UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/771,536	08/31/2015	Jack Rubinstein	UOC 272US	1004

26875 7590 10/08/2019

WOOD, HERRON & EVANS, LLP
2700 CAREW TOWER
441 VINE STREET
CINCINNATI, OH 45202

EXAMINER	
KANTAMNENI, SHOBHA	

ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
10/08/2019	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):

usptodock@whe-law.com

UNITED STATES PATENT AND TRADEMARK OFFICE

_____

BEFORE THE PATENT TRIAL AND APPEAL BOARD

_____

Ex parte JACK RUBINSTEIN and W. KEITH JONES

_____

Appeal 2019-002610
Application 14/771,536[1]
Technology Center 1600

_____

Before DONALD E. ADAMS, ERIC B. GRIMES, and
RACHEL H. TOWNSEND, *Administrative Patent Judges*.

TOWNSEND, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a method of treating heart failure with preserved ejection fraction, which have been rejected as obvious and for obviousness-type double patenting. We have jurisdiction under 35 U.S.C. § 6(b).

We reverse.

STATEMENT OF THE CASE

Heart failure with preserved ejection fraction is a heart failure where the heart lacks the capacity "to expand adequately and fill during diastole,

---

[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 University of Cincinnati, a University of the State of Ohio. (Br. 4.)

even though it is capable of contracting appropriately (i.e., normal systolic function)." (Spec. ¶ 3.) According to Appellant's Specification "there are no known drug therapies that improve the diastolic function of the heart (though there are many that improve the systolic function)." (*Id.* ¶ 4.) Appellant's invention is directed at treating patients suffering from heart failure with preserved ejection fraction.

Claims 1, 5, 7, 10–14, 18, 19, 23, and 24 are on appeal. Claim 1 is representative and reads as follows:

> 1. A method of treating heart failure with preserved ejection fraction (HFpEF) in a subject comprising intravenously infusing an amount of probenecid to achieve a plasma concentration effective to treat the cardiac dysfunction heart failure with preserved ejection fraction in the subject.

(Br. 13.)

The following grounds of rejection by the Examiner are before us on review:

Claims 1, 5, 7, 10–14, 18, 19, 23, and 24 under 35 U.S.C. § 103(a) as unpatentable over Bang,[2] Anjak,[3] Jones,[4] and Chiang.[5]

---

[2] Bang, S. et al., *Transient receptor potential V2 expressed in sensory neurons is activated by probenecid*, 425 Neuroscience Letters 120–125 (2007).

[3] Anjak, A. et al., *Transient receptor potential vanilloid 2 (TRPV2) stimulation is cardioprotective*, 58:4 Journal of Investigative Medicine, (2010).

[4] Jones et al., US 2010/0292755 A1, published Nov. 18, 2010.

[5] Chiang, C.W. et al., *Dose-Dependent Kinetics of Probenecid in Rhesus Monkeys-Infusion Studies*, 28 Pharmacology 181–187 (1984).

Claims 1, 5, 7, 10–14, 18, 19, 23, and 24 on the ground of nonstatutory obviousness-type double patenting over claims 1, 3, 7–10, and 21–27 of copending Application No. 13/584,713.

DISCUSSION

The Examiner finds that Bang teaches that transient receptor potential vanilloid 2 receptor ("TRPV2 receptor") expressed in sensory neurons is activated by probenecid. (Non-Final Action[6] 3.) The Examiner also finds that Bang teaches a dose response curve determining EC50 and maximum efficacy. (*Id.*) The Examiner recognizes that Bang does not teach treating heart failure with preserved ejection fraction but concludes that use of probenecid in such a method would have been obvious in light of Anjak and Jones. (*Id.* at 3–4.)

In particular, the Examiner finds that Anjak teaches that TRPV2 is expressed in heart and peripheral nerves and that stimulation of TRPV2 with probenecid stimulates cardiac contractility and initiates a cardioprotective effect against myocardial infarction. (*Id.* at 4.) The Examiner indicates that increasing cardiac contractility is related to an increase in the rate of cardiac relaxation. (Ans. 4.) The Examiner also notes that Anjak teaches treatment with a gel. (Non-Final Action 4.)

The Examiner finds that Jones teaches a method of treating ischemic injury and teaches cardiac tissue protection by delivering a TRP agonist. (*Id.*) The Examiner finds that Jones teaches that TRP includes TRPV2. (*Id.*) The Examiner further finds that Jones teaches mice treated with probenecid had a significantly reduced infarct size as a percent of risk region. (*Id.*)

---

[6] The Non-Final Action is dated April 3, 2018.

