UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

UNITED STATES OF AMERICA	Criminal No. 17-10288
v.	Violation:
AEGERION PHARMACEUTICALS, INC.,	21 U.S.C. §§ 331(a), 333(a)(1), 352(f), (y) (Introduction into interstate commerce of misbranded drugs)
Defendant.	18 U.S.C. § 982(a)(7) (Forfeiture)

INFORMATION

The Acting United States Attorney charges that:

1. At all relevant times, the defendant, AEGERION PHARMACEUTICALS, INC. ("AEGERION"), a Delaware corporation with a principal place of business in Cambridge, Massachusetts, made and manufactured the drug Juxtapid (generic name lomitapide).

2. At all relevant times, the United States Food and Drug Administration ("FDA") was an agency of the United States responsible for protecting the health and safety of the public by assuring that, among other things, drugs intended for use in people were safe and effective for their intended uses and the labeling of the drugs was true and accurate. FDA regulates the manufacture, labeling, and shipment in interstate commerce of drugs.

Commercial Development and FDA Approval of Juxtapid

3. Starting in 2007, AEGERION sought to develop the medication Juxtapid for the treatment of "moderate hypercholesterolemia," and in 2008, AEGERION began overseeing a study of Juxtapid as a treatment for high cholesterol in patients with homozygous familial hypercholesterolemia, a rare form of familial hypercholesterolemia ("FH").

4. FH is a genetic disorder that prevents the removal of LDL-C, often called the "bad" cholesterol, from the blood, causing abnormally high levels of circulating LDL-C. Persons who inherit a defective LDL receptor gene (or a defective gene associated with the LDL receptor function) from one parent had heterozygous FH ("HeFH"). Persons who inherit defective LDL receptor genes from both parents had homozygous FH ("HoFH"). Persons with HoFH develop dramatically early and severe atherosclerotic cardiovascular disease ("CVD"). Symptomatic CVD typically presents during the first two decades of life, often leading to heart attack, stroke, and death. If untreated, most HoFH patients do not survive past age 30 due to death from CVD.

5. Throughout the approval process for Juxtapid, AEGERION represented to FDA that the estimated prevalence of HeFH was 1 in 500 (roughly 638,000 persons in the United States based on a population of about 319 million). Based on HeFH prevalence, AEGERION represented to FDA that the prevalence of HoFH is roughly 1-in-1 million (roughly 319 persons based on the current United States population).

6. AEGERION sought approval for Juxtapid for the treatment of HoFH under FDA's Orphan Drug Designation program, which encourages the development of medical products intended to treat rare diseases and conditions affecting fewer than 200,000 people in the United States. 21 U.S.C. § 360cc.

7. In 2009, AEGERION discussed with FDA the possibility of obtaining approval for Juxtapid not only for HoFH but also for refractory (resistant to treatment) HeFH based on an ongoing clinical trial of Juxtapid in 29 HoFH patients. FDA indicated that such an expanded indication would require an additional clinical trial, including potentially an outcomes study to determine whether Juxtapid treatment reduced the risk of heart attack or stroke.

8. In 2010, AEGERION told FDA that it would abandon an expanded indication covering refractory HeFH due to financial constraints and said that it would accept whatever post-approval supply constraints were necessary to ensure that Juxtapid would only be available to HoFH patients.

9. However, soon after deciding to abandon pursuit of an indication for HeFH, AEGERION redefined HoFH to include "HoFH-like" HeFH, which it called "functional" HoFH. AEGERION estimated there could be up to 3,000 "functional" HoFH patients in the United States.

10. In June 2011, in a face-to-face meeting, FDA rejected AEGERION's "functional" HoFH definition because it closely resembled what was considered to be severe refractory HeFH. FDA explained to AEGERION that use of the "functional" HoFH definition would expand the potential population using the drug, shifting the risk-benefit calculation for a new drug application based on a study of only 29 HoFH patients. AEGERION told FDA that it would not seek to expand the indication population to include severe refractory HeFH patients and accepted that the indicated population would have to align with the criteria used to identify HoFH patients for AEGERION's ongoing Juxtapid study.

