Document	Title	Abstract	Claims	Patentee	Granted	Priority
EP1660001B1	CROSSLINKING REAGENT FOR TREATING VERTEBRAL DISC DISORDERS	A method of improving the resistance of collagenous tissue to mechanical degradation in accordance with the present invention comprises the step of contacting at least a portion of a collagenous tissue with an effective amount of a crosslinking reagent. Methods and devices for enhancing the body's own efforts to stabilize discs in scoliotic spines by increasing collagen crosslinks. This stability enhancement is caused by reducing the bending hysteresis and increasing the bending stiffness of scoliotic spines, by injecting non-toxic crosslinking reagents into the convex side of discs involved in the scoliotic curve. Alternatively, contact between the tissue and the crosslinking reagent is effected by placement of a time-release delivery system directly into or onto the target tissue. Methods and devices that use crosslinking agents for increasing the permeability of an intervertebral disc, improving fluid flux to the intervertebral disc, and increasing the biological viability of cells within the intervertebral disc are provided.	1. Use of an effective amount of a crosslinking reagent for manufacturing a medicament for improving the stabilization of invertebrate discs by reducing the bending hysteresis of scoliotic spines comprising contacting at least a portion of a collagenous tissue within the discs with the crosslinking reagent, being genipin and/or proanthocyanidin. 2. Use of an effective amount of a crosslinking reagent for manufacturing a medicament for improving the stabilization of invertebrate discs by increasing the bending stiffness of scoliotic spines comprising contacting at least a portion of a collagenous tissue within the discs with the crosslinking reagent, being genipin and/or proanthocyanidin. 10. A device for improving the stabilization of invertebrate discs by reducing the bending hysteresis of scoliotic spines comprising: a crosslinking reagent, being genipin and/or proanthocyanidin. 11. A device for improving the stabilization of invertebrate discs by increasing the bending stiffness of scoliotic spines comprising: a crosslinking reagent, being genipin and/or proanthocyanidin. 17. A sterile reagent and application tray enclosed in packaging with a sterile inner surface, for improving the stabilization of invertebrate discs by reducing the bending hysteresis of scoliotic spines comprising one or more of the following: container containing an effective amount of a crosslinking reagent, being genipin and/or proanthocyanidin, or container containing premeasured amount of a solvent for dissolving the crosslinking reagent; syringe with needle, or other means for in injecting a crosslinking reagent, being genipin and/or proanthocyanidin; time release capsule for releasing a crosslinking reagent, being genipin and/or proanthocyanidin; time release capsule insertion device for aiding in the delivery of a crosslinking reagent, being genipin and/or proanthocyanidin; container of gel or ointment comprising a crosslinking reagent, being genipin and/or proanthocyanidin, or gel or ointment application device for applying the crosslinking reagent; treated patch comprising a crosslinking reagent, being genipin and/or proanthocyanidin; minimally invasive device for application of crosslinking reagent, being genipin and/or proanthocyanidin via a treated patch, gel, ointment, time release capsule, or injectable. 18. A sterile reagent and application tray enclosed in packaging with a sterile inner surface, for improving the stabilization of invertebrate discs by increasing the bending stiffness of scoliotic spines comprising one or more of the following: container containing an effective amount of a crosslinking reagent, being genipin and/or proanthocyanidin, or container containing premeasured amount of a solvent for dissolving the crosslinking reagent; syringe with needle, or other means for in injecting a crosslinking reagent, being genipin and/or proanthocyanidin; time release capsule for releasing a crosslinking reagent, being genipin and/or proanthocyanidin; time release capsule insertion device for aiding in the delivery of a crosslinking reagent, being genipin	Orthopeutics LP, Lexington, KY 40511, US, 101224107	2019-10-09	2001-08-31

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			and/or proanthocyanidin; container of gel or ointment comprising a crosslinking reagent, being genipin and/or proanthocyanidin, or gel or ointment application device for applying the crosslinking reagent; treated patch comprising a crosslinking reagent, being genipin and/or proanthocyanidin; minimally invasive device for application of crosslinking reagent, being genipin and/or proanthocyanidin via a treated patch, gel, ointment, time release capsule, or injectable. 19. Use of an effective amount of a crosslinking reagent for manufacturing a medicament for increasing the permeability of the outer region of an intervertebral disc, the annulus fibrosus, wherein the fluid flux to and from the central region, or nucleus pulposus, of the intervertebral disc is improved, wherein at least a portion of a collagenous tissue within the disc is contacted with the crosslinking reagent, being genipin and/or proanthocyanidin. 20. Use of an effective amount of a crosslinking reagent for manufacturing a medicament for increasing the permeability of an intervertebral disc and increasing the fluid flux to the central region of the disc, wherein the flow of nutrients to cells within the central region of the disc is increased and the flow of cell waste products and degraded matrix molecules from the cells within the central region of the disc are increased, comprising contacting at least a portion of a collagenous tissue within the disc with the crosslinking reagent, being genipin and/or proanthocyanidin. 21. Use of an effective amount of a crosslinking reagent for manufacturing a medicament for increasing the biological viability of cells in the central region of the intervertebral disc, comprising contacting at least a portion of a collagenous tissue within the disc with the crosslinking reagent, being genipin and/or proanthocyanidin. 22. A device for increasing the permeability of the outer region of an intervertebral disc, the annulus fibrosus, wherein the fluid flux to and from the central region, or nucleus pulposus, of the intervertebral disc is improved, comprising: a crosslinking reagent, being genipin and/or proanthocyanidin. 23. A device for increasing the permeability of an intervertebral disc and increasing the fluid flux to the central region of the disc, wherein the flow of nutrients to cells within the central region of the disc is increased and the flow of cell waste products and degraded matrix molecules from the cells within the central region of the disc are increased, comprising: a crosslinking reagent, being genipin and/or proanthocyanidin. 24. A device for increasing the biological viability of cells in the central region of the intervertebral disc, comprising: a crosslinking reagent, being genipin and/or proanthocyanidin. 27. A sterile reagent and application tray enclosed in packaging with a sterile inner surface, for increasing the permeability of the outer region of an intervertebral disc, the annulus fibrosus, wherein the fluid flux to and from the central region, or nucleus pulposus, of the intervertebral disc is improved comprising one			

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			or more of the following: container containing an effective amount of a crosslinking reagent, being genipin and/or proanthocyanidin, or container containing premeasured amount of a solvent for dissolving the crosslinking reagent; syringe with needle, or other means for in injecting a crosslinking reagent, being genipin and/or proanthocyanidin time release capsule for releasing a crosslinking reagent, being genipin and/or proanthocyanidin; time release capsule insertion device for aiding in the delivery of a crosslinking reagent, being genipin and/or proanthocyanidin; container of gel or ointment comprising a crosslinking reagent, being genipin and/or proanthocyanidin, or gel or ointment application device for applying the crosslinking reagent; treated patch comprising a crosslinking reagent, being genipin and/or proanthocyanidin; minimally invasive device for application of crosslinking reagent, being genipin and/or proanthocyanidin via a treated patch, gel, ointment, time release capsule, or injectable. 28. A sterile reagent and application tray enclosed in packaging with a sterile inner surface, for increasing the permeability of an intervertebral disc and increasing the fluid flux to the central region of the disc, wherein the flow of nutrients to cells within the central region of the disc is increased and the flow of cell waste products and degraded matrix molecules from the cells within the central region of the disc are increased comprising one or more of the following: container containing an effective amount of a crosslinking reagent, being genipin and/or proanthocyanidin, or container containing premeasured amount of a solvent for dissolving the crosslinking reagent; syringe with needle, or other means for in injecting a crosslinking reagent, being genipin and/or proanthocyanidin; time release capsule for releasing a crosslinking reagent, being genipin and/or proanthocyanidin; time release capsule insertion device for aiding in the delivery of a crosslinking reagent, being genipin and/or proanthocyanidin; container of gel or ointment comprising a crosslinking reagent, being genipin and/or proanthocyanidin, or gel or ointment application device for applying the crosslinking reagent; treated patch comprising a crosslinking reagent, being genipin and/or proanthocyanidin; minimally invasive device for application of crosslinking reagent, being genipin and/or proanthocyanidin via a treated patch, gel, ointment, time release capsule, or injectable. 29. A sterile reagent and application tray enclosed in packaging with a sterile inner surface, for increasing the biological viability of cells in the central region of the intervertebral disc comprising one or more of the following: container containing an effective amount of a crosslinking reagent, being genipin and/or proanthocyanidin, or container containing premeasured amount of a solvent for dissolving the crosslinking reagent; syringe with needle, or other means for in injecting a crosslinking reagent, being genipin and/or proanthocyanidin; time release capsule for releasing a crosslinking reagent, being genipin and/or proanthocyanidin; time release capsule insertion device for aiding in the delivery of a crosslinking reagent; container of gel or ointment			

