U.S. FOOD & DRUG ADMINISTRATION

NOTICE OF NONCOMPLIANCE ISSUED PURSUANT TO 42 U.S.C. 282(j)(5)(C)(ii)

VIA UNITED PARCEL SERVICE AND E-MAIL

December 19, 2024

FADOI Foundation
Attention: Dario Manfellotto, M.D., President
Via Felice Grossi Gondi 49
Rome, Italy, 00162
segretaria@fadoi.org
centrostudi@fadoi.org

Re: Noncompliance with the Requirements for Submission of Clinical Trial Results Information for "Apixaban for the Treatment of Venous Thromboembolism in Patients With Cancer: A Prospective Randomized Open Blinded End-Point (Probe) Study" (NCT03045406)
FDA Reference Number: CDER-2023-128

Dear Dr. Manfellotto:

The U.S. Food and Drug Administration (FDA) sent you a letter dated September 22, 2023, alerting you and FADOI Foundation to potential noncompliance with the requirement to submit clinical trial results information to the ClinicalTrials.gov data bank, operated by the National Library of Medicine (NLM) (a part of the National Institutes of Health) for the above-referenced clinical trial. FADOI Foundation is the "responsible party"[1] for the above-referenced clinical trial, which is an "applicable clinical trial"[2] subject to the requirements in section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA), 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

[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."
[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."

completion date[3] of the applicable clinical trial, unless the responsible party has submitted a timely certification of delay, a request for an extension for good cause, or a request for a waiver of the requirements for submission of results information.[4]

In our September 22, 2023, letter, we requested that your organization review its records for this clinical trial and submit all required results information promptly. We also stated that we intended to further review and assess this clinical trial beginning 30 calendar days after you received our September 22, 2023, letter, and that we might take regulatory action if we determined that your organization was not in compliance at that time. Despite extensive email correspondence between your organization, FDA, and/or NLM after FADOI Foundation received the September 22, 2023, letter, results information has not been submitted.

FDA has determined that your organization failed to submit results information for the applicable clinical trial referenced above, as required under section 402(j) of the PHS Act (42 U.S.C. 282(j)) and 42 CFR 11.48.[5] Moreover, FDA has determined that your organization failed to update the responsible party contact information for this clinical trial as required under 42 CFR 11.64(a)(1)(ii)(L).[6] Pursuant to section 402(j)(5)(C)(ii) of the PHS Act (42 U.S.C. 282(j)(5)(C)(ii)), FDA is notifying you that your organization is not in compliance with FDAAA's results information submission requirements, which include the requirements in 42 CFR part 11, and FDA is providing your organization with the opportunity to remedy its noncompliance by submitting the required clinical trial results information and updating the responsible party contact information within 30 calendar days after you receive this Notice of Noncompliance (Notice).

Because failure to submit 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, 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 may initiate an administrative action seeking a civil money penalty against your organization. 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

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[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 purposes of 42 CFR part 11.

[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 submission requirements.

[5] We acknowledge that, as recently as November 8, 2023, your organization entered results information for NCT03045406 into NLM's Protocol Registration and Results System (PRS); however, your organization did not complete the process for submitting results information, and the preliminary steps taken by your organization do not constitute submission of results information under 42 CFR 11.44(a).

[6] For applicable clinical trials initiated on or after January 18, 2017, such as the referenced clinical trial, 42 CFR 11.64(a)(1)(ii)(L) requires that responsible party contact information be "updated not later than 30 calendar days after a change in the responsible party or the contact information for the responsible party."

subject to a civil money penalty of not more than $10,000 for all violations adjudicated in a single proceeding."[7]

If your organization does not submit the required clinical trial results information in the manner and format specified at http://prsinfo.clinicaltrials.gov or at https://clinicaltrials.gov/ct2/manage-recs/how-report within 30 calendar days after receiving this Notice, FDA may also seek additional civil money penalties against your organization. Specifically, 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 receipt of a [notice issued] 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 money penalty of not more than $10,000 for each day of the violation after such period until the violation is corrected."

In addition to civil money penalties, 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.

If you have any questions about this Notice, you may call Laurie Muldowney, M.D., at (301) 796-1571. Please have the FDA reference number provided at the top of this Notice availablei when you call. Alternatively, you may e-mail Dr. Muldowney at CDER-OSI-Advisory@fda.hhs.gov. Please include the FDA reference number with any e-maili communications.

We request that your organization submit a written response to FDA within 30 calendar days after you receive this Notice, stating the actions your organization has taken in response to this Notice.

[7] The civil money penalty amounts in this Notice 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.

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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Deputy Director
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Sincerely yours,

Michael C. Rogers, M.S.
Associate Commissioner for Inspections and Investigations
Office of Inspections and Investigations
U.S. Food and Drug Administration

Cc: FADOI Foundation
Via Rodolfo Lanciani 62
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