11. At the June 2011 meeting, FDA encouraged AEGERION to provide information about a potential Risk Evaluation Mitigation Strategy ("REMS") for Juxtapid, specifically, detailed plans of how distribution would be restricted to the HoFH population as defined in the Juxtapid study. REMS programs were required risk management plans that used risk mitigation strategies to ensure that the benefits of prescription drugs outweigh their risks.

12. Although AEGERION abandoned its "functional" definition of HoFH in communications with FDA, AEGERION continued to develop marketing plans for Juxtapid using the "functional" definition of HoFH that included severe refractory HeFH. AEGERION

leadership also continued to promise Wall Street and other investors that Juxtapid would have an addressable market of at least 3,000 patients.

13. In October 2012, just prior to Juxtapid's approval, AEGERION again represented to FDA that the expected prevalence of HoFH was roughly one person per million (that is, approximately 319 people in the U.S.). At an October 2012 meeting of an FDA Advisory Committee to discuss whether to recommend Juxtapid's approval, a senior AEGERION executive stated that AEGERION was "totally focused" on HoFH; that everything AEGERION would do upon approval would be "focused on making sure that [HoFH patients] are the patients who receive the drug"; and that AEGERION had "no intention of promoting the drug outside of that very narrow, very small patient population, and [would] discourage its use outside of that patient population."

14. In December 2012, FDA approved Juxtapid as an adjunct to other lipid-lowering therapies to treat adult patients with HoFH. Juxtapid's label included information stating that the drug's safety and effectiveness had not been established in patients with hypercholesterolemia who do not have HoFH and that the effect of Juxtapid on cardiovascular morbidity and mortality had not been determined.

15. A boxed warning on the FDA-approved label cautioned prescribers about the risk of hepatotoxicity (liver toxicity) when taking Juxtapid, including elevations in transaminases (enzymes indicative of liver damage) and hepatic steatosis (the accumulation of fat in the liver), which can lead to liver disease, including steatohepatitis (fatty liver disease) and cirrhosis (chronic liver damage).

16. As a condition of approval of Juxtapid, FDA determined that a REMS program was necessary to ensure that the benefits of the drug outweighed the risk of hepatotoxicity. The purpose of the Juxtapid REMS program was "to educate prescribers about the risks of

hepatotoxicity associated with the use of Juxtapid and the need to monitor patients during treatment with Juxtapid as per product labeling" and "to restrict access to therapy with Juxtapid to patients with a clinical or laboratory diagnosis consistent with HoFH."

17. Juxtapid was only available through the FDA-mandated Juxtapid REMS program if the following requirements were met:

a. Prescribers were trained on the risks associated with Juxtapid, appropriate patient selection and monitoring, and the REMS requirements, and upon completion of the training, prescribers enrolled in the REMS program;

b. Prescribers attested to the safe use of Juxtapid for each new prescription by completing a Prescription Authorization Form stating that Juxtapid was indicated as an adjunct treatment for HoFH and that the patient had "a clinical or laboratory diagnosis consistent with HoFH," among other attestations; and

c. Only specially certified pharmacies dispensed Juxtapid to patients.

18. The Juxtapid REMS program further required AEGERION to be responsible for the implementation, maintenance, monitoring, and evaluation of the REMS program to assure the drug's safe use, and to be responsible for taking reasonable steps to improve implementation of and compliance with the Juxtapid REMS program. FDA required AEGERION to submit REMS Assessments or reports to FDA six months and then twelve months after the initial approval of the REMS, and annually thereafter.

19. At market launch in January 2013, Juxtapid cost roughly $295,000 per patient per year. The annual cost of Juxtapid later increased to over $330,000 per patient per year.

Misbranding

20. Under the Federal Food, Drug, and Cosmetic Act ("FDCA"), a drug was misbranded if the labeling did not bear "adequate directions for use." 21 U.S.C. § 352(f)(1).