According to the Examiner, these cardioprotective effects of Jones are "treating cardiac dysfunction." (Ans. 4–5.)

The Examiner relies on Chiang for its teaching of intravenous infusion of probenecid that falls within the range of "'the therapeutically effective amount of probenecid . . . , about 1 mg/kg/day to about 100 [m]g/kg/day' as cited in instant claim 10." (Non-Final Action 4–5.)

The Examiner asserts that one of ordinary skill in the art would have been motivated to administer probenecid in an amount to achieve a plasma concentration effective to treat heart failure because Anjak teaches stimulating TRPV2 is cardioprotective and stimulation with probenecid stimulates contractility and initiates a cardioprotective effect against myocardial infarct and Jones demonstrates that when probenecid is added in an animal model for myocardial infarct that the infarct size is reduced significantly. (*Id.* at 6.)

The Examiner asserts that one of ordinary skill in the art would reasonably have expected that the administration of probenecid to TRPV2 receptors as an agonist would treat heart failure because Jones teaches cardiac tissue protection with a TRP agonist and reduction in infarct size when probenecid was administered in an animal model. (*Id.* at 5.) According to the Examiner, the fact that probenecid is taught to stimulate cardiac muscle means that one of ordinary skill in the art would have reasonably expected "improve[ment in] cardiac muscle to properly expand resulting in a therapeutic effect for heart failure with preserved ejection fraction." (Ans. 5.)

We disagree with the Examiner's factual findings and conclusion of obviousness. As Appellant explains, in heart failure with preserved ejection fraction, the heart's capability to contract appropriately for normal systolic

function is not impaired. (Br. 5) What is impaired is the "heart's capacity to expand adequately enough to fill during diastole." (*Id.*) Anjak does not teach, contrary to the Examiner's assertion, that the stimulation of cardiac contractility with probenecid "will improve cardiac muscle to properly expand" (Ans. 5). That is, while systolic function may be improved, that fact does not speak to an improvement in diastolic function. Thus, we disagree with the Examiner that Anjak's teaching that probenecid stimulates cardiac contractility would have provided one of ordinary skill in the art with the motivation to use probenecid to treat heart failure with preserved ejection fraction or with a reasonable expectation that such would be successful.

Similarly, we do not find that Jones's teaching regarding a reduced infarct size after treatment with probenecid would have motivated one of ordinary skill in the art to treat heart failure with preserved ejection fraction. That is because an infarct is damaged area due to lack of oxygen. (*See* Amendment and Response dated July 6, 2017 at 6.) While it may be the case, as the Examiner posits, that the cardioprotective effects of Jones are "treating cardiac dysfunction" (Ans. 4–5), the Examiner has not explained why the fact that cardiac tissue is protected from a lack of oxygen would have reasonably apprised one of ordinary skill in the art that this effect was due to an improvement in heart's capacity to expand to fill during diastole, which is the problem that needs correcting in treating heart failure with preserved ejection fraction (*see* Spec. ¶ 3).

"[T]he examiner bears the initial burden, on review of the prior art . . . , of presenting a *prima facie* case of unpatentability." *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992). In light of the foregoing, we conclude that the Examiner has not established that the combination of Bang

Anjak, Jones, and Chiang suggests the claimed method of treating heart failure with preserved ejection fraction. Thus, we reverse the Examiner's rejection of claims 1, 5, 7, 10–14, 18, 19, 23, and 24 as being obvious.

Regarding the provisional obviousness-type double patenting rejection, as of the writing of this opinion, the co-pending application has not issued as a patent. Thus, we decline to reach the rejection as the issue is not ripe for decision. *Ex parte Moncla*, 95 USPQ2d 1884, 1885 (BPAI 2010) (precedential) (Where the co-pending, reference application has not issued, it is "premature for the original Board panel to address the Examiner's provisional rejection of the claims."); Manual of Patent Examining Procedure § 804(I)(B) ("The 'provisional' double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application *unless* that 'provisional' double patenting rejection is the only rejection remaining in at least one of the applications").

CONCLUSION

In summary:

Claims Rejected	35 U.S.C. §	Basis	Affirmed	Reversed
1, 5, 7, 10–14, 18, 19, 23, and 24	103	Bang, Anjak, Jones, and Chiang		1, 5, 7, 10–14, 18, 19, 23, and 24

REVERSED