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22 August 2019

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J & E Davy
Davy House
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Re: **Patent Report**
Aegerion Pharmaceuticals, Inc.

Dear Sirs:

Aegerion Pharmaceuticals, Inc. Patent Report

1. This Report

We have prepared this report for the directors of Amryt Pharma plc (**Amyrt**); Amryt's nominated adviser, Shore Capital & Corporate Limited; and Amryt's ESM Adviser, J & E Davy (**Report**).

Haug Partners LLP (**Haug Partners**) has been commissioned to review the registered patent rights of Aegerion Pharmaceuticals, Inc. (**Aegerion**). We have acted as intellectual property counsel providing counseling and services to Aegerion for several years.

This Report summarizes the details and status of the issued patents and pending patent applications that are either (i) owned by Aegerion, or (ii) in-licensed by Aegerion, as shown in Schedules 1 and 2.

Haug Partners is an IP-focused law firm that provides litigation and procurement services for technology and life sciences companies.

In providing this Report, we are aware that individuals and entities beyond Aegerion will have access to the information set forth herein. It is to be understood that the information disclosed herein shall not constitute a waiver of the attorney-client and/or attorney work product privileges that exist with respect to the advice and counsel provided to Aegerion beyond the limited opinions and representations specifically set forth herein.

We declare that we are responsible for this Report and that we have taken all reasonable care to ensure that the information contained in this Report is, to the best of our knowledge and belief, in accordance with the facts and contains no omissions likely to affect its import.

2. Executive Summary

Our review focused on Aegerion's patent portfolios that relate to its marketed products: Myalept® (metreleptin for injection, marketed in certain non-U.S. countries as Myalepta®) and Juxtapid® (lomitapide capsules, marketed in certain non-U.S. countries as Lojuxta®). Aegerion owns or in-licenses the patents and patent applications identified herein, which are organized into 11 patent families. The patents and applications are typically in major markets worldwide, including the U.S., Europe, Canada, and Japan.

Aegerion's patent rights include: (i) patents and patent applications owned by Aegerion, and (ii) patents and patent applications that are in-licensed to Aegerion. Aegerion's current intellectual property rights may be expanded in the future based on additional development by Aegerion personnel and/or through further licensing and/or strategic partnerships.

3. Scope of Report

This Report relates only to intellectual property of Aegerion in the form of patents and patent applications. Throughout the Report, patents and patent applications have been grouped into "families."

For each patent family, we have included a brief summary of the claimed invention. This information is subjective and is intended to provide a useful summary, rather than to be relied on in a factual sense. More detailed information about each patent family is provided in Schedule 1 (for patents and patent applications relating to metreleptin) and Schedule 2 (for patents and patent applications relating to lomitapide). In the schedules, certain exemplary claims have been selected for each patent family. Care has been taken to copy claims (or translations thereof) accurately, but errors cannot be excluded. Interested parties are encouraged to review granted patents and published patent applications referred to herein, and which are publically available, e.g., from the relevant patent office websites. No single claim can completely reflect the scope of the various claims in the different members of the patent family. Therefore, the exemplary claim in each case is intended to provide the reader with an example from the patent family in question. In particular, it cannot be assumed that

other members of the patent family share the same scope as that of the exemplary claim provided herein.

In the schedules we have also noted whether individual patents are granted or pending. This summary is based on our best assessment of the relevant facts and information as known to us, and represents our honest belief. This report is not intended as a substitute for reviewing the publicly available prosecution files, which in the case of the U.S. Patent & Trademark Office (USPTO) and the European Patent Office (EPO) are available online (for patents and published patent applications). Reports from the PCT procedure are also available online from the World Intellectual Property Organization (WIPO).

For the pending patent applications, it is not yet clear what rights will ultimately be granted in respect of such applications, as such applications are in various stages of prosecution. Patent applications are examined by the applicable national (e.g., USPTO, EPO, etc.) or international (e.g., WIPO) IP office (IPO). As a consequence, during the examination process the patent claims in the original patent application may be amended to comply with the patentability requirements of an IPO. Further, patent applications can be the subject of third party objections.

Even after patent applications are granted as patents, they can be the subject of post-grant reviews or oppositions before the corresponding IPO, or be subject to third-party revocation claims in front of an applicable national court. It is possible that the entire patent may be held as invalid and revoked.

This Report does not include a list or any details of the results of any searches conducted by an IPO, or the examination reports of an IPO. The reader is invited to view the results of IPO searches, examination reports, and cited documents, which are available from the public prosecution file for each case (and accessible online at least for U.S. and European patent applications).

We have not been asked to conduct, and have not conducted, freedom-to-operate (FTO) searches of USPTO, EPO, or Patent Cooperation Treaty (PCT) databases with respect to any product marketed by Aegerion. At the same time, we are not aware of any third-party patents or patent applications that would pose an obstacle to Aegerion's countined commercialization of any marketed products.

To the extent necessary to understand Aegerion's ownership or in-licensed rights, we have reviewed license agreements relevant to the patents and patent applications listed in Schedule 1 and 2. We have not reviewed any other agreements that may affect or encumber the IP estate of Aegerion. This Report also does not include a review of commercial, technical, regulatory, or financial issues that relate to the business or their respective intellectual property estates.

The information used in this Report was compiled up to 20 August 2019. Any change in the status of the patent families and any documents executed after 20 August 2019 may not be included in this Report unless Aegerion informed us explicitly in writing.

4. Aegerion's Intellectual Property Rights

4.1. Metreleptin

Family 1: Use of Leptin for Treating Human Lipoatrophy

Family 1 consists of issued patents and pending patent applications that are directed to various methods of treatment, including a method of treating a patient with a condition of lipoatrophy. The patents and applications were filed in the U.S., Europe, Australia, Canada, and Japan.

The patents will expire in 2022, with the exception of the U.S. Patent No. 7,183,254 ("'254 patent"), which was granted a 1,445-day patent term extension that will extend its expiration date to 2027. In the U.S., this patent's claims read on the approved Myalept® (metreleptin for injection) product.

Family 1 is co-owned by Amgen, University of Texas, and the National Institutes of Health under the Department of Health and Human Services. Aegerion acquired its patent rights through an in-license from Amgen. Aegerion's rights to Family 1 will expire in accordance with the license agreement from Amgen.

Family 2: Pegylated Leptin

Family 2 consists of issued patents that are directed to pegylated leptin. The patents were filed in Europe, Australia, Canada, Japan, and Mexico, and expire in October 2019. Family 2 is owned by Amgen, and Aegerion acquired its patent rights through an in-license from Amgen. Aegerion's rights to Family 2 will expire in accordance with the Amgen license agreement.

Family 3: Chimeric Leptin Polypeptides

Family 3 consists of issued patents and pending patent applications that are directed to chimeric polypeptides having seal and human leptin sequences. The patents and applications were filed in the U.S., Europe, Australia, Brazil, Canada, China, Eurasia, Israel, Japan, Mexico, New Zealand, India, and South Korea. The patents will expire in 2031. Aegerion owns the rights to the patents and patent applications in Family 3.

Family 4: Albumin-Leptin Polypeptide

Family 4 consists of issued patents and pending patent applications that are directed to polypeptides having albumin and leptin domains. The patents and applications were filed in the U.S., Europe, Brazil, Canada, China, Eurasia, Mexico, and South Korea. The patents will expire in 2031. Aegerion owns the rights to the patents and patent applications in Family 4.

Family 5: Albumin-Leptin Polypeptides with Reduced Immunogenicity

Family 5 consists of issued patents and pending patent applications that are directed to polypeptides having albumin and leptin domains with reduced immunogenicity. The patents and applications were filed in the U.S., Europe, China, Japan, and South Korea. The patents will expire in 2032. Aegerion owns the rights to the patents and patent applications in Family 5.

Family 6: Detection of Anti-Leptin Neutralizing Antibodies

Family 6 consists of pending patent applications that are directed to a method of detecting neutralizing antibodies to leptin. The applications (including published and unpublished applications) were filed in the U.S., Europe, Brazil, Canada, China, Eurasia, India, Japan, and Mexico. Aegerion owns the rights to the pending patent applications in Family 6.

Family 7: Treatment of Overweight/Obesity Associated with Leptin Deficiency

Family 7 consists of a PCT application that is directed to the use of metreleptin to treat hypoleptinemic metabolic disorder. The application was filed in the United States Receiving Office. The deadline for entering national phase is in February and March 2020. Aegerion owns the rights to the PCT application in Family 7.

4.2. Lomitapide

Family 8: MTP Inhibitors

Family 8 consists of one issued U.S. patent that is directed to the composition of matter of lomitapide. This patent was issued a five-year patent term extension that extended its expiration from early 2015 to 2020.

In the U.S., the issued patent is listed in the FDA's Center for Drug Evaluation and Research's Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the Orange Book) for the approved drug, Juxtapid® (lomitapide).

Family 8 is owned by The Trustees of the University of Pennsylvania (**Penn**), and Aegerion acquired its patent rights through an in-license from Penn. Aegerion's rights to Family 8 will expire in accordance with the license agreement with Penn.

Family 9: Use of MTP Inhibitors for Treating Hyperlipidemia/Hypercholesterolemia

Family 9 consists of issued patents and pending patent applications that are directed to the administration of lomitapide using various dosing regimens. The patents and applications were filed in the U.S., Europe, Australia, Canada, India, Japan, Mexico, New Zealand, and South Korea.

The patent term for the granted patents worldwide is generally to 2025, with some exceptions. One U.S. patent received a patent term adjustment issued by the USPTO, which extended its patent term to August 2027. One Japanese patent received a patent term extension from the Japanese Patent Office that extended its patent term to October 2026. In addition, patents in several European countries received a supplemental protection certificate, which extended their patent term to July or August of 2028.

In the U.S., the issued patents are listed in the FDA's Orange Book under the approved drug, Juxtapid® (lomitapide).

Family 9 is owned by Penn, and Aegerion acquired its patent rights through an in-license from Penn. Aegerion's rights to Family 9 will expire in accordance with the license agreement with Penn.

Family 10: Use of MTP Inhibition for Treating Atherosclerosis

Family 10 consists of one issued U.S. patent that is directed to a method of treating atherosclerosis. The patent will expire in December 2019.

The patent is listed in the FDA's Orange Book under the approved drug, Juxtapid® (lomitapide).

Family 10 is owned by Penn, and Aegerion received its patent rights through an in-license from Penn. Aegerion's rights to Family 10 will expire in accordance with the license agreement with Penn.

Family 11: Lomitapide Impurities

Family 11 consists of one issued U.S. patent and pending patent applications that are directed to impurities of lomitapide and methods of analyzing the impurities. The pending applications (including published and unpublished applications) were filed in Europe, Brazil, Canada, and Japan. The patent will expire in 2036. Aegerion owns the rights to the patent and patent applications in Family 11.

5. Ownership and Third Party Rights

For all issued patents owned or in-licensed by Aegerion, we confirmed the existence of assignments made from each inventor of each U.S. patent to the respective entities, as disclosed by the USPTO's website. We did not review underlying assignments agreements, nor did we review any contracts (e.g., employment, consulting) between the inventors and the entities.

We are not aware of any patent ownership dispute raised by an inventor for the patent families covering metreleptin or lomitapide.

