U.S. FOOD & DRUG ADMINISTRATION

VIA UNITED PARCEL SERVICE AND E-MAIL

Pacira Pharmaceuticals, Inc.
Attention: Christine Brozyniak
5 Sylvan Way
Parsippany, New Jersey 07054
Christine.Brozyniak@pacira.com

Re: Submission of Clinical Trial Results Information Pursuant to 42 U.S.C. 282(j)
FDA Reference Number: CDER-2020-115
NCT02713178, NCT02713230, NCT02713490, NCT03015961, and NCT02922582

Dear Ms. Brozyniak:

Based on an initial review of Food and Drug Administration (FDA) records; information from the ClinicalTrials.gov data bank operated by the National Library of Medicine, a part of the National Institutes of Health; and any available public information, it appears that Pacira Pharmaceuticals, Inc. is the "responsible party"[1] for the above-identified clinical trials, which appear to be "applicable clinical trials"[2] subject to the requirements of section 801 of the Food and Drug Administration Amendments Act of 2007, including its implementing regulations in 42 CFR part 11. A responsible party for an applicable clinical trial is required to submit to the ClinicalTrials.gov data bank certain results information for the trial; such results information generally must be submitted no later than one year after the primary completion date of the applicable clinical trial, unless the responsible party has submitted a certification of delay.[3]

FDA has identified potential noncompliance related to each of the following clinical trials:

- Protocol 402-C-326, "A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy, Safety, and Pharmacokinetics of Femoral Nerve Block with

[1] *See* section 402(j)(1)(A)(ix) of the Public Health Service Act (PHS Act) (42 U.S.C. 282(j)(1)(A)(ix)) and 42 CFR 11.10 for the definition of *responsible party*.
[2] *See* section 402(j)(1)(A)(i) and (iii) of the PHS Act (42 U.S.C. 282(j)(1)(A)(i) and (iii)) and 42 CFR 11.10 for definitions of *applicable clinical trial*.
[3] *See* section 402(j)(3)(E) of the PHS Act (42 U.S.C. 282(j)(3)(E)) and 42 CFR part 11 subpart C for results information submission requirements.

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EXPAREL® for Postsurgical Analgesia in Subjects Undergoing Total Knee Arthroplasty," evaluating the magnitude and duration of the analgesic effect achieved following a single-dose-injection femoral nerve block with EXPAREL® (bupivacaine liposome injectable suspension), an FDA-approved drug, in subjects undergoing primary unilateral total knee arthroplasty (TKA); and Protocol 402-C-327, "A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy, Safety and Pharmacokinetics of Brachial Plexus Nerve Block with EXPAREL® for Postsurgical Analgesia in Subjects Undergoing Total Shoulder Arthroplasty or Rotator Cuff Repair," evaluating the magnitude and duration of the analgesic effect achieved following a single-dose-injection brachial plexus nerve block with EXPAREL® (bupivacaine liposome injectable suspension), an FDA-approved drug, in subjects undergoing total shoulder arthroplasty or rotator cuff repair

- Protocol 402-C-331 (PILLAR Study), "A Multicenter, Randomized, Double-Blind, Controlled Trial Comparing Local Infiltration Analgesia with EXPAREL® to Local Infiltration Analgesia Without EXPAREL® to Manage Postsurgical Pain Following Total Knee Arthroplasty," comparing the pain control and total opioid consumption following local infiltration analgesia (LIA) with EXPAREL®, to the pain control and total opioid consumption following LIA without EXPAREL®, in adult subjects undergoing primary unilateral TKA

- Protocol 402-C-409, "A Multicenter, Randomized, Double-Blind, Controlled Study of EXPAREL® for Postsurgical Pain Management in Subjects Undergoing Open Lumbar Spinal Fusion Surgery," comparing postsurgical pain control following LIA with EXPAREL® admixed with bupivacaine HCl, to postsurgical pain control following LIA with bupivacaine HCL alone, in adult subjects undergoing open lumbar posterior spinal fusion surgery