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			comprising a crosslinking reagent, being genipin and/or proanthocyanidin, or gel or ointment application device for applying the crosslinking reagent; treated patch comprising a crosslinking reagent, being genipin and/or proanthocyanidin; minimally invasive device for application of crosslinking reagent, being genipin and/or proanthocyanidin via a treated patch, gel, ointment, time release capsule, or injectable.			
EP2446903B1	Compositions for treating itch	The invention features a method for inhibiting one or more voltage-gated ion channels in a cell by contacting the cell with (i) a first compound that activates a channel-forming receptor that is present on nociceptors and/or pruriceptors; and (ii) a second compound that inhibits one or more voltage-gated ion channels when applied to the internal face of the channels but does not substantially inhibit said channels when applied to the external face of the channels, wherein the second compound is capable of entering nociceptors or pruriceptors through the channel-forming receptor when the receptor is activated. The invention also features a quarternary amine derivative or other permanently or transiently charged derivative of a compound that inhibits one or more voltage-gated ion channels when applied to the internal face of the channels but does not substantially inhibit said channels when applied to the external face of the channels.	1. A composition for use in treating itch in a patient comprising a compound selected from N-methyl lidocaine, N, N-dimethyl prilocaine, N, N, N-trimethyl tocainide, N-methyl etidocaine, N-methyl ropivacaine, N-methyl bupivacaine, N-methyl levobupivacaine, N-methyl mepivacaine, QX-314, and QX-222.	President and Fellows of Harvard College, Cambridge, MA 02138, US, 101121798 | The General Hospital Corporation, Boston, MA 02114, US, 101247849	2019-10-09	2006-11-20
EP2732819B1	Compounds that enhance Atoh-1 expression	This invention generally provides compounds, pharmaceutical compositions, and methods for their use, which include methods that result in increased expression in an Atoh1 gene (e.g., Hath1) in a biological cell. More specifically, the invention relates to the treatment of diseases and/or disorders that would benefit from increased Atoh1 expression, e.g. a hearing impairment or imbalance disorder associated with a loss of auditory hair cells, or a disorder associated with abnormal cellular proliferation.	1. A pharmaceutical composition for use in the treatment of a hearing impairment or imbalance disorder associated with loss of auditory hair cells in a subject in need of treatment, the composition comprising a compound of the following formula, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier: wherein: R 43 is C 6 -C 10 aryl or heteroaryl including 5-10 atoms, each of which is optionally substituted with from 1-5 R m ; R 44 is: (i) C 6 -C 10 aryl or heteroaryl including 5-10 atoms, each of which is optionally substituted with from 1-5 R m ; or (ii) -Z 4 -(C 1 -C 6 alkyl), wherein: Z 4 is a bond or NH; and the C 1 -C 6 alkyl is substituted with one of the following: (a) heterocyclyl including 5-6 atoms, which is optionally substituted with from 1-3 substituents independently selected from oxo and C 1 -C 6 alkyl; or (b) phenoxy, which is optionally substituted with from 1-5 R m ; and R m at each occurrence is, independently: (i) halo; NH 2 ; NH(C 1 -C 3 alkyl); N(C 1 -C 3 alkyl) 2 ; hydroxy; C 1 -C 6 alkoxy or C 1 -C 6 haloalkoxy; nitro; or cyano; or (ii) C 1 -C 6 alkyl or C 1 -C 6 haloalkyl. | 2. A pharmaceutical composition comprising a compound selected from: 5-((4-chloro-2-methylphenoxy)methyl)-3-(pyridin-4-yl)-1, 2, 4-oxadiazole; 5-(2-methoxyphenyl)-3-p-tolyl-1, 2, 4-oxadiazole; 5-(phenoxymethyl)-3-(pyridin-2-yl)-1, 2, 4-oxadiazole; 5-(2-chloro-4-methylphenyl)-3-(pyridin-3-yl)-1, 2, 4-oxadiazole; 3-(2-chlorophenyl)-5-p-tolyl-1, 2, 4-oxadiazole; 5-(piperidin-1-ylmethyl)-3-p-tolyl-1, 2, 4-oxadiazole; 5-(4-bromophenyl)-3-(pyridin-3-yl)-1, 2, 4-oxadiazole; 5-(2-bromophenyl)-3-(4-bromophenyl)-1, 2, 4-oxadiazole; 5-(2-bromo-5-methoxyphenyl)-3-(thiophen-2-yl)-1, 2, 4-oxadiazole; and 3-(2-	MASSACHUSETTS EYE & EAR INFIRMARY, Boston, MA 02114, US, 100173163 | The Brigham and Women's Hospital, Boston, MA 02115, US, 100235631	2019-10-16	2008-02-07

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			fluorophenyl)-N-(3-(piperidin-1-yl)propyl)-1, 2, 4-oxadiazol-5-amine; or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.			
EP2352494B1	NOVEL AND POTENT TAPENTADOL DOSAGE FORMS	The present invention provides a dosage form comprising at least one form of tapentadol, with or without a second analgesic, and at least one opioid antagonist, wherein tapentadol is present in an optimal or suboptimal amount and the said antagonist is present in an amount effective to improve the efficacy and or reduce the side effects of tapentadol. The present invention further provides a method of treating pain and pain related conditions by administering to a patient in need thereof, a dosage form comprising at least one form of tapentadol, with or without a second analgesic, and at least one opioid antagonist, wherein tapentadol is present in an optimal or suboptimal amount and the said antagonist is present in an amount effective to improve the efficacy and or reduce the side effects of tapentadol.	1. A slow release dosage form comprising at least one form of tapentadol selected from the group consisting of tapentadol base, optically active enantiomers of tapentadol, and pharmaceutically acceptable salts of tapentadol, and at least one opioid antagonist selected from the group consisting of naloxone and naltrexone and pharmaceutically acceptable salts thereof, wherein the antagonist improves the efficacy and/or reduces the side effects of tapentadol and wherein the said dosage form provides effective pain relief for at least 12 hours, when administered to a human patient.	Grünenthal GmbH, 52078 Aachen, DE, 100133822	2019-10-09	2008-10-30
EP2434886B1	INJECTABLE MELPHALAN COMPOSITIONS COMPRISING A CYCLODEXTRIN DERIVATIVE AND METHODS OF MAKING AND USING THE SAME	The present invention is directed to pharmaceutical compositions comprising melphalan and a cyclodextrin derivative, and methods of making and using the same. The present invention is directed to pharmaceutical compositions comprising melphalan and a cyclodextrin derivative, and methods of making and using the same.	1. A dilute pharmaceutical composition for use in a method of treating a subject suffering from a neoplastic disorder, by administering the dilute pharmaceutical composition by injection to the subject in need thereof, wherein the dilute pharmaceutical composition is prepared by diluting a composition with an aqueous diluent to provide a dilute pharmaceutical composition comprising 25 mg to 125 mg of melphalan and a cyclodextrin derivative of formula I: wherein n is 4, 5 or 6; wherein R 1 , R 2 , R 3 , R 4 , R 5 , R 6 , R 7 , R 8 and R 9 are independently a straight-chain or branched C 1 -C 8 -(alkylene)-SO 3 - group having an average degree of substitution of about 6.5 per cyclodextrin derivative, and the remaining substituents are -H; wherein the dilute pharmaceutical composition has a pH of 4 to 6; wherein the cyclodextrin derivative is present in a concentration of at least 50:1 (w/w) relative to the melphalan; wherein the melphalan in the dilute pharmaceutical composition degrades by 2% or less at 25° C within 5 hours after the diluting. 12. A pharmaceutical composition comprising: melphalan as a hydrochloride salt; an optional buffer; and a cyclodextrin derivative of formula I: wherein n is 4, 5 or 6; wherein R 1 , R 2 , R 3 , R 4 , R 5 , R 6 , R 7 , R 8 and R 9 are independently a straight-chain or branched C 1 -C 8 -(alkylene)-SO 3 - group having an average degree of substitution of about 6.5 per cyclodextrin derivative, and the remaining substituents are -H; wherein the pharmaceutical composition has a pH of 4 to 6, wherein dilution of the pharmaceutical composition with an aqueous solution provides a dilute pharmaceutical composition in which the melphalan degrades by 2% or less at about 25° C within 5 hours after the dilution; and wherein the pharmaceutical composition comprises 25 mg to 125 mg of melphalan salt and the cyclodextrin derivative is present in a ratio of 50:1 to 100:1 (w/w) relative to the melphalan. 19. A pharmaceutical kit comprising: a first container comprising melphalan as a hydrochloride salt and an optional water-	CyDex Pharmaceuticals Inc., San Diego, CA 92121, US, 101618229	2019-10-16	2009-05-29

