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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

OSI PHARMACEUTICALS, LLC
and GENENTECH, INC.,

Petitioner,

v.

ARCH DEVELOPMENT CORP. and
DANA-FARBER CANCER INSTITUTE, INC.,

Patent Owner.

Case IPR2016-01034
Patent 7,838,512 B1

Before LORA M. GREEN, TINA E. HULSE, and
ROBERT A. POLLOCK, *Administrative Patent Judges*.

POLLOCK, *Administrative Patent Judge*.

DECISION
Denying Request for Rehearing
37 C.F.R. §42.71

I. INTRODUCTION

A. Background

In our Final Written Decision (Paper 43, "Dec."), we held that claims 1–3, 5, and 6 (collectively, "the challenged claims") of U.S. Patent No. 7,838,512 B1 (Ex. 1001, "the '512 patent") were unpatentable over Akinaga,[1] in view of the knowledge of a person of ordinary skill in the art, Seynaeve,[2] Friedman,[3] and Tam[4] (Ground IV). *See* Dec. 38–39.[5] Patent Owner timely filed a Request for Rehearing requesting that we vacate the portion of our Decision relating to that Ground. Paper 44 ("Reh'g Req.").[6] We did not authorize any response to the Request for Rehearing.

For the reasons that follow, we deny Patent Owner's Request for Rehearing.

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[1] Shiro Akinaga et al., *Enhancement of Antitumor Activity of Mitomycin C In Vitro and In Vivo by UCN-01, a Selective Inhibitor of Protein Kinase C*, 32 CANCER CHEMOTHERAPY AND PHARMACOLOGY 183–89 (1993). Ex. 1004.
[2] Caroline M. Seynaeve et al., *Cell Cycle Arrest and Growth Inhibition by the Protein Kinase Antagonist UCN-01 in Human Breast Carcinoma Cells*, 53 CANCER RES. 2081–86 (1993). Ex. 1014.
[3] BethAnn Friedman et al., *Regulation of the Epidermal Growth Factor Receptor by Growth-Modulating Agents: Effects of Staurosporine, a Protein Kinase Inhibitor*, 50 CANCER RES. 533–38 (1990). Ex. 1031.
[4] Sun W. Tam and Robert Schlegel, *Staurosporine Overrides Checkpoints for Mitotic Onset in BHK Cells*, 3 CELL GROWTH & DIFFERENTIATION 811–17 (1992). Ex. 1012.
[5] We note that Paper 43, the Final Written Decision, issued September 11, 2017, contains font changes introduced during the uploading process. Paper 43 is hereby republished to eliminate the unintended font changes.
[6] We further found claim 6 invalid for reasons not at issue here.

B. Standard for Reconsideration

The applicable standard for a request for rehearing is set forth in 37 C.F.R. § 42.71(d), which provides in relevant part:

> A party dissatisfied with a decision may file a request for rehearing, without prior authorization from the Board. The burden of showing a decision should be modified lies with the party challenging the decision. The request must specifically identify all matters the party believes the Board misapprehended or overlooked, and the place where each matter was previously addressed in a motion, an opposition, or a reply.

II. ANALYSIS

Patent Owner argues that we should grant its Request for Rehearing because our conclusion is based on findings that 1) staurosporine was known to inhibit the tyrosine kinase c-src in human and animal cells; and 2) that staurosporine has a structure and mechanism of action similar to UCN-01, such that one of ordinary skill in the art would expect UCN-01 to likewise inhibit tyrosine kinases such as c-src. *See* Reh'g Req. 1–2. As an initial matter, we reject the premise of Patent Owner's argument that our Decision stands or falls on whether one of ordinary skill in the art would have understood that UCN-01 inhibits the tyrosine kinase c-src in human and animal cells.

