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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte ANANTHA HARIJITH, VISWANATHAN NATARAJAN, ROBERTO F. MACHADO, and JEFFREY JACOBSON

Appeal 2020-001340
Application[1] 15/527,103
Technology Center 1600

Before DONALD E. ADAMS, RICHARD M. LEBOVITZ, 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 a pulmonary disease or condition, which have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We reverse.

STATEMENT OF THE CASE

Appellant's Specification indicates that there is a known "correlation between sphingosine kinase (SphK) activity and lung injury." (Spec. ¶ 4.) For example "increased expression of sphingosine kinase 1 (SphKl) has

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[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 The Board of Trustees of the University of Illinois. (Appeal Br. 1.)

been found in lung tissues from patients with idiopathic pulmonary fibrosis." (*Id.*)

The Specification also states that selective inhibitors of SphK1 are known in the prior art. (*Id.* ¶ 5.) Appellant's invention is directed at treating pulmonary diseases or conditions with a selective SphK1 inhibitor having 20-fold greater selectivity for SphK1 than SphK2 and a 50% inhibition at less than 10 μM. (*Id.* ¶6.)

Claims 1–5 and 11–13 are on appeal.[2] Claim 1 is illustrative and reads as follows:

> 1. A method of treating a pulmonary disease or condition in a subject comprising administering to a subject in need of treatment an effective amount of a SphKl inhibitor to treat the subject's pulmonary disease or condition, wherein the SphKl inhibitor
>
> (a) exhibits at least a 20-fold greater selectivity for SphKl than SphK2; and
>
> (b) is cell permeable, has an IC_{50} value of less than 10 μM, or has a K_i of less than 10 μM, or a combination thereof.

(Appeal Br. 16.)

[2] Claims 6–8 remain pending, but are withdrawn from consideration.

The prior art relied upon by the Examiner is:

Name	Reference	Date
Santos et al.	WO2013/119946 A1	Aug. 15, 2013
Mark E. Schnute et al., *Modulation of cellular S1P levels with a novel, potent and specific inhibitor of sphingosine kinase-1*, 444 Biochem J., 79–88 (2012).		

The following ground of rejection by the Examiner is before us on review:

Claims 1–5 and 11–13 under 35 U.S.C. § 103(a) as unpatentable over Santos and Schnute.

DISCUSSION

The Examiner finds that Santos teaches administering "an effective amount of a SphK1 inhibitor to prevent or treat [a] subject's pulmonary disease or condition." (Final Action 6.) The Examiner further finds that Santos teaches "the SphK1 inhibitor is cell permeable and has a . . . [K_i] of less than 10 μm (para [0130[]]), Table 2, pg 46, Compound 64, . . . Compound 64 of the invention is a potent and selective Inhibitor of SphK1)." (*Id.*)

The Examiner finds that Santos does not teach the SphK1 inhibitor to be PF-543 (the compound recited in claims 3 and 11). (*Id.*) The Examiner concludes, however, that substituting Compound 64 of Santos with PF-543 would have been obvious in light of the teachings of Schnute. (*Id.* at 6–7.) In particular, the Examiner finds that Schnute teaches PF-543 is "a potent and selective inhibitor of SphK1 activity" and as such substitution of PF-543 for Compound 64 would have been obvious "to enhance the efficacy of inhibiting SphK1 activity and to thereby improve therapeutic efficacy of treating a pulmonary disease in a subject." (*Id.*)

We disagree with the Examiner's factual findings and conclusion that the claims are obvious over Santos and Schnute. In particular, we disagree that Santos teaches treating a pulmonary disease or condition with a selective SphK1 inhibitor. As Appellant notes, Santos is directed to using compounds of formula 1 for treating a myriad of diseases or conditions. (*See* Appeal Br. 12; Reply Br. 2; Santos ¶¶ 15, 36, 37.) Those conditions include neoplastic diseases (Santos ¶ 39), diseases that involves excess vascular growth, such as macular degeneration (*id.* ¶ 40), inflammatory diseases (*id.* ¶¶ 42–43), allergic diseases (*id.* ¶ 41), sepsis (*id.* ¶ 46), as well as fibrotic diseases, such as pulmonary fibrosis (*id.* ¶ 45).