"Adequate directions for use" meant directions under which a layperson could use a drug safely and for the purposes for which it was intended. 21 C.F.R. § 201.5. A prescription drug, by definition, could not bear adequate directions for use by a layperson, but was exempt from the adequate-directions-for-use requirement if it, among other things, had FDA-approved labeling that provided adequate information for its safe and effective use by practitioners for all the purposes for which it was intended, including all purposes for which it was advertised or represented. 21 C.F.R. §§ 201.100(c)(1), 201.100(d).

21. A drug's "intended use" included the "objective intent of the persons legally responsible for the labeling of the drugs," which could be demonstrated by, among other things, evidence concerning "oral or written statements by such persons or their representatives" and "the circumstances that the article [was], with the knowledge of such persons or their representatives, offered and used for a purpose for which it [was] neither labeled nor advertised." 21 C.F.R. § 201.128.

22. A drug was also misbranded under the FDCA if it was subject to a REMS program and the manufacturer failed to comply with certain REMS requirements, such as, for example, the implementation of the elements to assure safe use. 21 U.S.C. § 352(y).

23. The FDCA prohibited the introduction or delivery for introduction, or causing the introduction or delivery for introduction, of misbranded drugs into interstate commerce. 21 U.S.C. § 331(a).

COUNT I

21 U.S.C. §§ 331(a), 333(a)(1), 352(f) (Misbranding); 18 U.S.C. § 2 (Aiding and Abetting)

24. The allegations in paragraphs 1 to 23 are herein re-alleged and incorporated in full.

25. From in or about December 2012 to in or about December 2015, in the District of Massachusetts and elsewhere, the defendant

AEGERION PHARMACEUTICALS, INC.

did introduce and deliver for introduction and cause to be introduced and delivered for introduction into interstate commerce the drug Juxtapid, which was misbranded in that it lacked adequate directions for use, and did not qualify for any exemptions from this requirement, under 21 U.S.C. § 352(f).

26. Prior to Juxtapid's approval, based on extensive market research, AEGERION trained its sales force that the United States market for hypercholesterolemia could be clinically segmented into ranges based on a patient's LDL cholesterol level while on optimal or maximum lipid-lowering therapies: "refractory HeFH" from 100 to 200; "severe refractory (SR) HeFH" from 200 to 300; "phenotypic HoFH" from 300 to 450; and "classic HoFH" over 400.

27. In January 2013, senior AEGERION executives and sales managers trained the AEGERION sales force to abandon the documented clinical segmentation of refractory HeFH, severe refractory HeFH, phenotypic HoFH, and classic HoFH that was central to general sales force training in December 2012; instead, senior AEGERION executives and sales managers trained the sales force to sell Juxtapid as a treatment for severe high cholesterol in general without respect to peer-reviewed standards for diagnosing HoFH. Specifically, AEGERION executives and managers trained the sales force to market Juxtapid based on "The Art of Not Defining" HoFH and reinforced that strategy on weekly conference calls and in further trainings. The purpose of "The Art of Not Defining" HoFH was to render the diagnosis of HoFH as

indefinite as possible: first, by discouraging the use of genetic testing (notwithstanding information in AEGERION's possession that genetic testing was the best and most reliable method for diagnosis and that testing capacity and availability in the United States was more than sufficient to test suspected HoFH patients); and second, by discouraging the use of any established, published, peer-reviewed diagnostic criteria. AEGERION management trained the sales force to sell Juxtapid for the treatment of "severe refractory lipid" patients, including those with HoFH, severe refractory HeFH, statin intolerance, or other diseases, such as diabetes, associated with treatment-resistant high cholesterol.

28. AEGERION sales managers trained sales representatives to sell Juxtapid without mentioning HoFH. Many sales representatives told doctors that Juxtapid was approved for treatment of "FH" (*i.e.*, both HoFH and HeFH regardless of severity) and that appropriate Juxtapid patients included any who had not reacted adequately to other lipid-lowering therapies, because, AEGERION claimed, poor response to therapy was "consistent" with HoFH.

29. Initially, AEGERION sought to market Juxtapid to lipidologists at elite academic centers; however, AEGERION soon found that academic lipidologists resisted AEGERION's efforts to "not define" HoFH so it would include a broader population of refractory high cholesterol patients.