6. Overview of Intellectual Property Protection

The term "intellectual property" refers to a group of registrable and non-registrable rights, including rights in patents, designs, trademarks, plant varieties, copyright, confidential information, and trade secrets. Intellectual property has many of the characteristics possessed by real and personal property. In particular, intellectual property is an asset, which may be bought, sold, licensed, exchanged, or otherwise transferred as other forms of property. Accordingly, an intellectual property owner has the right to prevent the unauthorized use or sale of its property.

Patents

A patent is a term-limited exclusive right to an invention. To be patentable, the invention must meet certain requirements, set forth by jurisdiction (e.g., novel and nonobvious). Generally, a patent right is granted by national governments through their patent office following an application and, in most cases, examination procedure. The process of guiding a patent application through the application and examination procedure is generally known as patent prosecution.

Patent ownership and entitlement

Typically, the right to be granted a patent primarily belongs to the inventor or joint inventors. However, that right may pass to the employer of the inventor by operation of law (provided certain conditions are met). Moreover, ownership of a patent may be transferred by assignment.

Patent term

The basic term of a patent is twenty years from the earliest date of filing, depending on the jurisdiction (the date of grant does not affect patent term in most jurisdictions). Most notably, in the U.S., the twenty-year term may be adjusted or extended, e.g., due to delays on the part of the USPTO during prosecution. However, the calculation of such term adjustments, and the interplay with terminal disclaimers filed between commonly owned U.S. patents in certain situations, is complex and beyond the scope of this Report. As used herein, unless otherwise expressly noted, the expiry date is given for guidance only and is simply the filing date plus twenty years.

7. Filing and Maintenance of the Patents

Patent filing and prosecution

It is not cost effective for Aegerion to obtain patent protection for an invention in all possible jurisdictions. In common with industry norms, Aegerion balances geographical coverage against cost, taking into account effectiveness of IP legal regimes, market importance, and other factors. As a result, Aegerion typically aims to secure patent protection in major developed economies, most often in the United States, Europe, Canada, China, and Japan.

The strategy to obtain such patent protection makes use of legal systems and conventions across the globe. At least one, and sometimes more than one, "priority" patent application is prepared and filed, sometimes in the U.S. as a provisional patent application. Under applicable law, a later patent application filed within 12 months of the first priority patent application can benefit from the earlier filing date to the extent that the patent application and the priority patent application are directed to the same invention. At this 12-month point, Aegerion may file a U.S. non-provisional patent application and/or an international patent application under the Patent Cooperation Treaty (PCT). The PCT system provides for centralized application, search, publication, and limited, non-binding examination during the "international phase." At 30 or 31 months (jurisdiction-dependent) from the filing date of the priority patent application, it is necessary to convert the PCT application into one or more national patent applications by entering the national phase in each jurisdiction in which patent protection is sought. These jurisdictions may comprise a national patent office (for example, the USPTO, Canadian Patent Office, Japanese Patent Office, etc.) or, where available, a regional patent office (for example, EPO, Eurasian Patent Office, etc.).

Once filed, a patent office examiner typically reviews the patent application and determines whether the application complies with that jurisdiction's requirements for patentability. Usually, the examiner will issue objections and rejections, most often to the claims, and the claims can be amended as long as there is support for the amendments in the patent application as originally filed. Arguments, supplementary experimental data, and/or expert declarations can be filed in combination with, or as an alternative to, amending the claims. A primary objective is to secure strong protection for commercially important subject matter.

Haug Partners has replaced previous counsel(s) and is currently the attorney of record for all U.S. patents and patent applications of Aegerion. Haug Partners is responsible for the coordination of foreign patent prosecution carried out by local patent attorneys in the relevant jurisdictions.

The patent family members described in this Report are related because they share at least one common priority patent application and typically have the same or very similar technical content. However, each family member may have different claims, not least because the various jurisdictions have different requirements (both formal and substantive) for a patent to be granted. The phrase "priority" is intended to mean that the patent application has been filed in order to obtain a priority date and in certain cases such priority patent applications have or will be abandoned in favor of later applications in the family. Similarly, a PCT application marked as "closed" may mean that the international phase has ended and the application has converted into one or more national or regional patent applications.

After grant, a European patent must be converted into one or more national rights in European countries where patent protection is wanted by a process known as validation. The term "validated in" as used here is followed by a list of European countries (using two-letter codes such as GB for the

United Kingdom and DE for Germany) and shows those countries where the necessary formalities have been completed to secure patent protection on the basis of a European grant.

Patent renewals

Haug Partners employs a renewal fee service to monitor and, upon instruction from Aegerion, initiate payment of renewal fees that are due for granted patents and pending patent applications. We are not aware of any abandonment decision by Aegerion with respect to any granted patent and pending applications.

8. Freedom to Operate

Filing a patent application does not mean that the applicant is free to commercially use an invention, as it is possible that the intellectual property rights of another party may be infringed by doing so. Thus, it is possible to both obtain patent protection for an invention and yet still infringe the rights of an earlier granted patent (as the grant of a patent does not have any bearing on whether the invention described in the patent application would infringe the rights of any other third-party patent). The result therefore of prosecution of any of the patent applications mentioned in the current Report does not allow any conclusions to be drawn with regard to freedom-to-operate. FTO searches, typically, identify third-party rights by conducting a search in each relevant country or jurisdiction.

We have not been asked to conduct and have not conducted FTO searches with respect to any product marketed by Aegerion. At the same time, as of 20 August 2019, we are not aware of any third-party patents or patent applications that would pose an obstacle to Aegerion's countined commercialization of any marketed products. Further, we are not aware of any actual or threatened litigation being commenced with respect to any patent or patent application referred to in this Report.

Sincerely,

Russell A. Garman, Ph.D.
Partner

Haug Partners LLP

SCHEDULE 1

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claims	Status | Comments	Patent Family
FAMILY 1: Use of Leptin for Treating Human Lipoatrophy					
US 7183254 2007-02-27 Publication: US 2005/0020496 2005-01-27	Application No.: US 10/623189 2003-07-18 Priority: US 10/279129 2002-10-22 US 60/336394 2001-10-22	Amgen Inc. Board of Regents, The University of Texas System The Government of the United States of America, as Represented by the Secretary, Department of Health and Human Services Licensed under the Agreement between Amgen Inc. and Amylin Pharmaceuticals, Inc. (2006-02-07)	**Use of Leptin for Treating Human Lipoatrophy and Method of Determining Predisposition to Said Treatment** 1. A method of treating a human patient with a condition of lipoatrophy, which comprises administering to the patient a dose of leptin, leptin analog or leptin derivative effective to treat the condition of lipoatrophy. 11. The method of claim 1, wherein the condition of lipoatrophy comprises metabolic abnormalities. 24. A method of determining a predisposition of a lipoatrophic patient to respond to treatment with leptin, leptin analog, or leptin derivative, the method comprising: (a) determining a leptin level in the patient prior to said treatment; and (b) ascertaining whether the leptin level is less than or equal to approximately 4 ng/ml.	Granted Expires: 2027-07-17 (PTE of 1,445 days) 1st fee paid: 2010-07-02 2nd fee paid: 2014-07-30 3rd fee paid: 2018-08-27	Australia AU 2002359288 (GRANTED) Canada CA 2464277 (GRANTED) Europe EP 1444516 (GRANTED) Validated in: CH, DE, DK, ES, FR, GB, IT, NL, PL, SE EP 2219031 (GRANTED) Validated in: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LT, LU, LV, MC, MK, NL, PT, RO, SE, SI, SK, TR Japan JP 2016-108936 (PENDING) JP 2018-141461 (PENDING)

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claims	Status | Comments	Patent Family
					Mexico MX 279227 (GRANTED) MX 250445 (GRANTED) Poland PL 214862 (GRANTED) United States US 7183254 (GRANTED) US 8318666 (GRANTED) US 16/195661 (PENDING) WIPO PCT/US2002/033875 (CLOSED)
US 8318666 2012-11-27 Publication: US 2011/0306540 2011-12-15	Application No.: US 13/103294 2011-05-09 Priority: US 11/606805 2006-11-29 US 10/623189 2003-07-18 US 10/279129 2002-10-22 US 60/336394	Amgen Inc. Board of Regents, The University of Texas System The Government of the United States of America, as Represented by the Secretary, Department of Health and Human Services Licensed under the Agreement between Amgen Inc. and Amylin Pharmaceuticals, Inc.	**Use of Leptin to Treat Metabolic Abnormalities Associated with Lipoatrophy** 1. A method of treating diabetes associated with an inherited or an acquired form of lipoatrophy in a human in need thereof comprising administering to the human a therapeutically effective amount of recombinant methionyl human leptin to treat the diabetes. 10. A method of treating hypertriglyceridemia associated with an inherited or an acquired form of lipoatrophy in a human in need thereof comprising administering to the	Granted Expires: 2022-10-22 (Subject to a terminal disclaimer to '254 patent) 1st fee paid: 2016-05-27 2nd fee due: 2020-05-27 3rd fee due:	Same as US 7183254

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claims	Status | Comments	Patent Family
	2001-10-22	(2006-02-07)	human a therapeutically effective amount of recombinant methionyl human leptin to treat the hypertriglyceridemia. 18. A method of treating a metabolic abnormality associated with an inherited or an acquired fowl [sic] of lipoatrophy in a human in need thereof comprising administering to the human a therapeutically effective amount of recombinant methionyl human leptin to treat the metabolic abnormality.	2024-05-27	
Publication: Not yet published	Application No.: US 16/195661 2018-11-19 Priority: US 15/154749 2016-05-13 US 13/669324 2012-11-05 US 11/606805 2006-11-29 US 13/103294 2011-05-09 US 10/623189 2003-07-18 US 10/279129 2002-10-22 US 60/336394 2001-10-22	Amgen Inc. Board of Regents, The University of Texas System The Government of the United States of America, as Represented by the Secretary, Department of Health and Human Services Licensed under the Agreement between Amgen Inc. and Amylin Pharmaceuticals, Inc. (February 7, 2006)	**Use of Leptin for Treating Human Lipoatrophy and Method of Determining Predisposition to Said Treatment** Claims not yet published	Pending	Same as US 7183254

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claims	Status | Comments	Patent Family
EP 1444516 2010-07-21 Publication: EP 1444516 2004-08-11	Application No.: EP 02793811.7 2002-10-22 Priority: PCT/US2002/033875 2002-10-22 US 60/336394 2001-10-22	Amgen Inc. Board of Regents, The University of Texas System The Government of the United States of America, as Represented by the Secretary, Department of Health and Human Services Licensed under the Agreement between Amgen Inc. and Amylin Pharmaceuticals, Inc. (2006-02-07)	**Use of Leptin for Treating Human Lipoatrophy and Method of Determining Predisposition to Said Treatment** 1. A method of determining a predisposition of a lipoatrophic patient to respond to treatment with a leptin protein, the method comprising: (a) determining a leptin level in the patient prior to said treatment; (b) ascertaining whether the leptin level is less than or equal to approximately 4 ng/ml; and (c) assigning a predisposition for said patient to respond to a replacement therapy comprising said treatment with said leptin protein. 6. A pharmaceutical regimen for the treatment of a lipoatrophic patient by determining a predisposition of a lipoatrophic patient to respond to treatment with a leptin protein by a method according to any one of claims 1 to 5, and subsequently treating said patient with said regimen, said regimen comprising a pharmaceutical composition comprising said leptin protein. 7. A pharmaceutical regimen for treating lipoatrophy comprising a combination of protease inhibitor and a leptin protein. 8. A pharmaceutical regimen for treating lipoatrophy comprising a combination of a leptin protein and at least one compound selected from the group consisting of thiazolidinediones, fibrates, statins and metformin.	Granted Validated in: CH, DE, DK, ES, FR, GB, IT, NL, PL, SE Expires: 2022-10-22	Same as US 7183254