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			soluble polymer; and a second container comprising an aqueous diluent, an optional buffer, and a cyclodextrin derivative of formula I: wherein n is 4, 5 or 6; wherein R 1 , R 2 , R 3 , R 4 , R 5 , R 6 , R 7 , R 8 and R 9 are independently a straight-chain or branched C 1 -C 8 -(alkylene)-SO 3 - group having an average degree of substitution of about 6.5 per cyclodextrin derivative, and the remaining substituents are -H; wherein combining the first container and the second container provides a dilute pharmaceutical composition having a pH of 4 to 6 that degrades by 2% or less at about 25° C within 5 hours after the diluting; and wherein the first container comprises 25 mg to 125 mg of melphalan as a hydrochloride salt and the cyclodextrin derivative is present in the second container in a concentration of at least 50:1 (w/w) relative to the melphalan; preferably wherein the first container comprises povidone in an amount of 10 mg to 30 mg, and the second container comprises a pH-adjusting agent in a concentration sufficient to provide a pH of 4 to 6 when the first container and the second container are combined.			
EP3075386B1	FORMULATIONS FOR LYSOSOMAL ENZYMES	The present invention provides improved formulations for lysosomal enzymes useful for enzyme replacement therapy. Among other things, the present invention provides formulations that preserve or enhance the stability and/or efficacy of a lysosomal enzyme such as acid alpha-glucosidase.	1. A kit comprising (a) a pharmaceutical formulation for treating Pompe disease comprising an acid alpha-glucosidase and a poloxamer and (b) instructions for reconstitution and/or using of the pharmaceutical formulation.	BioMarin Pharmaceutical Inc., Novato, CA 94949, US, 100087720	2019-10-16	2009-06-17
EP3449926B1	COMPOSITIONS AND METHODS FOR MODULATION OF SMN2 SPLICING IN A SUBJECT	Disclosed herein are compounds, compositions and methods for modulating splicing of SMN2 mRNA in a subject. Also provided are uses of disclosed compounds and compositions in the manufacture of a medicament for treatment of diseases and disorders, including spinal muscular atrophy.	1. A pharmaceutical composition for use in treating a human subject having spinal muscular atrophy (SMA), wherein the pharmaceutical composition is administered into the cerebrospinal fluid in the intrathecal space of the human subject and the pharmaceutical composition comprises (i) an antisense compound comprising an antisense oligonucleotide complementary to intron 7 of a pre-mRNA encoding human SMN2 and (ii) a pharmaceutically acceptable diluent or carrier, wherein the antisense oligonucleotide has a nucleobase sequence consisting of the nucleobase sequence of SEQ ID NO: 1, wherein each nucleoside of the antisense oligonucleotide comprises a modified sugar moiety, wherein each modified sugar moiety is a 2'-O-methoxyethyl sugar moiety and wherein each internucleoside linkage is a phosphorothioate linkage.	Biogen MA Inc., Cambridge, MA 02142, US, 101654068 | COLD SPRING HARBOR LABORATORY, Cold Spring Harbor, NY 11724, US, 100101644	2019-10-09	2009-06-17
EP2575789B1	DIVERSION-RESISTANT MICROGRANULES AND MICROTABLETS	The invention relates to the use of an oral dosage form based on microgranules and/or microtablets to reduce the abusive use of at least one active principle contained therein. The aim of the invention is to prevent the diversion of an oral dosage form based on microgranules and/or microtablets containing at least one active principle capable of causing a dependency, a gelling agent, and a gelling activator. The gelling agent and the activator are only brought into contact with each other in the event of diversion by crushing. Said judiciously selected pair of excipients confers a viscosity to the formulation, such that said formulation cannot be administered by injection or does not release the active principle rapidly by forming a gel when it comes into contact with the mucous membrane if nasally administered.	1. Oral dosage form based on microgranules and/or microtablets comprising two populations of microgranules or microtablets with the same external appearance, the first population comprising at least one active principle that could create a dependency and a gelling agent, and the second population, without active principle and gelling agent, comprising at least one gelling activator, wherein the gelling activator, in association with the gelling agent, enables the formation of bridges at certain sites of the polymeric chains of the gelling agent or/and enables the reinforcement of the polymeric network of the gelling agent.	Ethypharm, 92210 Saint-Cloud, FR, 101240231	2019-10-23	2010-06-07

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EP2612671B1	A CLINICAL PREPARATION OF SCUTELLARIN AND THE PREPARATION METHOD THEREOF	A clinical preparation of scutellarin and the preparation method thereof. The active agent contains the compound shown as formula (I). The amount of said active agent in the injection is 0.01~0.03 g/mL and the amount of said active agent in the lyophilized powder for injection is 4.7~41.3% by weight percent, calculated on the basis of scutellarin. The preparation method thereof does not need a buffer pair of organic acid and organic alkali to adjust stable pH value, while contains the steps that adding meglumine into the suspension of scutellarin and agitating, forming a clear solution, cooling to -2~1□ and being settled for more than 8 hours, filtrating through 0.45~0.8μm filter membrane, then being made into scutellarin clinical preparation by conventional procedures.	1. A clinical solution preparation of scutellarin, characterized in that it comprises active ingredients and water for injection, and the active ingredient comprises a compound shown in Formula (I) wherein the molar ratio between scutellarin and meglumine is 1.0 : 1.0, and the pH of the preparation is 6.5~6.7.	KPC Pharmaceuticals Inc., Kunming, Yunnan 650106, CN, 101607266	2019-10-09	2010-09-02
EP3020409B1	FREEZE-DRIED PREPARATION CONTAINING HIGH-PURITY PTH AND METHOD FOR PRODUCING SAME	[Problem] Provided is a freeze-dried preparation containing high-purity PTH peptide and a method for the production thereof. Also provided is a test method for PTH analogs to confirm the purity of a freeze-dried preparation containing PTH peptide, and the like. [Solution] In the present invention, the presence of PTH analogs produced during the manufacturing process of a freeze-dried preparation containing PTH peptide was confirmed. The production of these PTH analogs was also discovered to be markedly prevented or reduced by controlling exposure of the solution containing PTH peptide and the like to air environments within a pharmaceutical production facility.	1. A method for producing a freeze-dried preparation containing high-purity human PTH(1-34), the method comprising controlling the exposure of the solution containing human PTH (1-34) to ozone contained in air environments within a sterile injection production facility during one or more steps starting with the step of preparing a solution containing the human PTH (1-34) up to the end of the step for loading into the freeze-drying means, wherein "high purity" means both that the amount of a PTH analog versus the sum of the amount of human PTH(1-34) and the total amount of PTH analogs in the preparation is 1.0% or less and that the total amount of PTH analogs versus the sum of the amount of human PTH(1-34) and the total amount of PTH analogs is 5.0% or less, wherein the PTH analog is one or more of 1) to 11) as follows: 1) analog 1: oxide of PTH peptide having a mass number 64 Da larger than the mass number of the PTH peptide contained in the preparation and producing digestion products corresponding to the following fragments (1-a) to (1-c) when the analog is digested by trypsin, (1-a) Mass number of Ser-Val-Ser-Glu-Ile-Gln-Leu-Met-His-Asn-Leu-Gly-Lys (SEQ ID NO: 1) +16 Da, (1-b) Mass number of His-Leu-Asn-Ser-Met-Glu-Arg (SEQ ID NO: 2) +16 Da, and (1-c) Mass number of Val-Glu-Trp-Leu-Arg (SEQ ID NO: 3) +4 Da; 2) analog 2: oxide of PTH peptide having a mass number 36 Da larger than the mass number of the PTH peptide contained in the preparation and producing digestion products corresponding to the following fragments (2-a) to (2-c) when the analog is digested by trypsin, (2-a) Mass number of Ser-Val-Ser-Glu-Ile-Gln-Leu-Met-His-Asn-Leu-Gly-Lys (SEQ ID NO: 1) +16 Da, (2-b) Mass number of His-Leu-Asn-Ser-Met-Glu-Arg (SEQ ID NO: 2) +16 Da, and (2-c) Mass number of Val-Glu-Trp-Leu-Arg (SEQ ID NO: 3) +4 Da; 3) analog 3: oxide of PTH peptide having a mass number 32 Da larger than the mass number of the PTH peptide contained in the preparation and producing digestion products corresponding to the following fragments (3-a) and (3-b) when the analog is digested by trypsin, (3-a) Mass number of Ser-Val-Ser-Glu-Ile-Gln-Leu-Met-His-Asn-Leu-Gly-Lys (SEQ ID NO: 1) +16 Da, (3-b) Mass number of His-Leu-Asn-Ser-Met-Glu-Arg (SEQ ID NO: 2) +16 Da; 4) analog 4: oxide of PTH peptide having a mass number 48 Da larger	Asahi Kasei Pharma Corporation, Chiyoda-ku, Tokyo 100-0006, JP, 101833984	2019-10-09	2011-06-07

