Filed on behalf of: Mylan Pharmaceuticals Inc.
By: Steven W. Parmelee
Michael T. Rosato
Jad A. Mills
WILSON SONSINI GOODRICH & ROSATI

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.,
Petitioner,

v.

BAYER Intellectual Property GmbH,
Patent Owner.

Case No. IPR2017-00041
Patent No. 7,157,456

PETITION FOR INTER PARTES REVIEW OF U.S. PATENT NO. 7,157,456

Table of Contents

I. INTRODUCTION

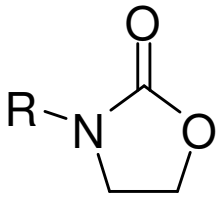
Mylan Pharmaceuticals Inc. ("Petitioner") requests *inter partes* review of U.S. Patent No. 7,157,456 to Straub *et al.* ("the '456 patent," EX1001), which issued on January 2, 2007. PTO records indicate the '456 patent is assigned to Bayer Intellectual Property GmbH ("Patent Owner"). This Petition demonstrates there is a reasonable likelihood that claims 1-8, 10-14, 16-22, 24, 26-28, and 30 of the '456 patent are unpatentable over prior art. Additional Petitions are being filed to address related patents that are terminally disclaimed over the '456 patent.

Multiple enzymes are involved in the blood clotting cascade, but one protein known as "factor X," via its active form, "Xa," is called upon at an essential point in both the intrinsic and extrinsic coagulation pathways. EX1014 at 6630. The '456 patent is directed to a class of compounds that bind to and inhibit "factor Xa." Because the crystal structure of factor Xa was known, the art had established the presence of dual binding pockets for inhibitors, termed the S1 and S4 pockets. *Id.*; *see also* EX1015 at 390. The S1 pocket was recognized as a narrow cleft that bound planar aromatic groups, while the S4 pocket was less selective, binding not only planar aromatic groups but also non-aromatic rings with heteroatoms, such as nitrogen and oxygen. *Id.*

Based on the detailed knowledge of the factor Xa binding pockets, the art had designed dozens of compounds which fit into these pockets and showed potent

inhibition of factor Xa. *See generally*, Ewing, EX1007. What these compounds lacked was not potency, but favorable pharmacokinetic profiles. *Id.* Oral bioavailability was especially sought after, as the art needed new, safe and effective, orally-active anticoagulants. Many viewed factor Xa inhibitors as attractive drug targets for developing effective oral anticoagulants. *Id.*

Oxazolidinones are a class of compounds comprising a 5-membered heterocycle (shown), and had long been known in the art to have various pharmacologic activities. EX1008.



The art described oxazolidinone compounds that inhibited platelet aggregation, and were said to be useful in the treatment of thrombosis and myocardial infarction. *Id.* The "most advanced" oxazolidinone compound, linezolid, was known to have very desirable pharmacokinetic and pharmacologic properties, including high oral bioavailability and patient tolerability. *Id.* at 626-27. Linezolid was safe in humans and had entered Phase III human clinical trials for antimicrobial uses.

It was known that oxazolidinone-based antibiotics could have dual uses for other indications, and that they could be optimized for other therapeutic activities, including as anti-depressants or as anticoagulants. EX1008 at 630; EX1018 at 136. Linezolid's 4'-morpholinophenyl arm was a known factor Xa binding moiety, and was present on a factor Xa inhibitor disclosed in Example 1 of PCT WO 00/39111 (the '111 publication, EX1009). This binding moiety is structurally similar to the

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