30. AEGERION shifted its marketing focus to community cardiologists, who were often much less knowledgeable about HoFH than academic lipidologists. By focusing on community cardiologists, AEGERION sales representatives were able to execute AEGERION's commercial strategy of distributing Juxtapid for use in patients who could not be diagnosed with HoFH but who had certain isolated characteristics consistent with aspects of HoFH.

31. One senior AEGERION executive explained, "[I]f you ask most clini[cal] card[iologists] if they have patients with FH they will say that do not know and if you ask if they

have HoFH [patients] they will say no. . . . [W]e start our calls and market research first asking if they have [patients] that are difficult to treat with [maximum tolerated treatment] and then lead them down the pathway that it could be HoFH [] showing the variability in [LDL] and other characteristics from our [Juxtapid] study."

32. AEGERION's commercial management trained sales representatives to mislead prescribers about the clinical profiles of patients in the Juxtapid HoFH study and about clinical characteristics typical of HoFH patients. For example, AEGERION's commercial management trained sales representatives to tell prescribers that the Juxtapid HoFH study included a genetically-tested patient with a treated LDL of 152, as though such an LDL level was typical of HoFH patients. AEGERION sales and marketing management directed sales representatives to tell prescribers that based on the existence of this one patient (of 29 in the Juxtapid study) with a treated LDL of 152, such a low LDL could be used to diagnose HoFH generally, even though AEGERION knew that no published, peer-reviewed clinical diagnostic criteria supported AEGERION's view. Moreover, AEGERION sales representatives did not provide material information regarding the particular patient's age (very young), medical history (diagnosis at age 2 and multiple cardiac interventions by age 18), or treatment history (maximum drug therapy for over ten years and weekly apheresis, a mechanical process similar to dialysis to clear cholesterol from the blood). Instead, AEGERION sales representatives were trained to tell and did tell prescribers that they could generalize this one, specific patient to the general population, including the elderly. At no time did AEGERION proactively provide prescribers with material information correlating LDL levels with age to put into context the one patient with an LDL level of 152. In fact, soon after launching Juxtapid, AEGERION removed such information from its marketing materials.

33. With managerial approval and pursuant to managerial direction, AEGERION sales representatives "helped" doctors identify Juxtapid patients whose clinical profiles did not correspond to the peer-reviewed and established clinical diagnostic criteria for HoFH, at times with LDL levels approaching the national average for healthy Americans. For example, one sales representative helped a doctor identify patients for treatment with Juxtapid who had treated LDL levels from 100 to 135. Another sales representative helped a provider identify numerous patients for treatment with Juxtapid who had treated LDL levels just over 100. These sales representatives told doctors that such LDL levels were consistent with HoFH.

34. AEGERION sales managers trained sales representatives to tell prescribers and patients that use of Juxtapid would "take patients out of harm's way" and prevent "impending" heart attacks or strokes, even though AEGERION possessed no data showing that use of Juxtapid had any meaningful effect on cardiovascular mortality or morbidity. For example, one sales representative told doctors and their patients that the patients would have strokes if they did not take Juxtapid. Such false and misleading statements deceived community cardiologists and patients into believing that Juxtapid by itself could save patients from death or injury.

35. AEGERION executives and sales managers also specifically trained sales representatives to sell Juxtapid to treat statin-intolerant patients, and many sales representatives did so.

36. AEGERION executives, including the then-Chief Executive Officer, and sales managers also specifically encouraged, approved, and oversaw distribution of Juxtapid for use in pediatric patients.

37. AEGERION further promoted and sold Juxtapid for use as a monotherapy, *i.e.*, not as an adjunct therapy to other lipid-lowering therapies.

38. AEGERION caused numerous health care providers to prescribe Juxtapid to numerous HeFH, statin-intolerant and diabetic patients, including elderly and pediatric patients, even though Juxtapid's labeling does not include, nor is it exempt from the requirement that it have, adequate directions for use in such patients or for use in lowering cardiac risk or for use as a monotherapy.

39. Numerous HeFH, statin-intolerant, and diabetic patients, including elderly and pediatric patients, suffered adverse events, including liver toxicity and gastrointestinal distress, and had to discontinue use of Juxtapid.