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			than the mass number of the PTH peptide contained in the preparation and producing digestion products corresponding to the following fragments (4-a) and (4-b) when the analog is digested by trypsin, (4-a) Mass number of Ser-Val-Ser-Glu-Ile-Gln-Leu-Met-His-Asn-Leu-Gly-Lys (SEQ ID NO: 1) +16 Da, (4-b) Mass number of Val-Glu-Trp-Leu-Arg (SEQ ID NO: 3) +4 Da; 5) analog 5: oxide of PTH peptide having a mass number 48 Da larger than the mass number of the PTH peptide contained in the preparation and producing digestion products corresponding to the following fragments (5-a) and (5-b) when the analog is digested by trypsin, (5-a) Mass number of His-Leu-Asn-Ser-Met-Glu-Arg (SEQ ID NO: 2) +16 Da, and (5-b) Mass number of Val-Glu-Trp-Leu-Arg (SEQ ID NO: 3) +4 Da; 6) analog 6: oxide of PTH peptide having a mass number 20 Da larger than the mass number of the PTH peptide contained in the preparation and producing digestion products corresponding to the following fragments (6-a) and (6-b) when the analog is digested by trypsin, (6-a) Mass number of His-Leu-Asn-Ser-Met-Glu-Arg (SEQ ID NO: 2) +16 Da, and (6-b) Mass number of Val-Glu-Trp-Leu-Arg (SEQ ID NO: 3) +4 Da; 7) analog 7: oxide of PTH peptide having a mass number 16 Da larger than the mass number of the PTH peptide contained in the preparation and producing a digestion product corresponding to the following fragment (7-a) when the analog is digested by trypsin, (7-a) Mass number of Ser-Val-Ser-Glu-Ile-Gln-Leu-Met-His-Asn-Leu-Gly-Lys (SEQ ID NO: 1) +16 Da; 8) analog 8: oxide of PTH peptide having a mass number 16 Da larger than the mass number of the PTH peptide contained in the preparation and producing a digestion product corresponding to the following fragment (8-a) when the analog is digested by trypsin, (8-a) Mass number of His-Leu-Asn-Ser-Met-Glu-Arg (SEQ ID NO: 2) +16 Da; 9) analog 9: oxide of PTH peptide having a mass number 32 Da larger than the mass number of the PTH peptide contained in the preparation and producing a digestion product corresponding to the following fragment (9-a) when the analog is digested by trypsin, (9-a) Mass number of Val-Glu-Trp-Leu-Arg (SEQ ID NO: 3) +4 Da; 10) analog 10: oxide of PTH peptide having a mass number 16 Da larger than the mass number of the PTH peptide contained in the preparation and producing a digestion product corresponding to the following fragment (10-a) when the analog is digested by trypsin, (10-a) Mass number of Val-Glu-Trp-Leu-Arg (SEQ ID NO: 3) +16 Da; or 11) analog 11: oxide of PTH peptide having a mass number 4 Da larger than the mass number of the PTH peptide contained in the preparation and producing a digestion product corresponding to the following fragment (11-a) when the analog is digested by trypsin, (11-a) Mass number of Val-Glu-Trp-Leu-Arg (SEQ ID NO: 3) +4 Da, wherein, the PTH analog is one detected as a peak different from the PTH peptide which is the active ingredient on the chromatogram when a sample from a freeze-dried preparation containing PTH peptide is subjected to HPLC.			

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EP2717914B1	SUSTAINED RELEASE FORMULATIONS FOR DELIVERY OF PROTEINS TO THE EYE AND METHODS OF PREPARING SAME	The present invention provides for injectable pharmaceutical sustained release formulations for delivery of active agents, particularly therapeutic proteins, to the eye. The formulations are biocompatible, biodegradable sustained release formulations comprising low- solubility liquid excipients and relatively small amounts (less than about 10%) of biocompatible, biodegradable polymer such as PLA or PLGA polymers. A unit dose of 5 µL to 100 µL of the formulation provides for sustained release of the agent for at least 14 days.	1. A liquid pharmaceutical formulation for injection into the eye for the sustained release of a therapeutic protein comprising: a therapeutic protein; a liquid, biodegradable, biocompatible non-polymeric excipient selected from the group consisting of triethyl citrate and acetyl triethyl citrate; and a biodegradable, biocompatible poly(D, L-lactide-co-glycolide) (PLGA) polymer, wherein the PLGA polymer has a lactide:glycolide ratio of 50:50, MW range 7, 000-17, 000, and an alkyl ester end group; wherein the ratio of non-polymeric excipient:polymer is 90:10 to 99:1 wt%, inclusive; wherein upon and following injection of 5 µl to 100 µl, inclusive, of the formulation through a 25, 27, 28, 30 gauge, or smaller, needle, the formulation maintains its monolithic integrity and liquid state; and wherein the formulation releases the therapeutic protein for a period of at least 14 days. | 5. A liquid pharmaceutical formulation for injection into the eye for the sustained release of a therapeutic protein comprising: a therapeutic protein; a liquid, biodegradable, biocompatible non-polymeric excipient, wherein said excipient is benzyl benzoate; and a biodegradable, biocompatible poly(D, L-lactide-co-glycolide) (PLGA) polymer, wherein the PLGA polymer has a lactide:glycolide ratio of 50:50, MW range 7, 000-17, 000, and an alkyl ester end group; wherein the ratio of non-polymeric excipient:polymer is 90:10 to 99:1 wt%, inclusive; wherein upon and following injection of 5 µl to 100 µl, inclusive, of the formulation through a 25, 27, 28, 30 gauge, or smaller, needle, the formulation maintains its monolithic integrity and liquid state; and wherein the formulation releases the therapeutic protein for a period of at least 14 days.	Ramscor Inc., Menlo Park, California 94025, US, 100798958 | Icon Bioscience Inc., Watertown, MA 02472, US, 101797384	2019-10-30	2011-06-10
EP2790733B1	NANOPARTICLES WITH ENHANCED MUCOSAL PENETRATION OR DECREASED INFLAMMATION	Nanoparticles formed by emulsion of one or more core polymers, one or more surface altering materials, and one or more low molecular weight emulsifiers have been developed. The particles are made by dissolving the one or more core polymers in an organic solvent, adding the solution of the one or more core polymers to an aqueous solution or suspension of the emulsifier to form an emulsion, and then adding the emulsion to a second solution or suspension of the emulsifier to effect formation of the nanoparticles. In the preferred embodiment, the molecular weight of the emulsifiers is less than 1500, 1300, 1200, 1000, 800, 600, or 500 amu. Preferred emulsifiers include cholic acid sodium salt, dioctyl sulfosuccinate sodium, hexadecyltrimethyl ammonium bromide, saponin, TWEEN® 20, TWEEN® 80, and sugar esters. The surface altering materials are present in an amount effective to make the surface charge of the particles neutral or essentially neutral when the one or more emulsifiers are charged. The emulsifiers have an emulsification capacity of at least about 50%, preferably at least 55, 60, 65, 70, 75, 80, 85, 90, or 95%.	1. Nanoparticles formed by emulsion of one or more core polymers, one or more surface altering materials, and one or more low molecular weight emulsifiers having a molecular weight less than 1500 amu, wherein the one or more surface altering materials are selected from the group consisting of polyethylene glycol (PEG) and poloxamer, or wherein the particles are formed from block copolymers containing PEG, wherein the nanoparticle possess a ζ-potential of between 10 mV and -10 mV when dispersed in 10 mM NaCl solution at pH 7; wherein the nanoparticles further comprise one or more therapeutic, prophylactic, or diagnostic agents, and wherein the nanoparticles penetrate cervicovaginal mucus (CVM) with effective speeds less than 25-fold slower than the same particles in water.	The Johns Hopkins University, Baltimore, MD 21218, US, 101243348	2019-10-30	2011-12-14
EP2806877B1	NEUROACTIVE STEROID FORMULATIONS COMPRISING A COMPLEX OF	Formulations of comprising a neuroactive steroid, e.g., allopregnanolone; and optionally a cyclodextrin, e.g., a β-cyclodextrin, e.g., a sulfo butyl ether β- cyclodextrin, e.g., a β-cyclodextrin, e.g.,	1. An aqueous pharmaceutical composition formulated for parenteral administration comprising a complex comprising allopregnanolone and sulfobutyl ether β-cyclodextrin, wherein the	Sage Therapeutics Inc., Cambridge,	2019-10-09	2012-01-23