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claims	Status | Comments	Patent Family
			9. A pharmaceutical regimen for treating a human patient with metabolic abnormalities associated with lipoatrophy, said regimen comprising a pharmaceutical composition comprising a leptin protein.		
EP 2219031 2013-04-24 Publication: EP 2219031 2010-08-18	Application No.: EP 10165256.8 2002-10-22 Priority: EP 02793811.7 2002-10-22 PCT/US2002/033875 2002-10-22 US 60/336394 2001-10-22	Amgen Inc. Board of Regents, The University of Texas System The Government of the United States of America, as Represented by the Secretary, Department of Health and Human Services Licensed under the Agreement between Amgen Inc. and Amylin Pharmaceuticals, Inc. (2006-02-07)	**Use of Leptin for Treating Human Lipoatrophy and Method of Determining Predisposition to Said Treatment** 1. A leptin protein for use in a method of treating lipoatrophy or a metabolic abnormality associated therewith in a human patient with lipoatrophy, wherein the method comprises administering to the patient a dose of the leptin protein effective to treat the lipoatrophy or the metabolic abnormality associated therewith.	Granted Validated in: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LT, LU, LV, MC, MK, NL, PT, RO, SE, SI, SK, TR Expires: 2022-10-22	Same as US 7183254
FAMILY 2: Pegylated Leptin					
EP 1121155 2010-04-07 Publication: EP 1121155 2001-08-08	Application No.: EP 99970331.7 1999-10-13 Priority: PCT/US1999/024401 1999-10-13 US 09/172644 1998-10-14	Amgen Inc. Licensed under the Agreement between Amgen Inc. and Amylin Pharmaceuticals, Inc. (2006-02-07)	**Site-Directed Dual Pegylation of Proteins** 1. A dual PEGylated-leptin bioconjugate comprising two polyethylene glycol moieties attached site-specifically at two locations to a leptin moiety, wherein at least one of said two locations is a cysteine residue, wherein the bioconjugate has leptin biological activity. 4. A dual PEGylated-leptin bioconjugate produced by the method comprising: (a) engineering a cysteine residue into a specific amino acid position within the amino acid sequence of a leptin moiety to provide an analog of said leptin moiety; (b) conjugating a polyethylene glycol at said	Granted Validated in: DE, FR, GB Expires: 2019-10-13	Australia AU 757860 (GRANTED) Canada CA 2345027 (GRANTED) Europe EP 1121155 (GRANTED) Validated in: DE, FR, GB Japan

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claims	Status | Comments	Patent Family
			cysteine residue to provide a monoPEGylated leptin moiety conjugate; (c) conjugating a second polyethylene glycol to the N-terminus of said conjugate to provide a dualPEGylated leptin moiety bioconjugate; and (d) collecting said dualPEGylated leptin moiety bioconjugate; wherein the bioconjugate has leptin biological activity. 7. A substantially homogenous composition comprising a dualPEGylated-leptin bioconjugate comprising two polyethylene glycol moieties attached site-specifically at two locations to a leptin moiety wherein at least one of said two locations is a cysteine residue, wherein the bioconjugate has leptin biological activity.		JP 4854851 (GRANTED) Mexico MX 231739 (GRANTED) WIPO PCT/US1999/024401 (CLOSED)
FAMILY 3: Chimeric Leptin Polypeptides					
US 10087228 2018-10-02 Publication: US 2016/0083446 2016-03-24	Application No.: US 14/703523 2015-05-04 Priority: US 13/852521 2013-03-28 PCT/US2011/053774 2011-09-28 US 61/422091 2010-12-10 US 61/387402 2010-09-28	Aegerion Pharmaceuticals, Inc.	**Chimeric Leptin Polypeptide and Method of Using the Same** 1. A chimeric polypeptide comprising a wild type seal leptin polypeptide wherein at least one contiguous region of 1-30 amino acids of a wild type seal leptin sequence has been replaced with a contiguous region of 1-30 amino acids of a mature human leptin sequence, and wherein the chimeric polypeptide comprises an amino acid sequence having at least 95% identity to the amino acid sequence of SEQ ID NO: 30. 6. A method for treating a disease or disorder in a subject, comprising administering a chimeric polypeptide of claim 1 to a subject in need thereof in an amount effective to treat	Granted Expires: 2031-09-28 1st fee due: 2022-04-04 2nd fee due: 2026-04-02 3rd fee due: 2030-04-02	Brazil BR 112013007385-3 (PENDING) Canada CA 2813038 (PENDING) China CN 103547590 (GRANTED) Eurasia EA 024507 (GRANTED) In force: AM, AZ, BY, KG,

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claims	Status | Comments	Patent Family
			said disease or disorder, wherein the disease or disorder is selected from the group consisting of: overweight, obesity, overweight, obesity, lipodystrophy, dyslipidemia, hyperlipidemia, hypothalamic amenorrhea, Alzheimer's disease, leptin deficiency, fatty liver disease, diabetes (including type I and type II), nonalcoholic steatohepatitis (NASH), nonalcoholic fatty liver disease (NAFLD), metabolic syndrome X, and Huntington's Disease.		KZ, MD, RU, TJ, TM Europe EP 2621515 (GRANTED) Validated in: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR EP 17163203.7 (PENDING) Hong Kong HK 1188711 (GRANTED) India IN 3351/DELNP/2013 (PENDING) Japan JP 6174489 (GRANTED) JP 2016-235165 (PENDING) Mexico MX 349054 (GRANTED) MX/A3/2017/008977 (PENDING) United States US 10087228

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claims	Status | Comments	Patent Family
					(GRANTED) WIPO PCT/US2011/053774 (CLOSED)
EP 2621515 2017-03-29 Publication: EP 2621515 2013-08-07	Application No.: EP 11833075.2 2011-09-28 Priority: PCT/US2011/053774 2011-09-28 US 61/422091 2010-12-10 US 61/387402 2010-09-28	Aegerion Pharmaceuticals, Inc.	**A Chimeric Seal-Human Leptin Polypeptide with Increased Solubility** 1. A chimeric polypeptide comprising a wild type seal leptin polypeptide wherein at least one contiguous region of 1-30 amino acids of a wild type seal leptin sequence has been replaced with a contiguous region of 1-30 amino acids of a mature human leptin sequence and wherein the chimeric polypeptide comprises an amino acid sequence having at least 95% identity to the amino acid sequence of SEQ ID NO: 32. 5. A chimeric polypeptide of any one of claims 1-4 for use in treating a disease or disorder in a subject.	Granted Validated in: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR Expires: 2031-09-28	Same as US 10087228
Publication: EP 3241558 2017-11-08	Application No.: EP 17163203.7 2011-09-28 Priority: EP 11833075.2 2011-09-28 PCT/US2011/053774 2011-09-28 US 61/422091 2010-12-10 US 61/387402 2010-09-28	Aegerion Pharmaceuticals, Inc.	**Highly Soluble Leptins** 1. A chimeric polypeptide comprising a wild type seal leptin polypeptide wherein at least one contiguous region of 1-30 amino acids of a wild type seal leptin sequence has been replaced with a contiguous region of 1-30 amino acids of a mature human leptin sequence, and wherein the chimeric polypeptide comprises an amino acid sequence having at least 95% identity to the amino acid sequence of SEQ ID NO: 61. 4. A chimeric polypeptide of any one of claims 1 to 3 for use in treating a disease or disorder in a subject.	Pending	Same as US 10087228

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FAMILY 4: Albumin-Leptin Polypeptides					
Publication: US 2016/0137709 2016-05-19	Application No.: US 14/800537 2015-07-15 Priority: US 13/852671 2013-03-28 PCT/US2011/053786 2011-09-28 US 61/422091 2010-12-10 US 61/387402 2010-09-28	Aegerion Pharmaceuticals, Inc.	**Engineered Polypeptides Having Enhanced Duration of Action** 1. An engineered polypeptide comprising: an albumin binding domain polypeptide (ABD) and a first peptide hormone domain (HD1) selected from a leptin, a leptin analog or an active fragment thereof, and a first linker (L1) covalently linked to said HD1; wherein said ABD comprises an amino acid sequence having at least 85% identity with SEQ ID NO: 49; and wherein said HD1 comprises an amino acid sequence having at least 70% identity with SEQ ID NO: 33.	Pending	Brazil BR 112013007388-8 (PENDING) Canada CA 2813087 (PENDING) China CN 103403019 (GRANTED) Eurasia EA 201390497 (PENDING) Europe EP 2621519 (GRANTED) Validated in: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR Hong Kong HK 1188924 (GRANTED) India IN 3199/DELNP/2013 (PENDING) Japan JP 6412183 (GRANTED)

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claims	Status | Comments	Patent Family
					Mexico MX 351128 (GRANTED) United States US 14/800537 (PENDING) WIPO PCT/US2011/053786 (CLOSED)
EP 2621519 2017-06-28 Publication: EP 2621519 2013-08-07	Application No.: EP 11833080.2 2011-09-28 Priority: PCT/US2011/053786 2011-09-28 US 61/422091 2010-12-10 US 61/387402 2010-09-28	Aegerion Pharmaceuticals, Inc.	**Leptin-ABD Fusion Polypeptides with Enhanced Duration of Action** 1. An engineered polypeptide comprising: an albumin binding domain polypeptide (ABD) that comprises an albumin binding motif (ABM) comprising the amino acid sequence: GVSD X_5 YK X_8 X_9 I X_{11} X_{12} A X_{14} TVEGV X_{20} AL X_{23} X_{24} X_{25} I (SEQ ID NO: 34), wherein, independently of each other, X_5 is selected from Y and F; X_8 is selected from N, R and S; X_9 is selected from V, I, L, M, F and Y; X_{11} is selected from N, S, E and D; X_{12} is selected from R, K and N; X_{14} is selected from K and R; X_{20} is selected from D, N, Q, E, H, S, R and K; X_{23} is selected from K, I and T; X_{24} is selected from A, S, T, G, H, L and D; and X_{25} is selected from H, E and D; and a first peptide hormone domain (HD1) having an amino acid sequence selected from: (a) SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID	Granted Validated in: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR Expires: 2031-09-28	Same as US 2016/0137709

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			NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, amino acids 2-147 of SEQ ID NO:31, and amino acids 2-147 of SEQ ID NO:33; or (b) the amino acid sequence 1-146 of a leptin selected from: SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, and SEQ ID NO:146; in which a different amino acid is substituted in one or more of the following positions and retaining the same numbering (even in the absence of a glutaminyl residue at position 28): 4, 32, 33, 35, 50, 64, 68, 71, 74, 77, 78, 89, 97, 100, 102, 105, 106, 107, 108, 111, 118, 136, 138, 142, and 145; (c) the amino acid sequence of subpart (b) in which the glutaminyl residue at position 28 is absent; (d) the amino acid sequence of subparts (b) or (c) in which a methionyl residue is added at		

