ROPES & GRAY ALERT

FDA Regulatory ▪ Government Enforcement / White Collar Crime ▪ Appellate & Supreme Court

December 16, 2015

Ropes & Gray Advises Pacira Pharmaceuticals in Reaching Landmark Settlement Agreement with FDA

A cross-disciplinary team of Ropes & Gray attorneys advised Pacira Pharmaceuticals on its December 14 settlement agreement with FDA. On behalf of Pacira, Ropes & Gray had filed suit against FDA in September 2015 in the U.S District Court for the Southern District of New York, alleging that the agency had violated Pacira's First and Fifth Amendment rights, as well as the Administrative Procedure Act, in issuing a Warning Letter in 2014 that had accused Pacira of engaging in off-label marketing of EXPAREL®, the company's flagship drug. In its complaint and motion for a preliminary injunction, Pacira contended that the marketing claims cited by FDA in the Warning Letter were "on-label," rather than "off-label" as alleged by the agency; additionally, Pacira argued that even if its speech were deemed off-label, the speech was truthful and non-misleading and thus deserving of First Amendment protection. The pharmaceutical industry has been following the litigation closely as an indication how this approach of combining administrative and constitutional claims might fare in the wake of recent favorable First Amendment decisions relating to pharmaceutical manufacturers' marketing.

By teaming its veteran appellate and government enforcement litigators up with its expert FDA regulatory attorneys, Ropes & Gray helped Pacira win a resounding victory in the case. As described below, under the terms of the settlement agreement, FDA took the unprecedented step of withdrawing its Warning Letter, confirming that Pacira's promotional claims for EXPAREL were in fact on-label. Additionally, to clarify ambiguities that gave rise to the Warning Letter, FDA agreed to approve significant revisions to the EXPAREL label.

Background on Litigation

On September 8, 2015, Pacira filed a lawsuit against FDA seeking to gain clarity about the scope of EXPAREL's approval and to exercise its rights to communicate truthful and non-misleading information. The lawsuit followed the company's previously unsuccessful attempts to engage FDA in a dialogue regarding allegations made by FDA in the 2014 Warning Letter. Although FDA had approved EXPAREL in 2011 for "administration into the surgical site to produce postsurgical analgesia," the Warning Letter alleged that Pacira could not promote EXPAREL for use in surgeries other than bunionectomy and hemorrhoidectomy, the two sites studied in Pacira's pivotal clinical trials. The Warning Letter also asserted that Pacira could not make claims about EXPAREL's duration of effectiveness over 72 hours, even though that was the primary endpoint of one of the drug's pivotal trials.

Three prominent experts submitted declarations supporting Pacira's lawsuit. Dr. Larry Goldkind, a former high-ranking FDA official, described how the Warning Letter was inconsistent with both FDA's 2011 approval of EXPAREL and the agency's long-standing policy and practices relating to approval of analgesic drugs more generally. Dr. Lee-Jen Wei, a tenured professor of biostatistics at Harvard, explained that one of EXPAREL's pivotal trials demonstrated a significant treatment effect for EXPAREL compared to placebo for up to 72 hours. And Dr. Alex Cahana, a specialist in pain medication, described the substantial public health benefits of communicating information about non-opioid pain drugs such as EXPAREL.

Highlights of Settlement Agreement

The settlement confirms, as Pacira had maintained throughout, that EXPAREL is, and has at all times been, broadly approved to provide postsurgical analgesia and that Pacira did not violate the law by marketing EXPAREL for use in surgical sites beyond the two sites studied in its pivotal clinical trials. The key features of the settlement are as follows:

First, in an unprecedented move, FDA rescinded the Warning Letter and issued a new letter to Pacira explaining the reasons for the withdrawal (the "rescission letter"). The rescission letter, signed by Janet Woodcock, Director of the Center for Drug Evaluation and Research, acknowledged that the EXPAREL label as initially approved "created ambiguity with respect to the scope of the approved indication" and that upon further review, FDA concluded that the Warning Letter was based on a misreading of the EXPAREL label. The rescission letter also conceded that the plain language of the Indications and Usage section in the EXPAREL label, as well as the pivotal clinical trials submitted to FDA, made clear that EXPAREL is approved for postsurgical analgesia in surgical sites generally, and that the approval is not limited to bunionectomy and hemorrhoidectomy procedures.

Second, FDA approved a significant revision to the EXPAREL label to address certain ambiguities in the EXPAREL label that gave rise to the Warning Letter. In particular, the new label makes clear that EXPAREL is indicated for use in surgical sites generally, not just the two sites studied in EXPAREL's pivotal trials. Additionally, the revised Dosing and Administration section provides general guidance on selecting the proper EXPAREL dose for the planned surgical site and indicates that the dosing information from the two pivotal trials provides examples from which practitioners may extrapolate for administration in other surgical sites. The label also deletes language characterizing the duration of effect of EXPAREL in one of the pivotal studies and replaces it with a more balanced explanation of the data regarding effectiveness.

Doug Hallward-Driemeier of Ropes & Gray LLP, attorney for Pacira, stated, "We have long argued that the FDA Warning Letter to Pacira was issued in error because it was based on FDA's misinterpretation of the approved indication for EXPAREL and the clinical evidence supporting the drug's approval. We are pleased that the agency took the extraordinary steps of withdrawing the Warning Letter and revising the EXPAREL label, both of which fully vindicate our client and its lawful and appropriate promotional practices."

The Ropes & Gray cross-practice team representing Pacira included appellate & Supreme Court partner Doug Hallward-Driemeier; FDA regulatory partner Joy Liu; government enforcement partner Joan McPhee; FDA regulatory counsel Kellie Combs; business & securities litigation counsel Justin Florence; business & securities litigation associate Julian Helisek; and litigation associates Emerson Siegle and John Dey. If you have questions about the Pacira settlement, please consult with the attorneys listed above or your usual Ropes & Gray advisor.