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	ALLOPREGNANOLONE AND SULFOBUTYL ETHER BETA-CYCLODEXTRIN	a sulfo butyl ether β-cyclodextrin, e.g., CAPTISOL®; and methods of use in treating CNS disorders.	allopregnanolone is at a concentration of 5 mg/ml and the sulfobutyl ether β-cyclodextrin is at a concentration between 25-400 mg/mL, wherein the formulation is buffered to a pH of 6 and the buffer is a citrate buffer.	MA 02142, US, 101378120		
EP3257526B1	TREATMENT OF MIGRAINE HEADACHES WITH PRESYNAPTIC NEUROTOXIN	The present invention provides a method for treating a patient for migraine headache, including symptoms associated with migraine headache, such as migraine associated vertigo, which comprises administering to the patient a therapeutically effective amount of an invertebrate presynaptic neurotoxin, e.g. Botulinum toxin in a pharmaceutically safe form.	1. A Botulinum toxin in a pharmaceutically safe form for use in the treatment of a migraine-associated vertigo.	Binder William J., Beverly Hills, CA 90212, US, 101411011	2019-10-16	2012-03-12
EP2832349B1	LACTATE-BASED FULVESTRANT OR FULVESTRANT DERIVATIVE OILY PREPARATION AND PREPARATION METHOD THEREOF	Fulvestrant or fulvestrant derivative oily preparation and preparation method thereof. The oily preparation comprises: fulvestrant or a fulvestrant derivative, the content being 10mg/ml to 170 mg/ml; a lactate compound, the content being 5% to 80% of the total weight of the preparation; vegetable oil or artificially-synthetic oil (grease) ester; a pain-killer; and an optional antioxidant.	1. An oily formulation of fulvestrant or derivatives thereof, characterized in that , the formulation comprises per ml: (a) fulvestrant or derivatives thereof, 10 to 170 mg; (b) ethyl lactate, 0.05 to 0.50 ml; (c) an analgesic, 3 to 5 mg/30 to 50 μl; and (d) a dispersant, balanced to 1 ml, the dispersant being selected from: 1) one, or a mixture of two or more of castor oil, polyoxyethylene castor oil (35, 40), hydrogenated castor oil and sulfonated castor oil at any ratio; 2) a mixture of one, or a mixture of two or more of castor oil, polyoxyethylene castor oil (35, 40), hydrogenated castor oil and sulfonated castor oil with one, two or more of other oils (esters) (purified for injection) at any ratio, wherein said other oils (esters) are glycerol triacetate, ethyl oleate, benzyl benzoate, soybean oil, sesame oil, corn oil, olive oil; wherein said fulvestrant or derivatives thereof has the following structure: wherein 1) both of R 1 and R 2 are -OH; 2) one of R 1 and R 2 is -H, and the other one should be -OH; and one, or a mixture of two or more of fulvestrant or derivatives thereof may be used in the formulation.	Xi'an Libang Pharmaceutical Co. Ltd., Shaanxi Province 710075, CN, 101836899	2019-10-02	2012-03-31
EP2900244B1	TAZOBACTAM ARGININE ANTIBIOTIC COMPOSITIONS	This disclosure provides compositions comprising a beta- lactam compound and crystalline tazobactam arginine, and related methods and uses of these compositions.	1. A pharmaceutical composition comprising crystalline tazobactam arginine and a beta-lactam compound which is (6R, 7R)-3-[(5-amino-4-{[(2-aminoethyl)carbamoyl]amino}-1-methyl-1H-pyrazol-2-ium-2-yl)methyl]-7-({(2Z)-2-(5-amino-1, 2, 4-thiadiazol-3-yl)-2-[(1-carboxy-1-methylethoxy)imino]acetyl}amino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate or a pharmaceutically acceptable salt thereof. 2. A method of making a pharmaceutical composition comprising combining crystalline tazobactam arginine and a beta-lactam compound which is (6R, 7R)-3-[(5-amino-4-{[(2-aminoethyl)carbamoyl]amino}-1-methyl-1H-pyrazol-2-ium-2-yl)methyl]-7-({(2Z)-2-(5-amino-1, 2, 4-thiadiazol-3-yl)-2-[(1-carboxy-1-methylethoxy)imino]acetyl}amino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate or a pharmaceutically acceptable salt thereof. 12. Crystalline tazobactam arginine and a beta-lactam compound which is (6R, 7R)-3-[(5-amino-4-{[(2-aminoethyl)carbamoyl]amino}-1-methyl-1H-pyrazol-2-ium-2-yl)methyl]-7-({(2Z)-2-(5-amino-1, 2, 4-thiadiazol-3-yl)-2-[(1-carboxy-1-methylethoxy)imino]acetyl}amino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate or a pharmaceutically	Merck Sharp & Dohme Corp., Rahway, NJ 07065, US, 101373466	2019-10-23	2012-09-27

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			acceptable salt thereof for use in a method of treating a bacterial infection in a mammal. 13. Crystalline tazobactam arginine for use in a method of treating a bacterial infection in a mammal, comprising administration of crystalline tazobactam arginine in combination with a beta-lactam compound which is (6R, 7R)-3-[(5-amino-4-{[(2-aminoethyl)carbamoyl]amino}-1-methyl-1H-pyrazol-2-ium-2-yl)methyl]-7-({(2Z)-2-(5-amino-1, 2, 4-thiadiazol-3-yl)-2-[(1-carboxy-1-methylethoxy)imino]acetyl}amino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate or a pharmaceutically acceptable salt thereof. 14. A beta-lactam compound for use in a method of treating a bacterial infection in a mammal, comprising administration of a beta-lactam compound which is (6R, 7R)-3-[(5-amino-4-{[(2-aminoethyl)carbamoyl]amino}-1-methyl-1H-pyrazol-2-ium-2-yl)methyl]-7-({(2Z)-2-(5-amino-1, 2, 4-thiadiazol-3-yl)-2-[(1-carboxy-1-methylethoxy)imino]acetyl}amino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate or a pharmaceutically acceptable salt thereof in combination with crystalline tazobactam arginine. 15. Crystalline tazobactam arginine and a beta-lactam compound which is (6R, 7R)-3-[(5-amino-4-{[(2-aminoethyl)carbamoyl]amino}-1-methyl-1H-pyrazol-2-ium-2-yl)methyl]-7-({(2Z)-2-(5-amino-1, 2, 4-thiadiazol-3-yl)-2-[(1-carboxy-1-methylethoxy)imino]acetyl}amino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate or a pharmaceutically acceptable salt thereof as a combined preparation for simultaneous, separate or sequential use in a method of treating a bacterial infection in a mammal.			
EP2958572B1	TREATMENT OF HYPERHIDROSIS	The present invention relates to a composition for reducing sweating in humans, characterized in that said composition comprises a compound capable of reduction of ITPR2 protein function and reduction of levels of ITPR2mRNA and/or ITPR2 protein, and optionally pharmaceutically acceptable carriers and/or excipients, as well as to methods of treatment and specific siRNA molecules and their use in therapy.	1. A composition comprising a nucleic acid molecule that targets ITPR2 mRNA, or a chemically modified derivative thereof, and optionally pharmaceutically acceptable carriers and/or excipients for use in treating hyperhidrosis.	Hidros Therapeutics International AB, 75108 Uppsala, SE, 101552002	2019-10-23	2013-01-03
EP2953667B1	NEEDLE ASSISTED JET INJECTION DEVICE HAVING REDUCED TRIGGER FORCE	An injector includes a trigger mechanism including: a trigger member disposed about an axis having an aperture and a protrusion, and a ram assembly having a ram configured to pressurize a medicament container for expelling a medicament therefrom, the ram assembly further having a trigger engagement member configured to engage the aperture of the trigger member when the trigger member is in a pre-firing condition; an energy source associated with the ram for powering the ram to expel the medicament; and a user-operable firing-initiation member having an aperture engaged with the protrusion of the trigger member and operable for causing an axial translation of the trigger member in a proximal direction from the pre-firing condition to a firing condition in which the trigger engagement	1. An injector (100), comprising: a trigger mechanism including: a trigger member (1400) disposed about an axis (170), the trigger member (1400) having a trigger member opening (1408) and a trigger member protrusion (1406), and a ram assembly (122) having a ram (1232) configured to pressurize a medicament container (110) for expelling a medicament therefrom, the ram assembly (122) further having a trigger engagement member (1230); an energy source (120) associated with the ram (1232) for powering the ram (1232) to expel the medicament; a user-operable guard (1500) including a firing-initiation member (1504), the user-operable guard having a guard aperture (1508) engaged with the trigger member protrusion (1406) and operable for causing an axial translation of the trigger member (1400) in a proximal direction from a pre-firing condition to a firing	Antares Pharma Inc., Ewing, NJ 08628, US, 101612936	2019-10-23	2013-02-11

