticles is systemic (e.g., "orally, parenterally, topically, or rectally."). *See* Answer 3; Appeal Br. 14; Davis '556 ¶ 163. If Davis '556's systemically administered therapeutic agent is to treat a "mental disorder," i.e., a disorder of the mind or brain, the brain must be treated and the BBB must be traversed by the drug. Appellant's unsupported assertions to the contrary are not persuasive. Davis '556's omitting any discussion of this specific path to the brain does not indicate, or even support, that it would not be required. Appellant's assertions to the contrary are not persuasive.

Davis '556 specifically identifies transferrin as a preferred targeting agent for its nanoparticles, which is the same targeting agent of focus in Appellant's Specification. Davis '556 Fig. 12; Spec. ¶¶ 37–38. "[I]t is beyond argument that no utility need be disclosed for a reference to be anticipatory of a claim to an old compound. The compound appellants are attempting to patent is not new." *In re Schoenwald*, 964 F.2d 1122, 1124 (Fed. Cir. 1992). Here, as in *Schoenwald*, it is not disputed that Davis '556 discloses the same compound (a pharmaceutical nanoparticle with a transferrin targeting agent) as claimed (once its liker is modified as taught by Lam). However, unlike *Schoenwald*, here Davis '556 actually teaches using this same nanoparticle in the same way as claimed, that is, by systemically administering it to treat a mental/brain disorder. Thus, Davis '556's transferrin targeting agent would necessarily function to transport the nanoparticle across the BBB, just as it would for the claimed invention. *See, e.g.*, Spec. ¶¶ 7, 13, 37–38, 52–54, 68 (transferrin is "a ligand for targeting brain endothelial cell"). Thus, the claimed method would have been obvious.

III. OBVIOUSNESS-TYPE DOUBLE PATENTING

Under the doctrine of obviousness-type double patenting, the Examiner determined that the claimed invention would have been obvious over the claims of Davis '097, without further elaboration. Final Action 9.

Appellant argues:

> The claims of the 097 patent recite various nanoparticle compositions, as well as methods of administering those nanoparticles such as "the method comprising administering to the individual the nanoparticle . . . ." None of the claims of the 097 patent refer to the blood-brain barrier in any way (or even

> "mental disorders"). As such, it is unclear why the examiner believes that the 097 patent claims would render obvious or be patentably indistinct from the process claimed in this application.

Appeal Br. 19.

Upon review, we do not observe that the claims of Davis '097 recite a targeting ligand having an affinity for binding to a receptor expressed by endothelial cells of the BBB, for example, transferrin. Davis '097, 85:38–93:10. We also do not observe that these claims recite a size for the nanoparticles, the zeta potential of the nanoparticles, or whether any claimed therapeutic agents are for treating neurological disorders. *Id.* Thus, it appears that there are substantial differences between the Davis '097 claims and the appealed claims that remain unaccounted for by the Examiner's rejection. The Examiner has not accounted for these differences in his rejection. For this reason, we find the Examiner has not established a prima facie case that the appealed claims would have been obvious over the claims of Davis '097 and, therefore, we reverse the rejection.

CONCLUSION

In summary:

Claims Rejected	35 U.S.C. §	Reference(s) /Basis	Affirmed	Reversed
1–8, 18–23, 28–36, 38, 40, 41, 46–49, 53, 54, 56, 57, 59	103	Davis '556, Lam	1–8, 18–23, 28–36, 38, 40, 41, 46–49, 53, 54, 56, 57, 59	
1–8, 18–23, 28–36, 38–41, 46–49, 52–54, 56–60	103	Davis '556, Lam, Pratt	1–8, 18–23, 28–36, 38–41, 46–49, 52–54, 56–60	

Claims Rejected	35 U.S.C. §	Reference(s) /Basis	Affirmed	Reversed
1–8, 18–23, 28–36, 38–41, 46–49, 51–54, 56–60	Obviousness-type double patenting	Davis '097		1–8, 18–23, 28–36, 38–41, 46–49, 51–54, 56–60
Overall Outcome			1–8, 18–23, 28–36, 38–41, 46–49, 52–54, 56–60	

TIME PERIOD FOR RESPONSE

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

AFFIRMED