- Protocol 404-C-201, "A Randomized, Single-Blind, Active-Controlled, Dose-Ranging Study to Evaluate PK [Pharmacokinetics], Safety, and Efficacy of Local Administration of DepoTXA for Reduced Post-Surgical Bleeding in Subjects Undergoing TKA," evaluating the pharmacokinetics, safety, and efficacy of DepoTXA, compared to the pharmacokinetics, safety, and efficacy of intravenous tranexamic acid, in reducing postsurgical bleeding

It appears that results information for the referenced applicable clinical trials has not been submitted to the ClinicalTrials.gov data bank. Your company should review records of these clinical trials and determine whether your company submitted all required results information. If your company determines that results information is required and due for these clinical trials, please submit the results information promptly.

Failure to submit clinical trial information required under section 402(j) of the Public Health Service Act (PHS Act) (42 U.S.C. 282(j)), including information required under the regulations found in 42 CFR part 11, is a prohibited act under section 301(jj)(2) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 331(jj)(2)). FDA intends to further review and assess the above-identified clinical trials beginning 30 calendar days after you receive this letter. If FDA determines that your company is not in compliance with all applicable requirements of section 402(j) of the PHS Act (42 U.S.C. 282(j)) and 42 CFR part 11, your company may receive from FDA a Notice of Noncompliance,[4] and FDA may thereafter initiate an administrative action seeking a civil monetary penalty.[5] In addition to civil monetary penalties, violations of section 301(jj) of the FD&C Act (21 U.S.C. 331(jj)) could also result in other regulatory action, such as injunction and/or criminal prosecution.

As requested, please review your company's clinical trial records and submit any required results information to the ClinicalTrials.gov data bank. You can access the ClinicalTrials.gov website at https://register.clinicaltrials.gov. If you have any questions about this letter, you may call Mark S. Miller, Pharm.D., at (301) 796-2798. Please have the FDA Reference Number provided at the top of this letter available when you call. Alternatively, you may e-mail him at CDER-OSI-Advisory@fda.hhs.gov. Please include the FDA Reference Number with any e-mail communications.

We request that you submit a written response to FDA within 30 calendar days after you receive this letter, stating the actions that you have taken in response to this letter. If you believe that your company has complied with applicable requirements, please provide us with your reasoning and include any supporting information for our consideration. Please direct your response to the address below and include the FDA Reference Number on all correspondence relating to this matter.

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[4] *See* section 402(j)(5)(C)(ii) of the PHS Act (42 U.S.C. 282(j)(5)(C)(ii)).

[5] Pursuant to section 303(f)(3)(A) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 333(f)(3)(A)), "[a]ny person who violates section 301(jj) [of the FD&C Act (21 U.S.C. 331(jj))] shall be subject to a civil monetary penalty of not more than $10,000 for all violations adjudicated in a single proceeding." Moreover, section 303(f)(3)(B) of the FD&C Act (21 U.S.C. 333(f)(3)(B)) provides that "[i]f a violation of section 301(jj) [of the FD&C Act (21 U.S.C. 331(jj))] is not corrected within the 30-day period following notification under section 402(j)(5)(C)(ii) [of the PHS Act (42 U.S.C. 282(j)(5)(C)(ii))], the person shall, in addition to any penalty under subparagraph (A), be subject to a civil monetary penalty of not more than $10,000 for each day of the violation after such period until the violation is corrected." The civil monetary penalty amounts listed in this letter reflect the amounts listed in the statute. These amounts are updated annually to reflect inflation, as required by the Federal Civil Penalties Inflation Adjustment Act of 1990 (Pub. L. No. 101-410, 104 Stat. 890 (1990) (codified as amended at 28 U.S.C. 2461 note 2(a)), as amended by the Federal Civil Penalties Inflation Adjustment Act Improvements Act of 2015 (Sec. 701 of the Bipartisan Budget Act of 2015, Pub. L. No. 114-74, November 2, 2015). For the most up-to-date amounts, please see 45 CFR 102.3.

Mark S. Miller, Pharm.D., BCPS, RAC
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Sincerely yours,

{See appended electronic signature page}

David C. Burrow, Pharm.D., J.D.
Director
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/s/

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