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			the N terminus; (e) a leptin consisting of a fragment of the amino acid sequence of (b), (c), or (d) selected from: i) amino acids 98-146; ii) amino acids 1-32; iii) amino acids 40-116; iv) amino acids 1-99 and 112-146; v) amino acids 1-99 and 112-146 in which one or more of amino acids 100-111 is placed between amino acids 99 and 112; vi) the amino acid sequence of subpart (i) wherein one or more of amino acids 100, 102, 105, 106, 107, 108, 111, 118, 136, 138, 142, and 145 is substituted with another amino acid; vii) the amino acid sequence of subpart (ii) wherein one or more of amino acids 4, 8 and 32 is substituted with another amino acid; viii) the amino acid sequence of subpart (iii) wherein one or more of amino acids 50, 53, 60, 64, 66, 67, 68, 71, 74, 77, 78, 89, 97, 100, 102, 105, 106, 107, 108, 111 and 112 is replaced with another amino acid; ix) the amino acid sequence of subpart (iv) wherein one or more of amino acids 4, 8, 32, 33, 35, 48, 50, 53, 60, 64, 66, 67, 68, 71, 74, 77, 78, 89, 97, 112, 118, 136, 138, 142, and 145 is replaced with another amino acid; and x) the amino acid sequence of subpart (v) wherein one or more of amino acids 4, 32, 33, 35, 50, 64, 68, 71, 74, 77, 78, 89, 97, 100, 102, 105, 106, 107, 108, 111, 118, 136, 138, 142, and 145 is replaced with another amino acid; xi) the amino acid sequence of any of subparts (i) (x) wherein a methionine has been added at the N terminus; (f) the amino acid sequence of any of		

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			subparts (b) through (e) wherein said amino acid sequence is attached to a chemical moiety; (g) the amino acid sequence of subpart (f) wherein said chemical moiety is a water soluble polymer moiety; (h) the amino acid sequence of subpart (g) wherein said water soluble polymer moiety is selected from: polyethylene glycol, an ethylene glycol/propylene glycol copolymer, a carboxymethylcellulose, a dextran, a polyvinyl alcohol, a polyvinyl pyrolidone, a poly-1,3-dioxolane, a poly-1,3,6-trioxane, an ethylene/maleic anhydride copolymer, a polyamino acid homopolymer, a polyamino acid random copolymer, an albumin, an Fc protein, a poly(n-vinyl pyrolidone) polyethylene glycol, a propylene glycol homopolymer, a polypropylene oxide/ethylene oxide copolymer, a polyoxyethylated polyol, a polyvinyl alcohol, a polyethylene glycol propionadehyde, a succinate, and a styrene; (i) the amino acid sequence of subpart (h) wherein said water soluble polymer moiety is a polyethylene glycol; and (j) the amino acid sequence of subpart (h) wherein said water soluble polymer is a polyamino acid selected from: an albumin, an antibody, an Fc protein, and a polylysine moiety; and a first linker (L1) covalently linked to said HD1, said linker comprising an amino acid sequence selected from Gly-Gly-Gly, $[Gly-Ser]_n$, $[Gly-Gly-Ser]_n$, $[Gly-Gly-Gly-Ser]_n$ and $[Gly-Gly-Gly-Gly-Ser]_n$, wherein n is 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10. 25. The engineered polypeptide according to		

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			any one of claims 1 to 24 for use in treating a disease or disorder in a subject.		
FAMILY 5: Albumin-Leptin Polypeptides with Reduced Immunogenicity					
US 9879063 2018-01-30 Publication: US 2016/0207974 2016-07-21	Application No.: US 14/837705 2015-08-27 Priority: US 14/129793 2014-04-03 PCT/US2012/045398 2012-07-03 US 61/540422 2011-09-28 US 61/506001 2011-07-08	Aegerion Pharmaceuticals, Inc.	**Engineered Polypeptides Having Enhanced Duration of Action and Reduced Immunogenicity** 1. An engineered polypeptide comprising: an albumin binding domain (ABD) polypeptide and a first peptide hormone domain (HD1) comprising a leptin, a leptin analog or an active fragment thereof, wherein said ABD comprises at least 95% identity to SEQ ID: 300, with the proviso that X_7 is not L, E or D; or alternatively, with the proviso that the amino acid sequence is not (SEQ ID NO: 679). 7. A method for treating a disease or disorder in a subject, comprising administering an engineered polypeptide according to claim 1 to a subject in need thereof in an amount effective to treat said disease or disorder.	Granted Expires: 2032-07-21 (PTA of 18 days) 1st fee due: 2021-07-30 2nd fee due: 2025-07-30 3rd fee due: 2029-07-30	China CN 103957926 (GRANTED) Hong Kong HK 14109560.5 (PENDING) Europe EP 2729160 (GRANTED) Validated in: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR Japan JP 6040464 (GRANTED) JP 2016-110954 (PENDING) United States US 9879063 (GRANTED) US 15/882919 (PENDING) WIPO PCT/US2012/045398

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claims	Status | Comments	Patent Family
					(CLOSED)
Publication: US 2018/0305430 2018-10-25	Application No.: US 15/882919 2018-01-29 Priority: US 14/837705 2015-08-27 US 14/129793 2014-04-03 PCT/US2012/045398 2012-07-03 US 61/540422 2011-09-28 US 61/506001 2011-07-08	Aegerion Pharmaceuticals, Inc.	**Engineered Polypeptides Having Enhanced Duration of Action and Reduced Immunogenicity** 1. An engineered polypeptide comprising: an albumin binding domain polypeptide (ABD) and a first peptide hormone domain (HD1) selected from a leptin, a leptin analog or an active fragment thereof, wherein said ABD comprises an amino acid sequence selected from the amino acid sequence comprising: (i) LA X3 AK X6 X7 AN X10 ELD X14 YGVSDF YKRLI X26 KAKT VEGVEALK X39 X40 IL X43 X44 LP (SEQ ID NO: 300) wherein independently of each other X3 is selected from E, S, Q and C; X6 is selected from E, S and C; X7 is selected from A and S; X10 is selected from A, S and R; X14 is selected from A, S, C and K; X26 is selected from D and E; X39 is selected from D and E; X40 is selected from A and E; X43 is selected from A and K; X44 is selected from A, S and E; the leucine at position 45 is present or absent; and the praline at position 46 is present or absent; and (ii) an amino acid sequence which has at least 95% identity to the sequence defined in (i); with the proviso that X7 is not L, E or D; or alternatively, with the proviso that the amino acid sequence is not defined by the following	Pending	Same as US 9879063

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			sequence, as defined in PCT Published Application No. WO 2009/016043: LAEAK X_a X_b A X_c X_d EL X_e KY GVSD X_5 YK X_8 X_9 I X_{11} X_{12} A X_{14} TVEGV X_{20} AL X_{23} X_{24} X_{25} ILAALP (SEQ ID NO: 679) wherein independently of each other, X_a is selected from V and E; X_b is selected from L, E and D; X_c is selected from N, L and I; X_d is selected from R and K; X_e is selected from D and K; and X_5 is selected from Y and F; X_8 is selected from N, R and S; X_9 is selected from V, I, L, M, F and Y; X_{11} is selected from N, S, E and D; X_{12} is selected from R, K and N; X_{14} is selected from K and R; X_{20} is selected from D, N, Q, E, H, S, R and K; X_{23} is selected from K, I and T; X_{24} is selected from A, S, T, G, H, L and D; and X_{25} is selected from H, E and D. 191. A method for treating a disease or disorder in a subject, comprising administering an engineered polypeptide according to claim 1 to a subject in need thereof in an amount effective to treat said disease or disorder.		

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claims	Status | Comments	Patent Family
EP 2729160 2019-03-27 Publication: EP 2729160 2014-05-14	Application No.: 12811361.0 2012-07-03 Priority: PCT/US2012/045398 2012-07-03 US 61/540422 2011-09-28 US 61/506001 2011-07-08	Aegerion Pharmaceuticals, Inc.	**Engineered Polypeptides Having Enhanced Duration of Action and Reduced Immunogenicity** 1. An engineered polypeptide comprising: an albumin binding domain polypeptide (ABD) and a first peptide hormone domain (HD1) comprising a leptin, a leptin analog having at least 50% sequence identity to the parent leptin, or an active fragment thereof, wherein said ABD comprises at least 95% identity to SEQ ID NO: 300, with the proviso that X_{14} is selected from A, S, and C; with the proviso that X_7 is not L, E or D; or alternatively, with the proviso that the amino acid sequence is not SEQ ID NO: 679. 14. An engineered polypeptide according to any one of claims 1 to 13 for use in a method for treating a disease or disorder in a subject, said method comprising administering the engineered polypeptide to a subject in need thereof in an amount effective to treat said disease or disorder.	Granted Validated in: AU, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR Expires: 2032-07-03	Same as US 9879063
FAMILY 6: Detection of Anti-Leptin Neutralizing Antibodies					
Publication: US 2018/0074073 2018-03-15	Application No.: US 15/702719 2017-09-12 Priority: US 62/393632 2016-09-12	Aegerion Pharmaceuticals, Inc.	**Methods of Detecting Anti-Leptin Neutralizing Antibodies** 1. A method of detecting neutralizing antibodies to leptin in a sample comprising the steps of: (a) inactivating leptin present in the sample; (b) adding a known quantity of labeled leptin to the sample; (c) contacting the sample containing labeled	Pending	Brazil BR 112019004715-8 (PENDING) Canada CA 3036551 (PENDING) China CN 201780069880.X

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			leptin of (b) with a substrate capable of binding the labeled leptin; (d) washing the substrate to remove unbound labeled leptin; and (e) measuring the label signal produced by the substrate-bound labeled leptin. 2. A method of identifying subjects having neutralizing antibodies to leptin in blood, serum, or plasma from the subject comprising the steps of: (a) inactivating leptin and leptin present in the sample of the subject's blood, serum, or plasma; (b) adding a known quantity of labeled leptin to the sample; (c) contacting the sample containing labeled leptin of (b) with a substrate capable of binding the labeled leptin; (d) washing the substrate to remove unbound labeled leptin; (e) measuring the label signal produced by the bound labeled leptin; (f) measuring a positive control signal, said positive control signal produced by completing steps (a)-(e), and further comprising adding a known quantity of anti-leptin antibody at step (b); and (g) comparing the signal from (e) with the signal from (f), wherein if the level of signal measured in step (e) is equal to or less than the level of signal measured in step (f), then the subject tests positive for anti-leptin neutralizing antibodies. 3. A method of identifying subjects having neutralizing antibodies to leptin in blood, serum, or plasma from the subject comprising the steps of:		(PENDING) Eurasia EA 201990720 (PENDING) Europe EP 17849795.4 (PENDING) India IN 201917013653 (PENDING) Japan JP 2019-513974 (PENDING) Mexico MX/a/2019/002818 (PENDING) WIPO PCT/US2018/04542 (CLOSED)