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		member is released from the retaining portion to allow the energy source to fire the ram.	condition in which the trigger engagement member (1230) is disengaged from the trigger member opening (1408) to allow the energy source (120) to fire the ram (1232); and an end cap (104); characterized in that the trigger engagement member (1230) is configured to engage the trigger member opening (1408) when the trigger member (1400) is in the pre-firing condition, wherein said end cap (104) comprises a ram holding member (1042) that engages the trigger engagement member (1230) to axially retain the ram assembly (122) in a proximal position against action of the energy source (120) in the pre-firing position.			
EP2967066B1	COMPOSITIONS, FORMULATIONS AND METHODS FOR TREATING OCULAR DISEASES	Disclosed herein are compounds effective for activation of Tie-2 and inhibition of HPTP-beta. The compounds can provide effective therapy for conditions associated with angiogenesis, for example, ocular conditions. Formulations for increased solubility are disclosed. Combination therapy with antibodies and PK/PD data are also disclosed.	1. A pharmaceutical composition comprising a compound that activates Tie-2 and 2-hydroxypropyl-beta cyclodextrin, for use in treating a condition, wherein the compound that activates Tie-2 is a compound of the formula: or a pharmaceutically-acceptable salt, or zwitterion thereof	Aerpio Therapeutics Inc., Cincinnati, OH 45242, US, 101411451	2019-10-23	2013-03-15
EP2994120B1	ALPHA ADRENERGIC AGONISTS FOR THE TREATMENT OF TISSUE TRAUMA	The present invention provides a method of treating tissue trauma (such as damage from radiation (such as solar and ultraviolet radiation), wounds, bruising, burns, blisters, excoriations, incisions, excisions, and ulcers) in a subject, comprising topically administering to the tissue area of the subject affected by said trauma a composition comprising a therapeutically effective amount of at least one alpha adrenergic agonist (such as oxymetazoline hydrochloride). The present invention also provides a method for alleviating the pain or discomfort associated with aesthetic or plastic surgery or cosmetology procedures in a subject comprising administering said alpha adrenergic agonist.	1. A composition comprising a therapeutically effective amount of at least one alpha adrenergic agonist, for use in a method of treating tissue trauma in a subject, the method comprising topically administering said composition to the tissue area of the subject affected by said trauma , wherein the tissue trauma is a burn that is severe enough to result in subsequent tissue damage characterized by at least one condition selected from the group consisting of epidermal necrosis, separation of the epidermis from the dermis and adaptive healing response, wherein the adaptive healing response is selected from epidermal proliferation and hyperplasia, wherein the alpha adrenergic agonist comprises a compound with an imidazoline structure, wherein the compound with the imidazoline structure is selected from the group consisting of oxymetazoline, xylometazoline, naphazoline, mivazerol and dexmedetomidine; or a pharmaceutically acceptable salt thereof.	ALLERGAN INC., Irvine, CA 92612, US, 100074706	2019-10-09	2013-05-06
EP2996713B1	COMPOSITIONS AND METHODS FOR TREATING POST-OPERATIVE COMPLICATIONS OF CARDIO-PULMONARY SURGERY	Disclosed herein are compositions and methods for treating damage inflicted by use of a cardio-pulmonary bypass (CPB) machine, particularly excessive bleeding and multi organ failure, by administering a pharmaceutical composition comprising alpha-1 antitrypsin (AAT).	1. A composition comprising a therapeutically effective amount of alpha-1 antitrypsin (AAT-1) for use in preventing organ injury or preventing excessive postoperative bleeding resulting from cardiac surgery, wherein the composition is administered to a subject before the cardiac surgery.	Mor Research Applications Ltd., 6971054 Tel Aviv, IL, 101491887	2019-10-02	2013-05-15
EP3030262B1	COMBINED PHARMACEUTICAL COMPOSITION	The present disclosure relates to a combined pharmaceutical composition, adapted for simultaneous, separate, or sequential administration for treating cancer in a subject comprising (a) a conjugate comprising (i) a polypeptide comprising the amino acid sequence of interleukin 15 or derivatives thereof, and ii) a polypeptide comprising the amino acid sequence of the sushi domain of IL-15Ra or derivatives thereof; a polynucleotide coding therefore, or a vector comprising such a polynucleotide; and (b) an antibody antagonizing an immune pathway implicated in the inhibition of T cell activation, or a fragment thereof, a	1. A combined pharmaceutical composition comprising: a) a conjugate comprising (i) a polypeptide comprising the amino acid sequence of interleukin 15 or derivatives thereof having at least 10% of the activity of human IL-15 on the proliferation induction of kit225 cell line, and (ii) a polypeptide comprising the amino acid sequence of the sushi domain of IL-15Rα or derivatives thereof having at least 10% of the binding activity of the sushi domain of human IL-15Rα to human IL-15, a polynucleotide coding therefore, or a vector comprising such a polynucleotide; and b) an antibody antagonizing an immune pathway implicated in the inhibition of T cell activation, or a fragment thereof	Cytune Pharma, 44100 Nantes, FR, 101547520 | Institut Gustave Roussy (IGR), 94805 Villejuif Cedex, FR, 100147103	2019-10-09	2013-08-08

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		polynucleotide coding therefore, or a vector comprising such a polynucleotide.	capable of reacting with the same antigen than its antibody counterpart, a polynucleotide coding therefore, or a vector comprising such a polynucleotide, wherein said antibody is a PD-1/PD-L1/PD-L2 antagonist, wherein said antibody is antagonizing either by binding the PD-1 receptor or by binding the PD-L1 or PD-L2 ligand; wherein said conjugate and the antibody or fragment thereof are not linked. 2. A pharmaceutical composition for use in treating cancer in a subject comprising (A) a conjugate comprising (i) a polypeptide comprising the amino acid sequence of interleukin 15 or derivatives thereof having at least 10% of the activity of human IL-15 on the proliferation induction of kit225 cell line, and (ii) a polypeptide comprising the amino acid sequence of the sushi domain of IL-15Rα or derivatives thereof having at least 10% of the binding activity of the sushi domain of human IL-15Rα to human IL-15, a polynucleotide coding therefore, or a vector comprising such a polynucleotide, wherein the use comprises simultaneously, separately, or sequentially administering (a) said pharmaceutical composition and (b) an antibody antagonizing an immune pathway implicated in the inhibition of T cell activation, or a fragment thereof which is capable of reacting with the same antigen than its antibody counterpart, a polynucleotide coding therefore, or a vector comprising such a polynucleotide, or (B) an antibody antagonizing an immune pathway implicated in the inhibition of T cell activation, or a fragment thereof which is capable of reacting with the same antigen than its antibody counterpart, a polynucleotide coding therefore, or a vector comprising such a polynucleotide, wherein the use comprises simultaneously, separately, or sequentially administering (a) said pharmaceutical composition and (b) a conjugate comprising (i) a polypeptide comprising the amino acid sequence of interleukin 15 or derivatives thereof having at least 10% of the activity of human IL-15 on the proliferation induction of kit225 cell line, and (ii) a polypeptide comprising the amino acid sequence of the sushi domain of IL-15Rα or derivatives thereof having at least 10% of the binding activity of the sushi domain of human IL-15Rα to human IL-15, a polynucleotide coding therefore, or a vector comprising such a polynucleotide, and wherein said antibody is a PD-1/PD-L1/PD-L2 antagonist, wherein said antibody is antagonizing either by binding the PD-1 receptor or by binding the PD-L1 or PD-L2 ligand. | 9. The pharmaceutical composition for use in treating cancer or the combined pharmaceutical composition of any one claims 1 to 8, wherein the polypeptides (i) and (ii) of the conjugate are covalently linked in a fusion protein.			
EP3035974B1	IMPLANTABLE MESHES FOR CONTROLLING THE MOVEMENT OF FLUIDS	Meshes for use to control the movement of bodily fluids, such as blood, are described herein. The mesh can be partially or completely biodegradable or non-biodegradable. In one embodiment, the mesh is formed from one or more self-assembling peptides. The peptides can be in the form of fibers, such as nanofibers. The peptides can be assembled prior to formation of the mesh or after the mesh has been formed but before it is applied.	1. A surgical mesh that is dried, consisting of woven or non-woven fibers of self-assembling peptides, wherein the self-assembling peptides comprise from 6 to 200 amino acid residues conforming to one or more of Formulas I-IV: ((Xaa neu -Xaa +) x (Xaa neu -Xaa -) y) n (I); ((Xaa neu -Xaa -) x (Xaa neu -Xaa +) y) n (II); ((Xaa + -Xaa neu) x (Xaa - -Xaa neu) y) n (III);	Arch Biosurgery Inc., Cambridge, Massachusetts 02142, US, 101511586	2019-10-09	2013-08-22

