IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

FRESENIUS KABI USA LLC

Petitioner,

v.

CUBIST PHARMACEUTICALS LLC

Patent Owner.

Case: IPR2015-01571

Patent No. 8,058,238

PATENT OWNER'S PRELIMINARY RESPONSE UNDER 37 C.F.R. § 42.107

TABLE OF CONTENTS

PAGE

TABLE OF AUTHORITIES

Page(s)

Cases

Statutes

Other Authorities

I. INTRODUCTION

Patent Owner Cubist Pharmaceuticals LLC's ("Cubist") U.S. Patent No. 8,058,238 (the "'238 patent") claims highly purified daptomycin compositions and pharmaceutical compositions thereof. The '238 patent discloses techniques that allow for the production of highly purified daptomycin compositions on a commercial scale. Previous purification techniques for daptomycin did not effectively remove these harmful impurities and resulted in extremely low yields, which made commercial-scale production of daptomycin infeasible.

Fresenius Kabi USA LLC ("Fresenius") filed the present Petition to invalidate certain claims of the '238 patent as obvious. Subsequently, the Board granted a joint motion to limit the present Petition to claims 98 and 187. *See* IPR2015-01571, Paper 15 (September 15, 2015). Therefore, the Petition is now narrowed to claims 98 and 187, challenged in Ground 1. The other claims and, consequently, Ground 2, are no longer at issue. Nevertheless, Fresenius's Petition, even as narrowed, should not be instituted as there is no reasonable likelihood that Petitioner will prevail on at least one claim.

Ground 1 fails to address motivation to combine the asserted references. This deficiency defeats Fresenius's proposed Ground 1, the only ground at issue, such that there is no reasonable likelihood that the Petitioner will prevail on at least one claim, and the Board should not institute review. 35 U.S.C. § 314; 37 C.F.R.

§ 42.108. Patent Owner also disagrees with the Petition on the merits, but will not address the substance of Petitioner's arguments in this paper.

A. State of the Art Prior to the Invention

Daptomycin is a potent antibiotic effective for treating serious infections caused by certain Gram-positive bacteria including *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* ("MRSA"). *See* CUBICIN® (daptomycin for injection) label approved November 26, 2014, at 2 (Ex. 2001). Daptomycin is obtained by fermenting the soil microorganism *Streptomyces roseosporus* (*S. roseosporus*). '238 patent at 1:60-63 (Ex. 1001). Fermenting *S. roseosporus* produces a complex mixture containing many undesirable compounds. Separating daptomycin from these compounds is difficult, particularly while obtaining quantities on a commercial scale.

The mixture resulting from fermentation of *S. roseosporus* may contain, among other things, endotoxins, saponins, and a group of daptomycin-related impurities identified in Table 3 of the '238 patent. *Id*. at 33:63-34:19. Each of these substances is undesirable in a pharmaceutical daptomycin composition. Even very small amounts of endotoxins (also referred to as pyrogens) can cause fever and other symptoms in humans. *See* U.S. Pharmacopeial Convention, The United States Pharmacopeia 90-91 & n.2 (36th prtg. 2012) (Ex. 2002). As a result, endotoxin levels are strictly limited in commercial pharmaceutical compositions.

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