As illustrated in claim 1, the challenged claims are generally directed to administering a chemotherapeutic DNA damaging agent in combination with a low molecular weight tyrosine kinase inhibitor.[7] According to the Specification, this combination is beneficial because treatment with a DNA damaging agent promotes cell cycle arrest, during which time cells attempt

[7] Patent Owner concedes that claim 1 is representative and does not argue claims 2, 3, 5, and 6 separately. *See*, *e.g.*, PO Resp. 3.

to repair DNA damage before undergoing mitosis and subsequent cell division. *See* Dec. 4–6. Tyrosine kinase inhibitors, however, force cells to override the cell cycle arrest checkpoint and enter mitosis before repairs are complete, thereby enhancing the cytotoxic effects of the DNA damaging agents. *Id.*

As discussed in our Decision, Akinaga examines the effect of UCN-01 alone, and in combination with the DNA damaging agent mitomycin C. *See* Dec. 27–28; Ex. 1004. Noting that the two compounds had 1) complementary effects in delaying cell cycle progression; and 2) synergistic cytotoxic and antitumor effects, Akinaga expressly suggests the combination of UCN-01 and DNA-damaging agents for cancer chemotherapy. *Id.* Seynaeve establishes that UCN-01 inhibits multiple tyrosine kinases in human breast cancer cells coincident with promoting cell cycle arrest. Dec. 28–29, 34–35; Ex. 1014. Accordingly, "Seynaeve proposes a link between UCN-01's inhibitory effects on tyrosine kinases and its inhibitory effects on the cell cycle." Dec. 29.[8]

Akinaga further suggests combining a chemotherapeutic DNA damaging agent with UCN-01 because the two compounds cause delays in different stages of the cell cycle and result in synergistic cytotoxic and antitumor effects, whereas Seynaeve examines the effects of UCN-01 on the cell cycle of human carcinoma cells and shows that UCN-01 is a tyrosine kinase inhibitor. *See* Dec. 37–38. Because both references

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[8] Considering Seynaeve teachings with respect to UCN-01, we reject Patent Owner's contention that "there is no evidence from which one can reasonably find that Petitioner carried its burden of proving that people of ordinary skill in the art considered either staurosporine or UCN-01 to be tyrosine kinase inhibitors." *See* Reh'g. Req. 6.

investigate the effect of UCN-01 on cell cycle arrest in human tumor cells, one of ordinary skill in the art would have found reason to combine their teachings. *See id.*

Accordingly, our Decision holding claims 1–3, 5, and 6 unpatentable under Ground IV is supported by substantial evidence irrespective of whether one of ordinary skill in the art would have understood that UCN-01 inhibits c-src in human and animal cells. We, nonetheless, address the specifics of Patent Owner's arguments.

A. Robinson

In our Decision, we rejected Patent Owner's contention that although Akinaga teaches that UCN-01 inhibits v-src (as does Seynaeve), one of ordinary skill in the art would have no reason to believe that UCN-01 would inhibit its cellular homolog c-src because v-src is "found only in chickens" and "is more difficult to inhibit." Dec. 28, 32. We instead credited the testimony of Petitioner's expert, Dr. Eastman that "[b]ecause v-Src and c-Src have similar structures, compounds that inhibit the tyrosine kinase activity of v-Src generally inhibit c-Src as well. Thus, a person of ordinary skill would have understood that an inhibitor of v-Src would also inhibit the c-Src protein present in A431 cells and other human tumors." *Id*. at 33 (quoting Ex. 1002 ¶ 202). Dr. Eastman testified that Robinson, for example, showed "that staurosporine, a molecule very similar to UCN-01, inhibited both v-Src and c-Src. . . . Thus, a person of ordinary skill in the art would have recognized that UCN-01 would inhibit tyrosine kinases in both animals and humans." *Id.*

According to Robinson, "[t]he elevation in the tyrosine-specific kinase activity of *pp60 c-src* in human carcinoma . . . is suggestive that appropriate tyrosine kinase inhibitors may represent a new class of cancer

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