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		Alternatively, the mesh can be prepared from unassembled peptides, which assemble at the time of application. The peptides can assemble upon contact with bodily fluids (e.g., blood) or can be contacted with an ionic solution to initiate assembly.	((Xaa - -Xaa neu) x (Xaa + -Xaa neu) y) n (IV); wherein Xaa neu represents an amino acid residue having a neutral charge under physiological conditions; Xaa + represents an amino acid residue having a positive charge under physiological conditions; Xaa - represents an amino acid residue having a negative charge under physiological conditions; x and y are integers having a value of 1, 2, 3, or 4, independently; and n is an integer having a value of 1-5.			
EP3054957B1	HEMATOCRIT MODULATION THROUGH NEEDLE ASSISTED JET INJECTION OF TESTOSTERONE	The present invention provides compositions and methods for treating a subject in need of treatment with testosterone, including introducing testosterone into the subject subcutaneously, intradermally, or intramuscularly, from a needle assisted jet injection device.	1. Testosterone or a pharmaceutically acceptable ester or salt thereof for use in a method of treating hypogonadism, reduced fertility, lack of libido or erectile dysfunction, osteoporosis or anemia in a subject, wherein the subject is susceptible to a change in his or her hematocrit blood levels in response to a change in testosterone blood levels and the method involves modulating or controlling the level of hematocrit in the subject, wherein the method comprises subcutaneously administering to the subject testosterone or a pharmaceutically acceptable ester or salt thereof, such that the maximum concentration of the testosterone or the pharmaceutically acceptable ester or salt thereof in the blood (serum or plasma) of the subject, following administration of a dose of the testosterone or of the pharmaceutically acceptable ester or salt thereof to the subject ("C max "), is maintained at a value from about 300 ng/dl to about 1800 ng/dl, and wherein the level of hematocrit produced in the subject following the subcutaneous administration of the dose of the testosterone or the pharmaceutically acceptable ester or salt thereof does not exceed 70%.	Antares Pharma Inc., Ewing, NJ 08628, US, 101506393	2019-10-02	2013-10-07
EP3079725B1	DELIVERY, USE AND THERAPEUTIC APPLICATIONS OF THE CRISPR-CAS SYSTEMS AND COMPOSITIONS FOR GENOME EDITING	The invention provides for delivery, engineering and optimization of systems, methods, and compositions for manipulation of sequences and/or activities of target sequences. Provided are delivery systems and tissues or organ which are targeted as sites for delivery. Also provided are vectors and vector systems some of which encode one or more components of a CRISPR complex, as well as methods for the design and use of such vectors. Also provided are methods of directing CRISPR complex formation in eukaryotic cells to ensure enhanced specificity for target recognition and avoidance of toxicity and to edit or modify a target site in a genomic locus of interest to alter or improve the status of a disease or a condition.	1. A composition comprising a CRISPR-Cas system for use in treating an ocular genetic disease by localized administration to a subject's eye, wherein the CRISPR-Cas system comprises: A. a polynucleotide encoding a CRISPR-Cas system RNA comprising: a) a guide sequence capable of hybridizing to an ocular genetic disease target sequence, b) a tracr mate sequence, and c) a tracr sequence wherein (a), (b) and (c) are arranged in a 5' to 3' orientation; and B. a polynucleotide encoding a Cas9; each of A and B are: formulated for delivery together in a delivery vehicle, the vehicle being an adeno-associated viral (AAV) vector, wherein the AAV is AAV1, AAV2 or AAV5; and capable, when administered together to the subject's eye, of forming a CRISPR-Cas complex comprising the Cas9, and the CRISPR-Cas system RNA.	The Broad Institute Inc., Cambridge, MA 02142, US, 101486043 | Massachusetts Institute of Technology, Cambridge, MA 02142, US, 101500173	2019-10-16	2013-12-12
EP3129001B1	HSP-FREE ALLERGEN PREPARATION	A pharmaceutical preparation comprising -10 to 200µg/ml of fragments of an antigenic structure which induces allergic reaction - 2 to 6% (w/v) mannitol - 0.5to2% (w/v) trehalose - water, wherein said preparation essentially does not comprise heat shock proteins.	1. A pharmaceutical preparation comprising - 10 to 200 µg/ml of fragments of an antigenic structure which induces allergic reaction - 2 to 6% (w/v) mannitol - 0.5 to 2% (w/v) trehalose - water, wherein the amount of heat shock proteins is less than 1 ng/ml, wherein the fragments of an antigenic structure are hydrolyzed allergens prepared by enzymatic hydrolysis of the antigenic structure, and wherein at least 70% by weight of the fragments are between 1, 000 and 10, 000 Da.	ASIT BioTech S.A., 1200 Bruxelles, BE, 101605099	2019-10-02	2014-04-10

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EP3191097B1	COMBINATION THERAPIES	Disclosed is a combination comprising an immunomodulator and a second therapeutic agent for use in treating cancer, wherein the immunomodulator is an inhibitor of an immune checkpoint molecule or an activator of a costimulatory molecule, or a combination thereof; and the second therapeutic agent is chosen from one or more of: 1) a c-MET inhibitor; 2) a CDK4/6 inhibitor; 3) a PI3K inhibitor; 4) a BRAF inhibitor; 5) an FGFR inhibitor; 6) a MEK inhibitor, or 7) a BCR-ABL inhibitor. The combination therapies can be used to treat or prevent cancerous conditions and/or disorders.	1. A combination comprising Nivolumab and a c-Met inhibitor for use in treating a cancer in a subject, wherein the c-MET inhibitor has the structure: wherein: L 1 is (CR 4 R 5) m , wherein R 4 and R 5 are independently H and m is 1; Cy 1 is heteroaryl; R 1 is H; R 2 is H; L 2 is (CR 7 R 8) r , wherein r is 0; and Cy 2 is aryl substituted with 2 W'-X'-Y'-Z'; R 7 and R 8 are independently selected from H, halo, OH, C 1-6 alkyl, C 2-6 alkenyl, C 2-6 alkynyl, C 1-6 alkoxy, C 1-6 haloalkyl, CN, and NO 2 ; or R 7 and R 8 together with the C atom to which they are attached form a 3, 4, 5, 6, or 7 - membered cycloalkyl or heterocycloalkyl ring, each optionally substituted by 1, 2, or 3 substituent independently selected from halo, OH, C 1-6 alkyl, C 2-6 alkenyl, C 2-6 alkynyl, C 1-6 alkoxy, C 1-6 haloalkyl, CN, and NO 2 ; W' is independently absent or independently selected from C 1-6 alkylene, C 2-6 alkenylene, C 2-6 alkynylene, O, S, NR h , CO, COO, CONR h , SO, SO 2 , SONR h and NR h CONR i , wherein each of the C 1-6 alkylene, C 2-6 alkenylene, and C 2-6 alkynylene is optionally substituted by 1, 2 or 3 substituents independently selected from halo, C 1-6 alkyl, C 1-6 haloalkyl, OH, C 1-6 alkoxy, C 1-6 haloalkoxy, amino, C 1-6 alkylamino, and C 2-8 dialkylamino; X'is independently absent or independently selected from C 1-6 alkylene, C 2-6 alkenylene, C 2-6 alkynylene, arylene, cycloalkylene, heteroarylene, and heterocycloalkylene, wherein each of the C 1-6 alkylene, C 2-6 alkenylene, C 2-6 alkynylene, arylene, cycloalkylene, heteroarylene, and heterocycloalkylene is optionally substituted by 1, 2 or 3 substituents independently selected from halo, CN, NO 2 , OH, C 1-6 alkyl, C 1-6 haloalkyl, C 2-8 alkoxyalkyl, C 1-6 alkoxy, C 1-6 haloalkoxy, C 2-8 alkoxyalkoxy, cycloalkyl, heterocycloalkyl, C(O)OR j , C(O)NR h R i , amino, C 1-6 alkylamino, and C 2-8 dialkylamino; Y' is independently absent or independently selected from C 1-6 alkylene, C 2-6 alkenylene, C 2-6 alkynylene, O, S, NR h , CO, COO, CONR h , SO, SO 2 , SONR h , and NR h CONR i , wherein each of the C 1-6 alkylene, C 2-6 alkenylene, and C 2-6 alkynylene is optionally substituted by 1, 2 or 3 substituents independently selected from halo, C 1-6 alkyl, C 1-6 haloalkyl, OH, C 1-6 alkoxy, C 1-6 haloalkoxy, amino, C 1-6 alkylamino, and C 2-8 dialkylamino; Z' is independently selected from H, halo, C 1-6 alkyl, C 2-6 alkenyl, C 2-6 alkynyl, C 1-6 haloalkyl, halosulfanyl, CN, NO 2 , N3, OR a2 , SR a2 , C(O)R b2 , C(O)NR c2 R d2 , C(O)OR a2 , OC(O)R b2 , OC(O)NR c2 R d2 , NR c2 R d2 , NR c2 C(O)R b2 , NR c2 C(O)NR c2 R d2 , NR c2 C(O)OR a2 , C(=NR 9)NR c2 R d2 , NR c2 C(=NR 9)NR c2 R d2 , P(R f2) 2 , P(OR e2) 2 , P(O)R e2 R f2 , P(O)OR e2 OR f2 , S(O)R b2 , S(O)NR c2 R d2 , S(O) 2 R b2 , NR c2 S(O) 2 R b2 , S(O) 2 NR c2 R d2 , aryl, cycloalkyl, heteroaryl, and heterocycloalkyl, wherein said C 1-6 alkyl, C 2-6 alkenyl, C 2-6 alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are optionally substituted by 1, 2, 3, 4 or 5 substituents independently selected from halo, C 1-6 alkyl, C 2-6 alkenyl, C 2-6 alkynyl, C 1-6 haloalkyl, halosulfanyl, CN, NO 2 , N 3 , OR a2 , SR a2 , C(O)R b2 , C(O)NR c2 R d2 , C(O)OR a2 , OC(O)R b2 , OC(O)NR c2 R d2 , NR c2 R d2 , NR c2 C(O)R b2 , NR c2 C(O)NR	Novartis AG, 4056 Basel, CH, 101062816	2019-10-23	2014-09-13