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			(a) inactivating leptin present in the sample of blood, serum, or plasma; (b) adding a known quantity of labeled leptin to the sample; (c) contacting the sample containing labeled leptin of (b) with a substrate capable of binding the labeled leptin; (d) washing the substrate to remove unbound labeled leptin; (e) measuring the label signal produced by the bound labeled leptin; (f) measuring a negative control signal, said negative control signal produced by completing steps (a)-(e), wherein the sample of blood, serum, or plasma does not contain anti-leptin neutralizing antibodies; and (g) comparing percent difference in the signal from (e) and the signal from (f) with a cutpoint, wherein if the percent difference in the signal from (e) and the signal from (f) is greater than the cutpoint, than the subject tests positive for anti-leptin neutralizing antibodies.		
Publication: EP 3509624 2019-07-17	Application No.: 17849795.4 2017-09-12 Priority: PCT/US2017/051232 2017-09-12 US 62/393632 2016-09-12	Aegerion Pharmaceuticals, Inc.	**Methods of Detecting Anti-Leptin Neutralizing Antibodies** 1. A method of detecting neutralizing antibodies to leptin in a sample comprising the steps of: (a) inactivating leptin present in the sample; (b) adding a known quantity of labeled leptin to the sample; (c) contacting the sample containing labeled leptin of (b) with a substrate capable of binding the labeled leptin; (d) washing the substrate to remove unbound labeled leptin; and (e) measuring the label signal produced by the substrate-bound labeled leptin.	Pending	Same as US 2018/0074073

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			2. A method of identifying subjects having neutralizing antibodies to leptin in blood, serum, or plasma from the subject comprising the steps of: (a) inactivating leptin and leptin present in the sample of the subject's blood, serum, or plasma; (b) adding a known quantity of labeled leptin to the sample; (c) contacting the sample containing labeled leptin of (b) with a substrate capable of binding the labeled leptin; (d) washing the substrate to remove unbound labeled leptin; (e) measuring the label signal produced by the bound labeled leptin; (f) measuring a positive control signal, said positive control signal produced by completing steps (a)-(e), and further comprising adding a known quantity of anti-leptin antibody at step (b); and (g) comparing the signal from (e) with the signal from (f), wherein if the level of signal measured in step (e) is equal to or less than the level of signal measured in step (f), then the subject tests positive for anti-leptin neutralizing antibodies. 3. A method of identifying subjects having neutralizing antibodies to leptin in blood, serum, or plasma from the subject comprising the steps of: (a) inactivating leptin present in the sample of blood, serum, or plasma; (b) adding a known quantity of labeled leptin to the sample; (c) contacting the sample containing labeled leptin of (b) with a substrate capable of binding the labeled leptin;		

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			(d) washing the substrate to remove unbound labeled leptin; (e) measuring the label signal produced by the bound labeled leptin; (f) measuring a negative control signal, said negative control signal produced by completing steps (a)-(e), wherein the sample of blood, serum, or plasma does not contain anti-leptin neutralizing antibodies; and (g) comparing percent difference in the signal from (e) and the signal from (f) with a cutpoint, wherein if the percent difference in the signal from (e) and the signal from (f) is greater than the cutpoint, than the subject tests positive for anti-leptin neutralizing antibodies. 35. A kit for use in detecting neutralizing antibodies to leptin in a sample, comprising (a) labeled leptin, and (b) a substrate capable of binding the labeled leptin.		
FAMILY 7: Treatment of Overweight/Obesity Associated with Leptin Deficiency					
Publication: WO 2019/032469 2019-02-14	Application No.: PCT/US2018/045425 2018-08-06 Priority: US 62/579819 2017-10-31 US 62/542175 2017-08-07	Aegerion Pharmaceuticals, Inc.	**Treatment of Overweight and Obesity Associated with Leptin Deficiency** 1. A method of treating an above-normal weight condition in a subject with a leptin deficiency, the method comprising administering a therapeutically effective amount of leptin to the subject. 15. The method of any one of claims 1-14, wherein the subject has a weight-related comorbidity. 43. A method of treating an above-normal weight condition in a subject with a leptin deficiency, the method comprising subcutaneously administering a	Pending	National phase filings are due in February and March 2020

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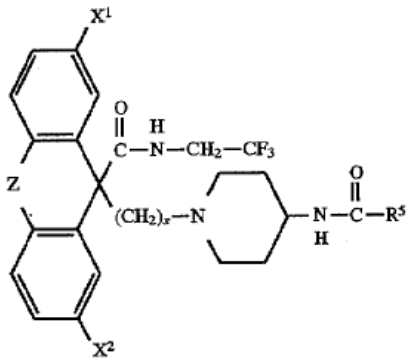
			therapeutically effective amount of leptin to the subject, wherein: (a) the subject is overweight and has a weight-related comorbidity, or the subject is obese; and (b) the leptin deficiency comprises a pre-treatment serum leptin concentration of: (i) ≤ about 16 ng/mL, if the subject is female, (ii) ≤ about 5 ng/mL, if the subject is male.		

SCHEDULE 2

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
FAMILY 8: MTP Inhibitors					
US 5712279 1998-01-27	Application No.: US 08/548811 1996-01-11 Priority: US 08/472067 1995-06-06 US 08/391901 1995-02-21	The Trustees of the University of Pennsylvania Licensed under the Agreement between Trustees of the University of Pennsylvania and Aegerion Pharmaceuticals, Inc. (2006-05-19)	**Inhibitors of Microsomal Triglyceride Transfer Protein and Method** 1. A compound having the structure  including the piperidine N-oxide thereof or a pharmaceutically acceptable salt thereof, wherein Z is a bond or S; X^1 and X^2 are independently selected from H or halo; x is an integer from 2 to 6, $(CH_2)_x$ is optionally substituted with 1, 2 or 3 substituents which are the same or different and are alkyl or halo; R^5 is heteroaryl, aryl, heterocycloalkyl or cycloalkyl, each R^5 group being optionally substituted with 1, 2, 3 or 4 substituents which may be the same or different, wherein one substituents is optionally attached to a ring carbon in the position adjacent to the carbon linked to 	Granted Expires: 2020-02-21 (PTE of 5 years) 1st fee paid: Date of payment is not available 2nd fee paid: Date of payment is not available 3rd fee paid: Date of payment is not available	No other pending patents or applications.

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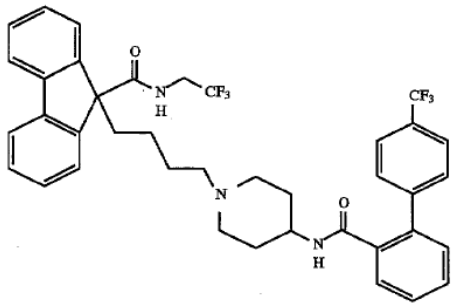
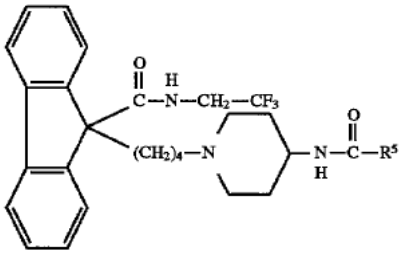
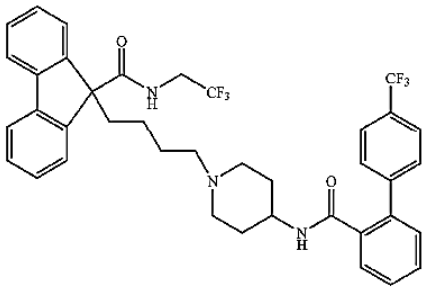
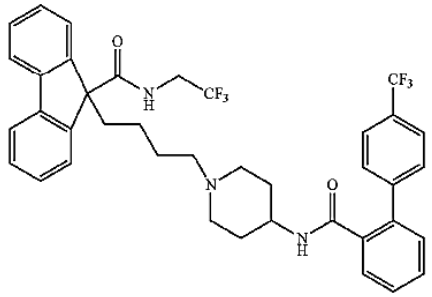
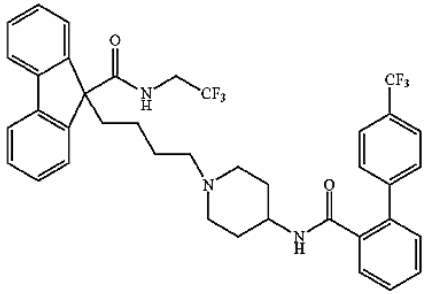
			13. A compound of the structure  or a pharmaceutically acceptable salt thereof or the piperidine N-oxide thereof. 14. A method for preventing or treating atherosclerosis; pancreatitis secondary to hypertriglyceridemia; hyperglycemia (1) by causing a reduced absorption of dietary fat through MTP inhibition, (2) by lowering triglycerides through MTP inhibition or (3) by decreasing the absorption of free fatty acids through MTP inhibition; or obesity by causing a reduced absorption of dietary fat through MTP, in a mammal species, which comprises administering to a patient in need of treatment a therapeutically effective amount of a compound as defined in claim 1 or 13. 15. A method of lowering serum lipid levels, cholesterol and/or triglycerides, or preventing and/or treating hyperlipemia, hyperlipidemia, hyperlipoproteinemia, hypercholesterolemia and/or hypertriglyceridemia, which comprises administering to a patient in need of treatment a therapeutically effective amount of a compound as defined in claim 1 or 13. 16. A compound having the structure		

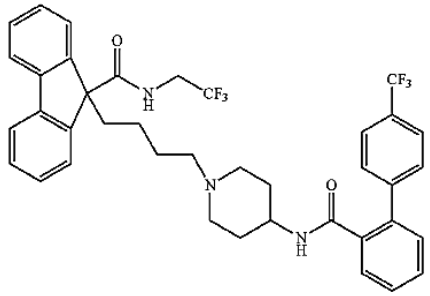
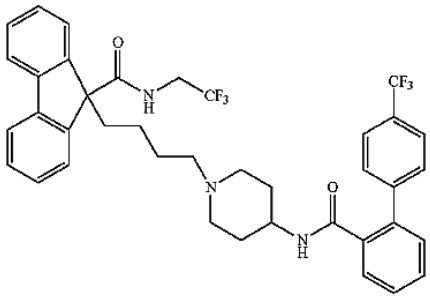
Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
			 including the piperidine N-oxide thereof or a pharmaceutically acceptable salt thereof, R^5 is heteroaryl, aryl, heterocycloalkyl or cycloalkyl, each R^5 group being optionally substituted with 1, 2, 3 or 4 substituents which may be the same or different wherein a substituent on R^5 is adjacent to a ring carbon attached to the  group.		
FAMILY 9: Use of MTP Inhibitors for Treating Hyperlipidemia-/Hypercholesterolemia-Associated Diseases					
US 7932268 2011-04-26 Publication: US 2009/0042941 2009-02-12	Application No.: US 10/591923 2007-06-21 Priority: PCT/US2005/007435 2005-03-07 US 60/550915 2004-03-05	The Trustees of the University of Pennsylvania Licensed under the Agreement between Trustees of the University of Pennsylvania and Aegerion Pharmaceuticals, Inc. (2006-05-19)	**Methods for Treating Disorders or Diseases Associated with Hyperlipidemia and Hypercholesterolemia While Minimizing Side Effects** 1. A method of treating a subject suffering hyperlipidemia or hypercholesterolemia, the method comprising administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises at least three step-wise, increasing dose levels of the MTP inhibitors wherein a first dose level is from about 2 to about 13 mg/day, a second dose level is from about 5 to about 30 mg/day, and a third dose level is from about 10 to about 50 mg/day; and wherein the MTP inhibitor is represented by:	Granted Expires: 2027-08-19 (PTA of 895 days) 1st fee paid: 2014-10-27 2nd fee paid: 2019-02-11 3rd fee due: 2022-10-26	Australia AU 2005221656 (GRANTED) AU 2011226862 (GRANTED) Canada CA 2910191 (PENDING) Europe EP 1725234 (GRANTED) Validated in: AL, AT, BA, BE,

