U.S. FOOD & DRUG ADMINISTRATION

VIA E-MAIL

Jenny C. Chang, M.D.
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Re: Submission of Clinical Trial Results Information Pursuant to 42 U.S.C. 282(j)
FDA Reference Number: CDER-2020-121
NCT01446016, NCT01931163, NCT02988986, and NCT02073487

Dear Dr. Chang:

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 you are 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 such clinical trials, which generally must be submitted no later than one year after the primary completion date of the applicable clinical trials, unless the responsible party has submitted a certification of delay.[3]

[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 the definition 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 11, subpart C for results information submission requirements.

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

- Pro00006423, "Phase II Study of The Efficacy and Safety of Chloroquine (C) in CombinAtion with Taxane or Taxane-like (T) Chemo Agents in the Treatment of Patients with Advanced or Metastatic Breast Cancer Who Have Failed Anthracycline Chemo Base Therapy," evaluating the anti-tumor activity of the combination of chloroquine plus taxane or taxane-like chemo agents (paclitaxel, docetaxel, Abraxane®, ixabepilone), all FDA-approved drugs, in subjects with advanced or metastatic breast cancer

- Pro00008952, "Neoadjuvant Phase II Study of Everolimus Plus Cisplatin in Triple Negative Breast Cancer Patients with Residual Disease After Standard Chemotherapy," evaluating tumor response to everolimus plus cisplatin, both FDA-approved drugs, in triple-negative breast cancer subjects with residual disease

- Pro00016065, "Open Label, Phase II Trial of Neoadjuvant TAK-228 Plus Tamoxifen in Patients with Estrogen Receptor (ER)-Positive, Human Epidermal Growth Factor Receptor 2 (HER2)-Negative Breast Cancer," evaluating the efficacy, toxicity, and safety of TAK-228 plus tamoxifen, an FDA-approved drug, in subjects with newly diagnosed ER-positive, HER2-negative breast cancer

- Pro00010074, "Randomized Open Label PhII Trial of Neoadjuvant Trastuzumab Emtansine (Te) in Combination w/Lapatinib (L) Followed by Abraxane® (A) Compared w/Trastuzumab Plus Pertuzumab Followed by Paclitaxel in Her2/Neu Over-Expressed Breast Cancer Patients," comparing the efficacy and safety of trastuzumab emtansine plus lapatinib followed by Abraxane® versus trastuzumab plus pertuzumab followed by paclitaxel, all FDA-approved drugs, in subjects with HER2-overexpressing breast cancer

It appears that results information for the referenced applicable clinical trials has not been submitted to the ClinicalTrials.gov data bank. You should review your records of these clinical trials and determine whether you submitted all required results information. If you determine 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 you are 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, you 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 result in other regulatory action without further notice, such as injunction and/or criminal prosecution.

As requested, please review your 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 you have taken in response to this letter. If you believe that you have 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 in 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] Under section 303(f)(3)(A) of the Federal Food, Drug, & 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.

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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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