40. Based on the above, AEGERION intended that Juxtapid be used in patients for purposes other than for HoFH, and for which Juxtapid's labeling did not bear adequate directions for use.

All in violation of 21 U.S.C. §§ 331(a), 333(a)(1), 352(f) and 18 U.S.C. § 2

COUNT II

21 U.S.C. §§ 331(a), 333(a)(1), 352(y) (Misbranding); 18 U.S.C. § 2 (Aiding and Abetting)

41. The allegations in paragraphs 1 to 23 and 26 to 40 are herein re-alleged and incorporated in full.

42. From in or about December 2012 to in or about December 2015, in the District of Massachusetts and elsewhere, the defendant

AEGERION PHARMACEUTICALS, INC.

did introduce and deliver for introduction and cause to be introduced and delivered for introduction into interstate commerce the drug Juxtapid while failing to comply with the requirements of the FDA-mandated Juxtapid REMS program under 21 U.S.C. § 355-1(f)(3) and (4), rendering Juxtapid misbranded under 21 U.S.C. § 352(y).

43. Among the elements to assure safe use of Juxtapid, required by FDA as part of the Juxtapid REMS program under 21 U.S.C. § 355-1(f)(3), was an attestation from a prescriber for each new prescription, including prescriptions to increase dosage, that a patient had a "laboratory or clinical diagnosis consistent with HoFH."

44. AEGERION sales representatives told doctors that it would be truthful to sign attestations that patients' diagnoses were consistent with HoFH if any isolated aspect of patients' diagnoses were consistent with the isolated characteristics of any genetically-diagnosed HoFH patient. For example, AEGERION routinely distributed Juxtapid based on a representation that a treated LDL level of 152 was consistent with a diagnosis of HoFH based on the existence of a single genetically-diagnosed HoFH patient in the Juxtapid study. AEGERION did not tell doctors that the study patient at issue was very young, with multiple physical manifestations of HoFH as a child, on multiple maximum treatments of other cholesterol-lowering drugs, and on apheresis. At the same time, AEGERION encouraged doctors to prescribe Juxtapid for patients with treated LDL levels of 152 and lower and to patients as old as 80 years old, without

providing doctors with material information regarding typical treated LDL levels in geriatric patients.

45. AEGERION sales representatives also caused the completion of attestations for prescribers by using prescribers' signature stamps, without the prescribers' knowledge.

46. AEGERION sales representatives also targeted nurse practitioners as Juxtapid prescribers and "REMS-trained" the nurse practitioners, but AEGERION sales representatives did not "REMS-train" the physicians who had to sign off on nurse practitioners' clinical work, with the result that physicians approved prescriptions without REMS required training and without knowing about the required REMS diagnostic attestation in violation of the Juxtapid REMS.

47. In order to make non-HoFH patients appear to be HoFH patients on forms submitted to FDA about the Juxtapid REMS program, AEGERION sales representatives filled out statements of medical necessity for physicians using false and misleading information, including total cholesterol levels (high density lipoprotein plus LDL) in place of LDL cholesterol levels; untreated LDL levels in place of treated LDL levels; and false medical histories (including the existence of xanthomas and tried-and-failed medications). As a result, AEGERION's implementation and monitoring of the REMS elements to assure safe use was fraudulent.

48. AEGERION's Juxtapid statements of medical necessity, which were not required by the Juxtapid REMS program, excluded specification that HoFH involves family history of disease from both parents; AEGERION used the statement of medical necessity to convince physicians that diagnoses were consistent with HoFH based on *any* family history (one or two parent or siblings, *i.e.*, consistent with HeFH or HoFH).

49. In late 2013, after AEGERION added a check-box for a diagnosis consistent with HoFH to the Juxtapid statement of medical necessity, AEGERION sales representatives checked the box for physicians while completing prescription documentation for the physicians.

50. In or around June 2013, AEGERION submitted a REMS Assessment Report to FDA.

51. In or around August 2013, FDA asked AEGERION to explain why the median age of the patients receiving Juxtapid was 57 years old when the median age of patients in the Juxtapid HoFH study was only 31.