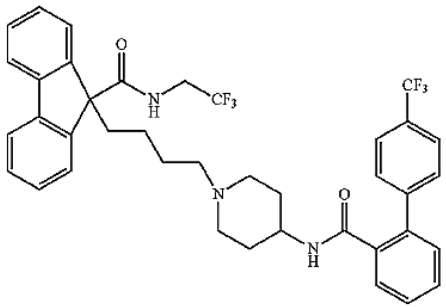
Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
			 or a pharmaceutically acceptable salt thereof or the piperidine N-oxide thereof, and wherein each dose level is administered to the subject for about 1 to 4 weeks.		BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, ME, MK, NL, PL, PT, RO, RS, SE, SI, SK, TR India IN 2826/KOLNP/2006 (PENDING) Japan JP 5697296 (GRANTED) PTE to 2026-10-14 for 5, 10, 20 mg capsules JP 5902760 (GRANTED) PTE to 2025-09-16 for 5, 10, 20 mg capsules JP 6189918 (GRANTED) New Zealand NZ 549721 (GRANTED) South Korea KR 10-1494067 (GRANTED) United States US 7932268 (GRANTED)

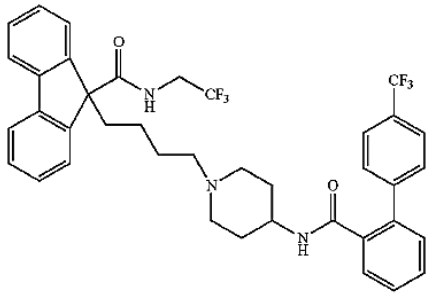
Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
					US 8618135 (GRANTED) US 9265758 (GRANTED) US 9364470 (GRANTED) US 9433617 (GRANTED) US 9861622 (GRANTED) US 10016404 (GRANTED) US 16/030703 (PENDING) WIPO PCT/US2005/007435 (CLOSED)
US 8618135 2013-12-31 Publication: US 2012/0010243 2012-01-12	Application No.: 13/046118 2011-03-11 Priority: US 10/591923 2007-06-21 PCT/US2005/007435 2005-03-07 US 60/550915 2004-03-05	The Trustees of the University of Pennsylvania Licensed under the Agreement between Trustees of the University of Pennsylvania and Aegerion Pharmaceuticals, Inc. (May 19, 2006)	**Methods for Treating Disorders or Diseases Associated with Hyperlipidemia and Hypercholesterolemia While Minimizing Side Effects** 1. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises at least three step-wise, increasing dose levels of the MTP inhibitor wherein a first dose level is from about 2 to about 13 mg/day, a second dose level is from about 5 to about 30 mg/day, and a third dose level is	Granted Expires: 2025-03-07 (Subject to a terminal disclaimer to '268 patent) 1st fee paid: 2017-06-30 2nd fee due: 2021-06-30 3rd fee due:	Same as US 7932268

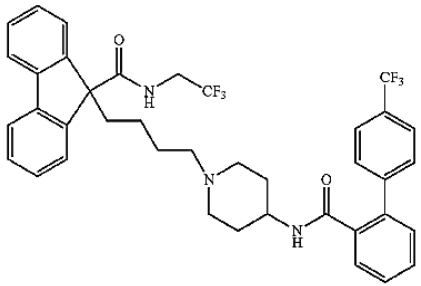
Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
			from about 10 to about 50 mg/day; and wherein the MTP inhibitor is represented by:  or a pharmaceutically acceptable salt thereof or the piperidine N-oxide thereof, and wherein each dose level is administered to the subject for about 1 to about 5 weeks. 9. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises at least three step-wise, increasing dose levels of the MTP inhibitor wherein a first dose level is from about 2 to about 13 mg/day, administered to the subject for about 2 weeks; a second dose level is from about 5 to about 30 mg/day, administered to the subject for about 2 weeks to about 4 weeks; and a third dose level is from about 10 to about 50 mg/day, administered to the subject for about 2 weeks to about 4 weeks; and wherein the MTP inhibitor is represented by:	2025-06-30	

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
			 or a pharmaceutically acceptable salt thereof or the piperidine N-oxide thereof. 10. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises at least three step-wise, increasing dose levels of the MTP inhibitor wherein a first dose level is from about 2 to about 13 mg/day, administered to the subject for about 1 to about 12 weeks; a second dose level is from about 5 to about 30 mg/day, administered to the subject for about 4 weeks; and a third dose level is from about 10 to about 50 mg/day, administered to the subject for about 4 weeks; and wherein the MTP inhibitor is represented by:		

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
			 or a pharmaceutically acceptable salt thereof or the piperidine N-oxide thereof.		
US 9265758 2016-02-23 Publication: US 2014/0303209 2014-10-09	Application No.: US 14/075483 2013-11-08 Priority: US 13/046118 2011-03-11 US 10/591923 2007-06-21 PCT/US2005/007435 2005-03-07 US 60/550915 2004-03-05	The Trustees of the University of Pennsylvania Licensed under the Agreement between Trustees of the University of Pennsylvania and Aegerion Pharmaceuticals, Inc. (2006-05-19)	**Methods for Treating Disorders or Diseases Associated with Hyperlipidemia and Hypercholesterolemia While Minimizing Side Effects** 1. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises at least three step-wise, increasing dose levels of the MTP inhibitor wherein the dose levels are from about 2 to about 13 mg/day, from about 5 to about 30 mg/day, and from about 10 to about 50 mg/day; and wherein the MTP inhibitor is represented by:  or a pharmaceutically acceptable salt thereof	Granted Expires: 2025-03-07 (Subject to a terminal disclaimer to '268 and '135 patents) 1st fee due: 2019-08-23 2nd fee due: 2023-08-23 3rd fee due: 2027-08-23	Same as US 7932268

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
			or the piperidine N-oxide thereof, and wherein each dose level is administered to the subject for about 1 to about 5 weeks. 7. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises at least three step-wise, increasing dose levels of the MTP inhibitor up to a maximum dose level, wherein a first starting dose level is from about 2 to about 13 mg/day, a second dose level is from about 5 to about 30 mg/day, and a third dose level is from about 10 to about 50 mg/day; and wherein the MTP inhibitor is represented by:  or a pharmaceutically acceptable salt thereof or the piperidine N-oxide thereof, and wherein each dose level is administered to the subject for about 1 to 4 weeks, wherein upon administration the patient has reduced steatorrhea as compared to a patient administered a starting dose of 25 mg/day. 9. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising administering to the subject an effective amount of an MTP		

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
			inhibitor, wherein said administration comprises at least three step-wise, increasing dose levels of the MTP inhibitor, wherein a first dose level is from about 2 to about 13 mg/day, a second dose level is from about 5 to about 30 mg/day, and a third dose level is from about 10 to about 50 mg/day; and wherein the MTP inhibitor is represented by:  or a pharmaceutically acceptable salt thereof or the piperidine N-oxide thereof, and wherein each dose level is administered to the subject for about 1 to 4 weeks, wherein the method reduces symptoms of steatorrhea and/or hepatic fat in the subject.		
US 9364470 2016-06-14 Publication: US 2016/0081994 2016-03-24	Application No.: US 14/959756 2015-12-04 Priority: US 14/075483 2013-11-08 US 13/046118 2011-03-11 US 10/591923 2007-06-21 PCT/US2005/007435	The Trustees of the University of Pennsylvania Licensed under the Agreement between Trustees of the University of Pennsylvania and Aegerion Pharmaceuticals, Inc. (2006-05-19)	**Methods for Treating Disorders or Diseases Associated with Hyperlipidemia and Hypercholesterolemia While Minimizing Side Effects** 1. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises at least three step-wise, increasing dose levels of the MTP inhibitor, wherein a first dose level is from about 0.02 to about 0.059 mg/kg/day, a second dose level is from about 0.06 to about 0.19 mg/kg/day, and a	Granted Expires: 2025-03-07 (Subject to a terminal disclaimer to '268, '135, and '758 patents) 1st fee due: 2019-12-16 2nd fee due: 2023-12-14	Same as US 7932268

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
	2005-03-07 US 60/550915 2004-03-05		third dose level is from about 0.2 to about 0.59 mg/kg/day; and wherein the MTP inhibitor is represented by:  or a pharmaceutically acceptable salt thereof or the piperidine N-oxide thereof, and wherein the first dose level is administered for about two weeks, and wherein the second and third dose levels are each administered for about 4 weeks.	3rd fee due: 2027-12-14	
US 9433617 2016-09-06 Publication: US 2016/0256446 2016-09-08	Application No.: US 15/155647 2016-05-16 Priority: US 14/959756 2015-12-04 US 14/075483 2013-11-08 US 13/046118 2011-03-11 US 10/591923 2007-06-21 PCT/US2005/007435 2005-03-07	The Trustees of the University of Pennsylvania Licensed under the Agreement between Trustees of the University of Pennsylvania and Aegerion Pharmaceuticals, Inc. (2006-05-19)	**Methods for Treating Disorders or Diseases Associated with Hyperlipidemia and Hypercholesterolemia While Minimizing Side Effects** 1. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising orally administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises three step-wise, increasing dose levels of the MTP inhibitor, wherein each dose level is 50% of the immediately following dose level, wherein the third dose level is about 0.2 to about 0.59 mg/kg/day, and wherein the MTP inhibitor is N-(2,2,2-trifluoroethyl)-9-[4-[4-[[[4'-(trifluoromethyl)[1,1'-biphenyl]-2-yl] carbonyl] amino]-1-piperidinyl]butyl]-9H-fluorene-9-carboxamide, methanesulfonate; and wherein	Granted Expires: 2025-03-07 (Subject to a terminal disclaimer to '268, '135, '758, and '470 patents) 1st fee due: 2020-03-06 2nd fee due: 2024-03-06 3rd fee due: 2028-03-06	Same as US 7932268

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
	US 60/550915 2004-03-05		each dose level is administered about 1 to about 12 weeks. 8. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia the method comprising administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises at least three step-wise, increasing dose levels of the MTP inhibitor, wherein each dose level is 50% of the immediately following dose level, wherein the second dose level is about 0.06 mg/kg/day to about 0.19 mg/kg/day, wherein the MTP inhibitor is N-(2,2,2-trifluoroethyl)-9-[4-[4-[[[4'-(trifluoromethyl)[l,r-biphenyl]-2-yl] carbonyl] amino]-l-piperidinyl]butyl]-9H-fluorene-9-carboxamide, methanesulfonate, and wherein each dose level is administered about 1 to about 12 weeks. 15. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises three step-wise, increasing dose levels of the MTP inhibitor, wherein each dose level is no more than 50% of the immediately following dose level, and wherein the first dose level is about 0.02 to about 0.059 mg/kg/day, the second dose level is about 0.06 mg/kg/day to about 0.19 mg/kg/day, and the third dose level is about 0.2 to about 0.59 mg/kg/day; wherein the MTP inhibitor is N-(2,2,2-trifluoroethyl)-9-[4-[4-[[[4'-(trifluoromethyl)[l,r-biphenyl]-2-yl] carbonyl] amino]-l-piperidinyl]butyl]-9H-fluorene-9-carboxamide, methanesulfonate;		