Compounds of formula I are required to be SphK enzyme inhibitors, but not necessarily selective SphK1 inhibitors as required by the claims. They may "have activity as selective inhibitors of the SphKl enzyme or the SphK2 enzyme or have activity as inhibitors of both SphKl and SphK2 enzymes." (Santos ¶ 37.)

It is true that Santos teaches Compound 64 selectively inhibits SphK1, decreasing S1P. (*Id.* ¶¶ 130 Table 2, 575.) However, Santos teaches a number of other compounds for use in treating any one of the identified diseases or conditions including, as Appellant explained, compound SLR080811 (Appeal Br. 12), which is an SphK2-selective inhibitor and increases S1P levels. (Santos ¶¶ 573–574, ¶ 57 (noting "compound (S)-2-(3-(4-octylphenyl)-1,2,4-oxadiazol-5-YL)pyrrolidine-1-carboximidamide (SLR080811)"); ¶ 130 Table 2 (noting compound (S)-2-(3-(4-octylphenyl)-1,2,4-oxadiazol-5-YL)pyrrolidine-1-carboximidamide is compound 49).)

Furthermore, Santos links pulmonary fibrosis treatment and compounds of Formula 1 that have activity to "improve the barrier function

of endothelial cells, which are identified as compounds "of Formula 1 that inhibit[] SphK2 enzymatic activity." (*Id.* ¶ 48.) The Examiner did not identify disclosure in Santos that ties the use of a selective inhibitor of the SphK1 enzyme as opposed to a selective inhibitor of the SphK2 enzyme for treating a pulmonary condition.

Thus, we do not agree with the Examiner that Santos teaches the use of compound 64, which is an SphK1 selective inhibitor, for use in treating pulmonary disease. Instead, we find the Examiner's position that Santos teaches compound 64 for treating a pulmonary condition amounts to an impermissible application of obvious to try. Nothing in Santos that we have been guided to indicates that SphK1 inhibition is critical for treating pulmonary conditions or provides any suggestion that compound 64 would be likely to be successful in treating pulmonary conditions as opposed to one of the other myriad conditions mentioned. *In re Kubin*, 561 F.3d 1351, 1359 (Fed. Cir. 2009) (identifying two categories of obvious-to-try situations that do not equate to prima facie obviousness under § 103: when what was "obvious to try" was (a) to vary all parameters or try every available option until one succeeds, where the prior art gave no indication of critical parameters and no direction as to which of many possibilities is likely to be successful; or (b) to explore a new technology or general approach in a seemingly promising field of experimentation, where the prior art gave only general guidance as to the particular form or method of achieving the claimed invention.).

We also agree with Appellant that the Examiner has not adequately established a reason that it would have been obvious to substitute PF-543 for compound 64 to treat a pulmonary condition. (Appeal Br. 12–13; Reply Br.

3.) Schnute determines "PF-543 is the most potent inhibitor of SphK1 described to date." (Schnute Abs.) However, the Examiner did not identify any teaching in Schnute to tie this fact to a reasonable expectation that this compound would be able to treat pulmonary conditions. Schnute does not attribute any treatment capabilities with this compound, despite recognizing that

> inhibitors of SphKl could potentially lead to the development of novel strategies for the treatment of autoimmune diseases, for cancer therapy and for neurodegenerative diseases.

(*Id.* at 85.) In fact, Schnute notes, with regard to the cancer cell line 1483 in which the compound was tested, that despite inhibiting SphK1 to a great extent, the cancer cell line grew at the normal rate. (*Id.* at 87.) Schnute also was also "unable to confirm growth inhibition by blockade of SphKl activity in U937 [leukemia] and LN229 [glioblastoma] cells." (*Id.*) After performing various experiments, Schnute concludes only that PF-543 "provides a new and valuable tool for the interrogation of biological effects of modulation of S1P signaling resulting from specific inhibition of SphK 1 catalytic activity." (*Id.* at 87.)

For the foregoing reasons, we do not affirm the Examiner's rejection of claims 1–5 and 11–13 as being obvious from Santos and Schnute.

DECISION SUMMARY

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1–5, 11–13	103	Santos, Schnute		1–5, 11–13

REVERSED