

VIA UNITED PARCEL SERVICE AND E-MAIL

Steven J. Isakoff, M.D., Ph.D.
Massachusetts General Hospital
55 Fruit Street, LRH306
Boston, Massachusetts 02114

Re: Submission of Clinical Trial Results Information Pursuant to 42 U.S.C. 282(j)
FDA Reference Number: CDER-2024-139
NCT01009788 and NCT01441947

Dear Dr. Isakoff:

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 the clinical trial; such results information generally must be submitted no later than one year after the primary completion date³ of the applicable clinical trial, unless the responsible party has submitted a timely certification of delay, a request

¹ See sections 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.” We recognize that Steven Isakoff, M.D., Ph.D., Massachusetts General Hospital is listed as the responsible party for these applicable clinical trials in the ClinicalTrials.gov data bank. Given the definition of “responsible party” in the statute and regulations, and the definition of “sponsor” in 21 CFR 50.3, we have concluded that you are the responsible party and sponsor for these applicable clinical trials.

² See sections 402(j)(1)(A)(i)-(iii) of the PHS Act (42 U.S.C. 282(j)(1)(A)(i)-(iii)) and 42 CFR 11.10 for the definition of “applicable clinical trial.”

³ See 42 CFR 11.10 for the definition of “primary completion date.” See also section 402(j)(1)(A)(v) of the PHS Act (42 U.S.C. 282(j)(1)(A)(v)), which defines “completion date.” As reflected in 42 CFR 11.10, the terms “primary completion date” and “completion date” are synonymous for the purposes of 42 CFR part 11.

for an extension for good cause, or a request for a waiver of the requirements for submission of results information.⁴

FDA has identified potential noncompliance related to the above-identified clinical trials, titled as follow:

- “A Phase 2 Study of ABT-888 and Temozolomide for Metastatic Breast Cancer and an Expansion Cohort in BRCA1/2 Mutation Carriers”
- “A Phase II Trial of Cabozantinib in Women With Metastatic Hormone-Receptor-Positive Breast Cancer With Involvement of Bone”

It appears that results information for the referenced trials have not been submitted to the ClinicalTrials.gov data bank. Moreover, it appears that you failed to update the clinical trial registration information with any changes, including the responsible party contact information for this clinical trial as required under 42 CFR 11.64(a)(1)(i)(A).⁵ You should review your records of these clinical trials and determine whether you submitted all required information. If you determine that information is required and due for these clinical trials, please submit the information promptly.

Failure to submit clinical trial information⁶ required under section 402(j) of the 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)). Beginning 30 calendar days after you receive this letter, FDA intends to further review and assess the above-identified clinical trials. If FDA determines that you have failed to submit any clinical trial information required under section 402(j) of the PHS Act (42 U.S.C. 282(j)), including its implementing regulations in 42 CFR part 11, you may receive from FDA a Notice of Noncompliance,⁷ and FDA may thereafter initiate an administrative action seeking a civil money penalty.⁸ In addition to civil money penalties,

⁴ See sections 402(j)(3)(E) and (H) of the PHS Act (42 U.S.C. 282(j)(3)(E) and (H)) and 42 CFR part 11, subpart C for results information submission requirements.

⁵ For applicable clinical trials initiated before January 18, 2017, such as the referenced clinical trial, section 402(j)(4)(C)(i)(I) of the Public Health Service Act (42 U.S.C. 282(j)(4)(C)(i)(I)) generally requires the responsible party to submit updates not less than once every 12 months to reflect any changes. See also 42 CFR 11.64(a)(1)(i)(A). If you are] no longer the responsible party for this clinical trial, you should notify FDA and must update this information in the ClinicalTrials.gov data bank.

⁶ See sections 402(j)(1)(A)(iv) of the PHS Act (42 U.S.C. 282(j)(1)(A)(iv)) and 42 CFR 11.10 for the definition of “clinical trial information.”

⁷ See section 402(j)(5)(C)(ii) of the PHS Act (42 U.S.C. 282(j)(5)(C)(ii)).

⁸ Pursuant to section 303(f)(3)(A) of the 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

violations of section 301(jj) of the FD&C Act (21 U.S.C. 331(jj)) could result in other regulatory action, such as injunction and/or criminal prosecution, without further notice.

As requested, please review your clinical trial records and submit any required results information to the ClinicalTrials.gov data bank. We also request that you review all applicable clinical trials for which you are the responsible party to ensure compliance with all ClinicalTrials.gov registration and results information submission requirements. You can access the ClinicalTrials.gov website at <https://register.clinicaltrials.gov>.

If you have any questions about this letter, you may e-mail FDA 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.

Brittany L. Garr-Colón, M.P.H.
Acting Branch Chief
Compliance Enforcement Branch
Division of Enforcement and Postmarketing Safety
Office of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
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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.” These civil money penalty amounts reflect the amounts found 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.

Sincerely yours,

{See appended electronic signature page}

Laurie Muldowney, M.D.
Deputy Director
Office of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

cc: (b) (6), M.S., Regulatory Affairs Coordinator III
Massachusetts General Hospital

(b) (6), CCRP, Senior Clinical Research Manager
Massachusetts General Hospital

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

LAURIE B MULDOWNNEY
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