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
			and wherein each dose level is administered about 1 to about 12 weeks.		
US 9861622 2018-01-09 Publication: US 2016/0331739 2016-11-17	Application No.: US 15/218670 2016-07-25 Priority: US 15/155647 2016-05-16 US 14/959756 2015-12-04 US 14/075483 2013-11-08 US 13/046118 2011-03-11 US 10/591923 2007-06-21 PCT/US2005/007435 2005-03-07 US 60/550915 2004-03-05	The Trustees of the University of Pennsylvania Licensed under the Agreement between Trustees of the University of Pennsylvania and Aegerion Pharmaceuticals, Inc. (2006-05-19)	**Methods for Treating Disorders or Diseases Associated with Hyperlipidemia and Hypercholesterolemia While Minimizing Side Effects** 1. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising orally administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises three step-wise, increasing dose levels of the MTP inhibitor, wherein each dose level is 50% of the immediately following dose level, wherein the third dose level is about 0.2 to about 0.59 mg/kg/day, and wherein the MTP inhibitor is N-(2,2,2-trifluoroethyl)-9-[4-[4-[[[4'-(trifluoromethyl)[1,1'-biphenyl]-2-yl] carbonyl] amino]-1-piperidinyl] butyl]-9H-fluorene-9-carboxamide, methanesulfonate; wherein each dose level is administered for a period of about 7 to about 35 days; and wherein the subject suffering from hyperlipidemia or hypercholesterolemia has homozygous familial hypercholesterolemia. 6. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia the method comprising administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises at least three step-wise, increasing dose levels of the MTP inhibitor, wherein each dose level is 50% of the immediately following dose level, wherein the second dose level is about 0.06 mg/kg/day to about 0.19 mg/kg/day, wherein the MTP inhibitor is N-	Granted Expires: 2025-03-07 (Subject to a terminal disclaimer to '268, '135, '758, '470, and '617 patents) 1st fee due: 2021-07-09 2nd fee due: 2025-07-09 3rd fee due: 2029-07-09	Same as US 7932268

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
			(2,2,2-trifluoroethyl)-9-[4-[4-[[[4'-(trifluoromethyl) [1,1'-biphenyl]-2-yl] carbonyl] amino]-1-piperidinyl] butyl]-9H-fluorene-9-carboxamide, methanesulfonate, wherein each dose level is administered for a period of about 7 to about 35 days, and wherein the subject suffering from hyperlipidemia or hypercholesterolemia has homozygous familial hypercholesterolemia. 11. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises three step-wise, increasing dose levels of the MTP inhibitor, wherein each dose level is no more than 50% of the immediately following dose level, and wherein the first dose level is about 0.02 to about 0.059 mg/kg/day, the second dose level is about 0.06 mg/kg/day to about 0.19 mg/kg/day, and the third dose level is about 0.2 to about 0.59 mg/kg/day; wherein the MTP inhibitor is N-(2,2,2-trifluoroethyl) -9-[4-[4[[[4'-(trifluoromethyl)[1,1'-biphenyl]-2-yl] carbonyl] amino]-1-piperidinyl] butyl]-9H-fluorene-9-carboxamide, methanesulfonate; wherein each dose level is administered for a period of about 7 to about 35 days; and wherein the subject suffering from hyperlipidemia or hypercholesterolemia has homozygous familial hypercholesterolemia.		
US 10016404 2018-07-10 Publication: US 2017/0258776 2017-09-14	Application No.: US 15/605548 2017-05-25 Priority: US 15/218670	The Trustees of the University of Pennsylvania Licensed under the Agreement between Trustees of the University of	**Methods for Treating Disorders or Diseases Associated with Hyperlipidemia and Hypercholesterolemia While Minimizing Side Effects** 1. A method of treating a human subject	Granted Expires: 2025-03-07 (Subject to a terminal disclaimer	Same as US 7932268

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
	2016-07-25 US 15/155647 2016-05-16 US 14/959756 2015-12-04 US 14/075483 2013-11-08 US 13/046118 2011-03-11 US 10/591923 2007-06-21 PCT/US2005/007435 2005-03-07 US 60/550915 2004-03-05	Pennsylvania and Aegerion Pharmaceuticals, Inc. (2006-05-19)	suffering from hyperlipidemia or hypercholesterolemia, the method comprising administering to the human subject an effective amount of an MTP inhibitor, the administration of the MTP inhibitor comprising three step-wise, increasing dose levels of the MTP inhibitor, wherein each of the dose levels is no more than 50% of the immediately following dose level; wherein each of the dose levels is administered for about 1 to about 12 weeks; wherein the MTP inhibitor is N-(2,2,2-trifluoroethyl)-9-[4-[4-[[[4' (trifluoromethyl) [1,1';-biphenyl]-2-yl] carbonyl] amino]-1-piperidinyl]butyl]-9H-fluorene-9 carboxamide, methanesulfonate; and wherein the administration of the MTP inhibitor reduces total cholesterol of the human subject by at least 30% as compared to control blood levels. 7. A method of treating a human subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising administering to the human subject an effective amount of an MTP inhibitor, the administration of the MTP inhibitor comprising three step-wise, increasing dose levels of the MTP inhibitor, wherein each of the dose levels is no more than 50% of the immediately following dose level; wherein each of the dose levels is administered for about 1 to about 12 weeks; wherein the MTP inhibitor is N-(2,2,2-trifluoroethyl)-9-[4-[4-[[[4' (trifluoromethyl) [1,1'-biphenyl]-2-yl] carbonyl] amino]-1-piperidinyl]butyl]-9H-fluorene-9 carboxamide, methanesulfonate; and wherein the administration of the MTP	to '268, '135, '758, '470, '617, and '622 patents) 1st fee due: 2022-01-10 2nd fee due: 2026-01-12 3rd fee due: 2030-01-10	

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
			inhibitor minimizes side effects as compared to administration of the MTP inhibitor to a human subject at a starting dose of 25 mg/day. 14. A method of treating a human subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising administering to the human subject an effective amount of an MTP inhibitor, the administration of the MTP inhibitor comprising three step-wise, increasing dose levels of the MTP inhibitor, wherein each of the dose levels is no more than 50% of the immediately following dose level; wherein each of the dose levels is administered for about 1 to about 12 weeks; wherein the first dose level is sub-therapeutic; wherein the MTP inhibitor is N-(2,2,2-trifluoroethyl)-9-[4-[4-[[[4' (trifluoromethyl) [1,1'-biphenyl]-2-yl] carbonyl] amino]-1-piperidinyl]butyl]-9H-fluorene-9 carboxamide, methanesulfonate; and wherein the administration of the MTP inhibitor reduces total cholesterol of the human subject by at least 30% as compared to control blood levels. 20. A method of treating a human subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising administering to the human subject an effective amount of an MTP inhibitor, the administration of the MTP inhibitor comprising three step-wise, increasing dose levels of the MTP inhibitor, wherein each of the dose levels is no more than 50% of the immediately following dose level; wherein each of the dose levels is		

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
			administered for about 1 to about 12 weeks; wherein the first dose level is sub-therapeutic; wherein the MTP inhibitor is N-(2,2,2-trifluoroethyl)-9-[4-[4-[[[4' (trifluoromethyl) [1,1'-biphenyl]-2-yl] carbonyl] amino]-1-piperidinyl]butyl]-9H-fluorene-9 carboxamide, methanesulfonate; and wherein the administration of the MTP inhibitor minimizes side effects as compared to administration of the MTP inhibitor to a human subject at a starting dose of 25 mg/day.		
Publication: US 2018/0318278 2018-11-08	Application No.: US 16/030703 2018-06-09 Priority: US 15/605548 2017-05-25 US 15/218670 2016-07-25 US 15/155647 2016-05-16 US 14/959756 2015-12-04 US 14/075483 2013-11-08 US 13/046118 2011-03-11 US 10/591923 2007-06-21 PCT/US2005/007435	The Trustees of the University of Pennsylvania Licensed under the Agreement between Trustees of the University of Pennsylvania and Aegerion Pharmaceuticals, Inc. (2006-05-19)	**Methods for Treating Disorders or Diseases Associated with Hyperlipidemia and Hypercholesterolemia While Minimizing Side Effects** 1. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising orally administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises three step-wise, increasing dose levels of the MTP inhibitor, wherein each dose level is 50% of the immediately following dose level, wherein the third dose level is about 0.2 to about 0.59 mg/kg/day, and wherein the MTP inhibitor is N-(2,2,2-trifluoroethyl)-9-[4-[4-[[[4'-(trifluoromethyl) [1,1'-biphenyl]-2-yl] carbonyl] amino]-1-piperidinyl]butyl]-9H-fluorene-9-carboxamide, methanesulfonate; and wherein each dose level is administered for a period of about 7 to about 35 days. 7. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia the method comprising administering to the subject an effective amount of an MTP	Pending	Same as US 7932268

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
	2005-03-07 US 60/550915 2004-03-05		inhibitor, wherein said administration comprises at least three step-wise, increasing dose levels of the MTP inhibitor, wherein each dose level is 50% of the immediately following dose level, wherein the second dose level is about 0.06 mg/kg/day to about 0.19 mg/kg/day, wherein the MTP inhibitor is N-(2,2,2-trifluoroethyl)-9-[4-[4-[[[4'-(trifluoromethyl)[1,1'-biphenyl]-2-yl] carbonyl] amino]-1-piperidinyl]butyl]-9H-fluorene-9-carboxamide, methanesulfonate, and wherein each dose level is administered for a period of about 7 to about 35 days. 13. A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises three step-wise, increasing dose levels of the MTP inhibitor, wherein each dose level is no more than 50% of the immediately following dose level, and wherein the first dose level is about 0.02 to about 0.059 mg/kg/day, the second dose level is about 0.06 mg/kg/day to about 0.19 mg/kg/day, and the third dose level is about 0.2 to about 0.59 mg/kg/day; wherein the MTP inhibitor is N-(2,2,2-trifluoroethyl)-9-[4-[4-[[[4'-(trifluoromethyl)[1,1'-biphenyl]-2-yl] carbonyl] amino]-1-piperidinyl]butyl]-9H-fluorene-9-carboxamide, methanesulfonate; and wherein each dose level is administered for a period of about 7 to about 35 days.		
EP 1725234 2012-11-21 Publication: EP 1725234	Application No.: EP 05724887.4 2005-03-07 Priority:	The Trustees of the University of Pennsylvania Licensed under the Agreement between Trustees	**Methods for Treating Disorders or Diseases Associated with Hyperlipidemia and Hypercholesterolemia While Minimizing Side Effects**	Granted Validated in: AL, AT, BA, BE, BG, CH, CY, CZ,	Same as US 7932268