52. In or around December 2013, AEGERION filed a second REMS Assessment Report in which it told the FDA that the age difference between the patients in the clinical study and those being prescribed Juxtapid post-approval could be attributed to the different standards of care used in academic centers, where most of the patients in the Juxtapid HoFH study had been treated, and the standards of care used in community cardiology practices, where AEGERION was finding its business. Aegerion did not disclose to the FDA that its commercial management had implemented a strategy to promote Juxtapid using a clinical definition of HoFH that did not correspond to AEGERION's pre-approval filings with the FDA and that did not correspond to any peer-reviewed clinical standard for diagnosing HoFH: Aegerion told prescribers that neither specific LDL levels nor history of disease in both parents was necessary for a diagnosis of HoFH and that HoFH really meant uncontrolled hypercholesterolemia. Neither did AEGERION tell the FDA that it was educating doctors that HoFH was as likely to appear in elderly populations as in pediatric populations. AEGERION refrained from telling FDA that, in the fall of 2013, AEGERION had obtained new marketing research based on AEGERION's marketing of Juxtapid that estimated over 900,000 potential Juxtapid patients. In short, AEGERION did not disclose to the FDA that its understanding of HoFH post-approval

was wholly different from AEGERION's representations to the FDA during the approval process for Juxtapid, including during discussions about the specific design and elements of the Juxtapid REMS program.

53. By providing health care providers with incomplete, inaccurate, and therefore misleading information about HoFH, AEGERION failed to comply with 21 U.S.C. § 355-1(f)(3), which authorized the elements to assure safe use of Juxtapid.

54. By seeking to render the diagnosis of HoFH as vague and indefinite as possible in order to capture the HeFH and statin-intolerant patient populations as markets for Juxtapid, AEGERION sought to obstruct and impede the implementation of the elements to assure safe use and failed to comply with 21 U.S.C. § 355-1(f)(4)(B), which required a company subject to a REMS to take reasonable steps to improve implementation of the REMS.

55. By filing a misleading REMS Assessment Report in December 2013, AEGERION further failed to comply with 21 U.S.C. § 355-1(f)(4)(B) by seeking to evade FDA scrutiny of AEGERION's fraudulent implementation of the Juxtapid REMS program.

All in violation of 21 U.S.C. §§ 331(a), 333(a)(1), 352(y) and 18 U.S.C. § 2.

PECUNIARY GAIN ALLEGATION

56. The defendant,

AEGERION PHARMACEUTICALS, INC.,

gained, during the time period relevant in this Information, revenue of not less than $15,451,827 in United States currency from the offenses set forth in Counts 1 and 2 of this Information, revenue that constitutes a pecuniary gain under the Alternative Fines Act, 21 U.S.C. § 3571(d).

FORFEITURE ALLEGATION
(18 U.S.C.§ 982(a)(7))

The United States Attorney further alleges that:

57. Upon conviction of one or more of the offenses in violation of Title 21, United States Code, Section 331(a), set forth in Counts One and Two of this Information,

AEGERION PHARMACEUTICALS, INC.,

defendant herein, shall forfeit to the United States, pursuant to Title 18, United States Code, Section 982(a)(7), any property, real or personal, that constitutes or is derived, directly or indirectly, from gross proceeds traceable to the commission of the offenses.

58. If any of the property described in Paragraph 57, above, as being forfeitable pursuant to Title 18, United States Code, Section 982(a)(7), as a result of any act or omission of the defendant:

a. cannot be located upon the exercise of due diligence;

b. has been transferred or sold to, or deposited with, a third party;

c. has been placed beyond the jurisdiction of the court;

d. has been substantially diminished in value; or

e. has been commingled with other property which cannot be divided without difficulty,

it is the intention of the United States, pursuant to Title 21, United States Code, Section 853(p), as incorporated by Title 18, United States Code, Section 982(b)(1), to seek forfeiture of any other property of the defendant up to the value of the property described in Paragraph 57 above.

All pursuant to 18 U.S.C.§ 982(a)(7).

Respectfully submitted,

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