

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

LUPIN LTD. and LUPIN PHARMACEUTICALS INC., INNOPHARMA
LICENSING, INC., INNOPHARMA LICENSING LLC, INNOPHARMA
INC., INNOPHARMA LLC, MYLAN PHARMACEUTICALS INC., and
MYLAN INC.
Petitioners

v.

SENJU PHARMACEUTICAL CO., LTD.
Patent Owner

Case IPR2015-01100¹
Patent 8,927,606

**PETITIONERS' REPLY TO PATENT OWNER'S
RESPONSE TO PETITION**

¹ Case IPR2016-00091 has been joined with this proceeding.

TABLE OF CONTENTS

| | | |
|------|---|----|
| I. | A POSA Would Have Combined Ogawa and Sallmann to Arrive at the Claimed Invention | 1 |
| A. | Bromfenac Was an NSAID with Superior Efficacy | 1 |
| B. | A POSA Would Have Considered Ogawa Example 6 | 2 |
| C. | A POSA Would Have Considered Sallmann Example 2..... | 3 |
| D. | One of ordinary skill would have been motivated to seek to replace polysorbate 80, and would have arrived at tyloxapol..... | 4 |
| A. | Ethoxylated Octylphenols Were Known to Solve the Complexation Problem..... | 12 |
| 1. | Tyloxapol Falls within the Class of Ethoxylated Octylphenols Disclosed in Fu | 13 |
| 2. | Tyloxapol and Polysorbate 80 were Among the Few Nonionic Surfactants..... | 14 |
| B. | BAC Was Commonly Used for Ophthalmic Products..... | 15 |
| III. | Patent Owner’s Evidence of Alleged Objective Indicia is Not Probative of Patentability | 16 |
| A. | Patent Owner’s Purported Unexpected Results Relating to Tyloxapol were Known in the Art..... | 16 |
| B. | The Data Relied Upon by Patent Owner Do Not Demonstrate More Chemical Stability Than The Closest Prior Art..... | 17 |
| C. | The Alleged Unexpected Benefits of The Claimed Invention Do Not Support Nonobviousness..... | 18 |
| D. | Patent Owner’s Test Data Should be Disregarded..... | 19 |
| E. | Evidence of Commercial Success Lacks Factual Support and Nexus with the Claims | 20 |

| | | |
|----|---|----|
| F. | Patent Owner’s Evidence of Secondary Considerations are Not Commensurate with the Scope of the Claims | 22 |
| G. | Patent Owner Did Not Compare the Closest Prior Art | 24 |
| H. | Patent Owner’s Arguments Regarding Licensing and Copying are Misplaced | 24 |
| I. | The Dependent Claims Are Not Separately Patentable | 25 |
| | CERTIFICATION OF SERVICE..... | 26 |

I. A POSA Would Have Combined Ogawa and Sallmann to Arrive at the Claimed Invention

One of skill in the art would have combined the teaching of Ogawa and Sallmann to arrive at the claims of the '606 patent. Based on the prior art, a POSA would have understood that replacing polysorbate 80 in Ogawa Example 6 with tyloxapol would have increased the stability of the formulation. Per Dr. Lawrence, a POSA would have understood that a function of polysorbate 80 in Ogawa formulation 6 is to stabilize the formulation against precipitation of bromfenac-BAC complexes known to occur. EX1094, ¶31. It was known that tyloxapol had improved properties over polysorbate 80, as well as antioxidant activity.

A. Bromfenac Was an NSAID with Superior Efficacy

Contrary to Patent Owner's assertions, one of ordinary skill would have chosen bromfenac as an ideal active agent for the treatment of ophthalmic conditions. Patent Owner does not dispute that Hara, which compared bromfenac sodium to pranoprofen, indomethacin, and diclofenac sodium, concluded that bromfenac "shows superior efficacy in treating anterior eye inflammation and post-operative inflammation." (EX1006, 3:2:2). Instead Patent Owner simply ignores the statement in Hara that "the range of applications [for diclofenac] is limited because the drug is indicated only for use in treating inflammation following cataract surgery." (EX1006, 2:2:5-3:1:1).

Patent Owner's allegation that the adverse events observed with the oral form of bromfenac would encourage a POSA to use diclofenac, is of little merit. Other NSAIDs, including diclofenac, were known to have similar issues. (EX1091, 2300:2:1; EX1092, 3:1:2; EX1093, 1:1:1, 4:2:2). Moreover, an ophthalmic dosage form of bromfenac was approved by the FDA. (EX2111, 2).

B. A POSA Would Have Considered Ogawa Example 6

Patent Owner's allegation that a POSA would not have been motivated to develop an improved bromfenac formulation is contrary to the prior art and the basic knowledge of a POSA. (Resp. at 8-10; EX1006, 2:1:2, 2:2:5-3:1:1, 3:2:2). Patent Owner would lead one to believe that a POSA would have simply stopped there and would have ignored the abundance of evidence that NSAID formulations can be further improved by using tyloxapol in place of polysorbate 80. Simply arguing that a POSA would not seek to improve something merely because it is "sufficient" is not the standard for obviousness. Moreover, as Dr. Lawrence testified, [REDACTED]

[REDACTED] (EX2316, 53:18-54:5).

[REDACTED]

[REDACTED]

(EX2316, 53:18-54:5, 148:14-20). By arguing that the formulation taught by Ogawa Example 6 is "stable" (Resp. at 9) and that one would not seek to improve

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.