Patent No. | Publication No.	Application No. | Priority	Assignee | Licensor	Title | Exemplary Claim	Status | Comments	Patent Family
2006-11-29	PCT/US2005/007435 2005-03-07 US 60/550915 2004-03-05	of the University of Pennsylvania and Aegerion Pharmaceuticals, Inc. (2006-05-19)	1. Use of an MTP inhibitor in the manufacture of a medicament for the treatment of a subject suffering from a disorder associated with hyperlipidemia and/or hypercholesterolemia, wherein said treatment comprises the administration of at least three step-wise, increasing dosages of said MTP inhibitor to said subject. 2. An MTP inhibitor for use in treating a subject suffering from a disorder associated with hyperlipidemia and/or hypercholesterolemia, wherein said treatment comprises the administration of at least three step-wise, increasing dosages of said MTP inhibitor to said subject. 21. Use of an MTP inhibitor in the manufacture of a medicament for the treatment of a subject suffering from a disorder selected from the group consisting or homozygous/heterozygous familial hypercholesterolemia or hypertriglyceridemia. 22. An MTP inhibitor for use in treating a subject suffering from a disorder selected from the group consisting of homozygous/ heterozygous familial hypercholesterolemia or hypertriglyceridemia. 27. A kit for treating a disorder associated with hyperlipidemia and/or hypercholesterolemia in a subject, comprising: a) at least four sets of pharmaceutical dosage units of an MTP inhibitor, wherein a first set of dosage units provides 6-25 mg/day for a first interval, a second set of dosage units provides 12.5 mg/day for a second interval, a third set of dosage units provides 37.5 mg/day	DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, ME, MK, NL, PL, PT, RO, RS, SE, SI, SK, TR <u>Expires:</u> AL: 2025-03-07 AT: 2028-08-05 (SPC granted) BA: 2025-03-07 BE: 2025-03-07 (SPC pending) BG: 2025-03-07 (SPC pending) CH: 2025-03-07 CY: 2028-07-31 (SPC granted) CZ: 2028-08-05 (SPC granted) DE:	

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			for a third interval, a fourth set of dosage units provides 50 mg/day for a fourth interval; and b) Instructions for use. 29. A kit for treating a disorder associated with hyperlipidemia and/or hypercholesterolemia in a subject, comprising; a) at least five sets of pharmaceutical dosage units of an MTP inhibitor, wherein a first set of dosage units provides from about 2 to about 13 mg/day for a first interval, a second set of dosage units provides from about 5 to about 30 mg/day for a second interval, a third set of dosage units provides from about 10 to about 50 mg/day for a third interval, a fourth set of dosage units provides from about 20 to about 60 mg/day for a fourth interval, and a fifth set of dosage units provides from about 30 to about 75 mg/day for a fifth interval; and b) instructions for use.	2028-08-05 (SPC granted) DK: 2028-08-05 (SPC granted) EE: 2028-08-05 (SPC granted) ES: 2028-08-05 (SPC granted) FI: 2028-08-05 (SPC granted) FR: 2028-08-05 (SPC granted) GB: 2025-03-07 (SPC pending) GR: 2028-08-06 (SPC granted) HR: 2025-03-07 (SPC pending) HU: 2025-03-07 (SPC pending)	

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				IE: 2028-08-04 (SPC granted) IS: 2028-08-04 (SPC granted) IT: 2028-07-30 (SPC granted) LI: 2025-03-07 LT: 2025-03-07 (SPC pending) LU: 2028-08-05 (SPC granted) LV: 2028-08-05 (SPC granted) MC: 2025-03-07 ME: 2025-03-07 MK: 2025-03-07 NL: 2028-08-04 (SPC granted)	

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				PL: 2028-08-05 (SPC granted) PT: 2028-08-05 (SPC granted) RO: 2025-03-07 (SPC pending) RS: 2025-03-07 SE: 2028-08-04 (SPC granted) SI: 2028-08-05 (SPC granted) SK: 2028-08-05 (SPC granted) TR 2025-03-07	
FAMILY 10: Use of MTP Inhibition for Treating Atherosclerosis					
US 6492365 2002-12-10	Application No.: US 08/486929 1995-06-07 Priority: US 08/117362 1993-09-03	The Trustees of the University of Pennsylvania Licensed under the Agreement between Trustees of the University of Pennsylvania and Aegerion	**Microsomal Triglyceride Transfer Protein** 1. A method for treating atherosclerosis in a mammalian species comprising administration of a therapeutically effective amount of an agent which decreases the amount or activity of microsomal triglyceride transfer protein,	Granted Expires: 2019-12-10	No other pending patents or applications.

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	US 08/015449 1993-02-22 US 07/847503 1992-03-06	Pharmaceuticals, Inc. (2006-05-19)	wherein said agent is not a polynucleotide compound. 2. A method for decreasing serum lipid levels in a mammalian species, which comprises administration of a therapeutically effective amount of an agent which decreases the amount or activity of microsomal triglyceride transfer protein, wherein said agent is not a polynucleotide compound. 6. A method for treating hyperglycemia in a mammalian species comprising administration of a therapeutically effective amount of an agent which decreases the amount or activity of microsomal triglyceride transfer protein, wherein said agent is not a polynucleotide compound. 7. A method for treating hypertriglyceridemia in a mammalian species comprising administration of a therapeutically effective amount of an agent which decreases the amount or activity of microsomal triglyceride transfer protein, wherein said agent is not a polynucleotide compound. 8. A method for treating hypercholesterolemia in a mammalian species comprising administration of a therapeutically effective amount of an agent which decreases the amount or activity of microsomal triglyceride transfer protein, wherein said agent is not a polynucleotide compound. 9. A method for treating hypertriglyceridemia and hypercholesterolemia in a mammalian species comprising administration of a therapeutically effective amount of an agent		

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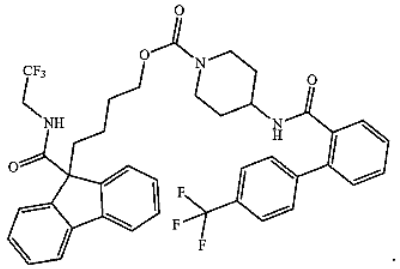
			which decreases the amount or activity of microsomal triglyceride protein, wherein said agent is not a polynucleotide compound. 10. A method of reducing gastrointestinal triglyceride, fatty acid cholesterol absorption in a mammalian species comprising administration of a therapeutically effective amount of an agent which decreases the amount or activity of microsomal triglyceride transfer protein, wherein said agent is not a polynucleotide compound.		
FAMILY 11: Lomitapide Impurities					
US 10213419 2019-02-26 Publication: US 2018-0133205 2018-05-17	Application No.: US 15/570246 2017-10-27 Priority: PCT/US2016/030397 2016-05-02 US 62/154906 2015-04-30	Aegerion Pharmaceuticals, Inc.	**Compound Impurities and Methods of Detecting Same** 1. A lomitapide product having the following structure:  6. A method for analyzing a lomitapide composition sample for the presence or amount of an impurity comprising: providing a lomitapide composition sample; using a spectral or toxicology analysis to determine the presence of a compound having the structure:	Granted Expires: 2036-05-02	Brazil BR 1020150255020 (PENDING) Canada CA 2983995 (PENDING) Europe EP 16787302.5 (PENDING) Japan JP 2017-556976 (PENDING) United States US 10213419 (GRANTED) WIPO PCT/US2016/030397 (CLOSED)

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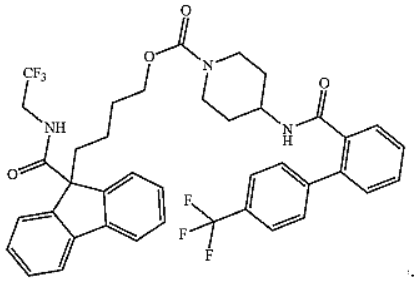
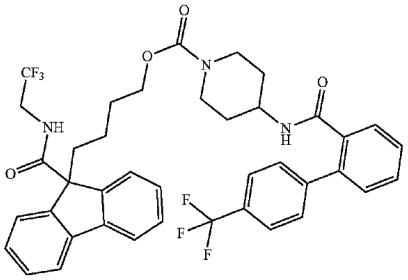
			 making a determination about the lomitapide composition sample based on a comparison of the compound and a reference standard for lomitapide or a pharmaceutically acceptable salt thereof; and determining the presence or amount of the compound thereby to analyze the lomitapide composition sample. 16. A method for determining an amount of an impurity in a composition sample comprising lomitapide or a pharmaceutically acceptable salt thereof, the method comprising: determining an amount of a compound having the structure:  in the sample; and correlating the amount the compound in the sample with the amount of lomitapide in the sample.		

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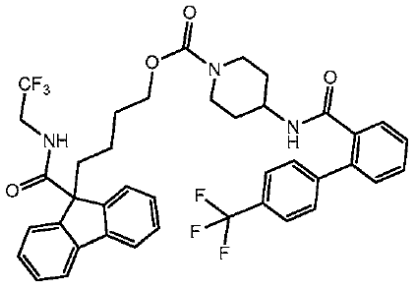
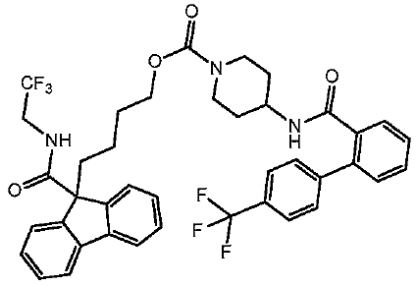
Publication: EP 3289085 2018-03-07	Application No.: EP 16787302.5 2016-05-02 Priority: PCT/US2016/030397 2016-05-02 US 62/154906 2015-04-30	Aegerion Pharmaceuticals	**Compound Impurities and Methods of Detecting Same** 1. A lomitapide composition comprising: lomitapide or a pharmaceutically acceptable salt thereof, and a carbamate product represented by  ; and a pharmaceutically acceptable excipient. 3. A method for analyzing a lomitapide composition sample for the presence or amount of an impurity comprising: providing a lomitapide composition sample; using a spectral or toxicology analysis to determine the presence of a compound having the structure:  ; making a determination about the lomitapide composition sample based on a comparison of a structural signal associated with the	Pending	Same as US 10213419

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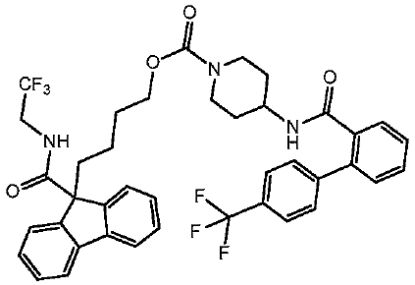
			compound to a reference standard for lomitapide or a pharmaceutically acceptable salt thereof; and determining the presence of the structural signature associated with the compound thereby to analyze the lomitapide composition sample. 9. A method for analyzing a lomitapide composition sample for the presence or amount of an impurity comprising: providing a lomitapide composition sample; using a spectral analysis to determine the presence of a compound having the structure:  ; making a determination about the lomitapide composition sample based on a comparison of the molecular weight associated with the compound to a reference standard for lomitapide or a pharmaceutically acceptable salt thereof; and determining the molecular weight associated with the compound thereby to analyze the lomitapide composition sample. 10. A method for determining an amount of an impurity in a composition sample comprising lomitapide or a pharmaceutically acceptable salt thereof, the method comprising: determining an amount of a compound having the structure:		

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			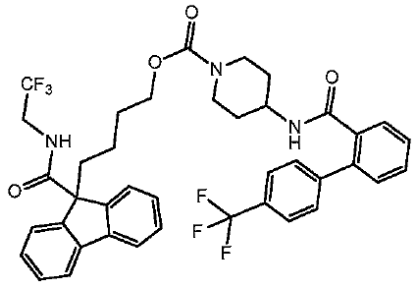 in the sample; and correlating the amount the compound in the sample with the amount of lomitapide in the sample.		