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			c2 R d2 , NR c2 C(O)OR a2 , C(=NR 9)NR c2 R d2 , NR c2 C(=NR g)NR c2 R d2 , P(R f2) 2 , P(OR e2) 2 , P(O)R e2 R f2 , P(O)OR e2 OR f2 , S(O)R b2 , S(O)NR c2 R d2 , S(O) 2 R b2 , NR c2 S(O) 2 R b2 , and S(O) 2 NR c2 R d2 ; wherein two adjacent -W'-X'-Y'-Z', together with the atoms to which they are attached, optionally form a fused 4-20 membered cycloalkyl ring or a fused 4-20 membered heterocycloalkyl ring, each optionally substituted by 1, 2, or 3 substituents independently selected from halo, C 1-6 alkyl, C 2-6 alkenyl, C 2-6 alkynyl, C 1-6 haloalkyl, halosulfanyl, CN, NO 2 , OR a3 , SR a3 , C(O)R b3 , C(O)NR c3 R d3 , C(O)OR a3 , OC(O)R b3 , OC(O)NR c3 R d3 , NR c3 R d3 , NF c3 C:(O)R b3 , NR c3 C(O)NR c3 R d3 , NR c3 C(O)OR a3 , C(=NR g)NR c3 R d3 , NR c3 C(=NR g)NR c3 R d3 , S(O)R b3 , S(O)NR c3 R d3 , S(O) 2 R b3 , NR c3 S(O) 2 b3 , S(O) 2 NR c3 R d3 , aryl, cycloalkyl, heteroaryl, and heterocycloalkyl; R a2 and R a3 are independently selected from H, C 1-6 alkyl, C 1-6 haloalkyl, C 2-6 alkenyl, C 2-6 alkynyl, aryl, cycloalkyl, heteroaryl, heterocycloalkyl, arylalkyl, heteroarylalkyl, cycloalkylalkyl, and heterocycloalkylalkyl, wherein said C 1-6 alkyl, C 1-6 haloalkyl, C 2-6 alkenyl, C 2-6 alkynyl, aryl, cycloalkyl, heteroaryl, heterocycloalkyl, arylalkyl, heteroarylalkyl, cycloalkylalkyl, or heterocycloalkylalkyl is optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, halo, C 1-6 alkyl, C 1-6 alkoxy, C 1-6 haloalkyl, and C 1-6 haloalkoxy; R b2 and R b3 are independently selected from H, C 1-6 alkyl, C 1-6 haloalkyl, C 2-6 alkenyl, C 2-6 alkynyl, aryl, cycloalkyl, heteroaryl, heterocycloalkyl, arylalkyl, heteroarylalkyl, cycloalkylalkyl, and heterocycloalkylalkyl, wherein said C 1-6 alkyl, C 1-6 haloalkyl, C 2-6 alkenyl, C 2-6 alkynyl, aryl, cycloalkyl, heteroaryl, heterocycloalkyl, arylalkyl, heteroarylalkyl, cycloalkylalkyl, or heterocycloalkylalkyl is optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, halo, C 1-6 alkyl, C 1-6 alkoxy, C 1-6 haloalkyl, and C 1-6 haloalkoxy; R c2 and R d2 are independently selected from H, C 1-10 alkyl, C 1-6 haloalkyl, C 2-6 alkenyl, C 2-6 alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, arylalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkylalkyl, arylcycloalkyl, arylheterocycloalkyl, arylheteroaryl, biaryl, heteroarylcycloalkyl, heteroarylheterocycloalkyl, heteroarylaryl, and biheteroaryl, wherein said C 1-10 alkyl, C 1-6 haloalkyl, C 2-6 alkenyl, C 2-6 alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, arylalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkylalkyl, arylcycloalkyl, arylheterocycloalkyl, arylheteroaryl, biaryl, heteroarylcycloalkyl, heteroarylheterocycloalkyl, heteroarylaryl, and biheteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, halo, C 1-6 alkyl, C 1-6 alkoxy, C 1-6 haloalkyl, C 1-6 haloalkoxy, hydroxyalkyl, cyanoalkyl, aryl, heteroaryl, C(O)OR a4 , C(O)R b4 , S(O) 2 R b3 , alkoxyalkyl, and alkoxyalkoxy; or R c2 and R d2 together with the N atom to which they are attached form a 4-, 5-, 6- or 7-membered heterocycloalkyl group or heteroaryl group, each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN,				

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			amino, halo, C 1-6 alkyl, C 1-6 alkoxy, C 1-6 baloalkyl, C 1-6 haloalkoxy, hydroxyalkyl, cyanoalkyl, aryl, heteroaryl, C(O)OR a4 , C(O)R b4 , S(O) 2 R b3 , alkoxyalkyl, and alkoxyalkoxy; R c3 and R d3 are independently selected from H, C 1-10 alkyl, C 1-6 haloalkyl, C 2-6 alkenyl, C 2-6 alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, arylalkyl, heteroarylalkyl, cycloalkylalkyl or heterocycloalkylalkyl, wherein said C 1-10 alkyl, C 1-6 haloalkyl, C 2-6 alkenyl, C 2-6 alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, arylalkyl, heteroarylalkyl, cycloalkylalkyl or heterocycloalkylalkyl is optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, halo, C 1-6 alkyl, C 1-6 alkoxy, C 1-6 haloalkyl, and C 16 haloatkoxy; or R c3 and R d3 together with the N atom to which they are attached form a 4-, 5-, 6- or 7-membered heterocycloalkyl group or heteroaryl group, each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, halo, C 1-6 alkyl, C 1-6 alkoxy, C 1-6 haloalkyl, and C 1-6 haloalkoxy; R e2 is independently selected from H, C 1-6 alkyl, C 1-6 haloalkyl, C 2-6 alkenyl, (C 1-6 alkoxy)-C 1-6 alkyl, C 2-6 alkynyl, aryl, cycloalkyl, heteroaryl, heterocycloalkyl, arylalkyl, cycloalkylalkyl, heteroarylalkyl, and heterocycloalkylalkyl; R f2 is independently selected from H, C 1-6 alkyl, C 1-6 haloalkyl, C 2-6 alkenyl, C 2-6 alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl; R g is H, CN, and NO 2 ; R h and R i are independently selected from H and C 1-6 alkyl; R j is H, C 1-6 alkyl, C 1-6 haloalkyl, C 2-6 alkenyl, C 2-6 alkynyl, aryl, cycloalkyl, heteroaryl, heterocycloalkyl, arylalkyl, heteroarylalkyl, cycloalkylalkyl, or heterocycloalkylalkyl.		
EP3235501B1	APPLICATION OF DERIVATIVE OF CLOSTRIDIUM GHONII	The invention relates to application of Derivatives of Clostridium ghonii, especially in the applicationof Derivatives of Clostridium ghonii MW-DCG-HNCv-18 in preparation of medicines for treating non-small cell lung carcinoma. The invention also discloses a medicine combining the Derivatives of Clostridium ghonii MW-DCG-HNCv-18 strain with Docetaxel as the active ingredients. According to the invention, the MW-DCG-HNCv-18 strain is found to have specific inhibition effect on non-small cell lung carcinoma for the first time, the inhibition effect on the non-small cell lung carcinoma is significantly superior to that of other known similar strains, and through screening, the MW-DCG-HNCv-18 strain is found to have more prominent inhibition effect on non-small cell lung carcinoma when combined with Docetaxel injection, so that a novel way is provided for the treatment of non-small cell lung carcinoma.	1. Spores of Clostridium ghonii MW-DCG-HNCv-18 for use in the treatment of non-small cell lung carcinoma. | 2. A medicine for treating non-small cell lung carcinoma, characterized by comprising a pharmaceutical composition prepared from spores of Clostridium ghonii MW-DCG-HNCv-18 and Docetaxel as active ingredients, as well as pharmaceutically acceptable excipients.	SHANDONG XINCHUANG BIOLOGICAL TECHNOLOGY CO. LTD, Jinan High-Tech Zone, Jinan, Shandong 250101, CN, 101726059	2019-10-16	2014-12-19
EP3316891B1	TREATMENT OF OTITIS MEDIA WITH RETROAURICULAR INJECTION OF AN ANTI-INFLAMMATORY DRUG	The present invention relates to the treatment of otitis media, in particularly secretory otitis media, with an anti-inflammatory drug such as a steroid or a non-steroid anti-inflammatory drug, wherein said anti-inflammatory drug is formulated as a depot formulation for retroauricular injection.	1. Anti-inflammatory drug for use in the treatment or prophylaxis of otitis media in an individual, wherein said anti-inflammatory drug is formulated as a depot formulation for retroauricular injection. 12. Unit dose comprising an anti-inflammatory drug for use of any of the claims 1-11, comprising 0.1 - 2.0 mL of said anti-inflammatory drug.	Region Nordjylland Aalborg University Hospital, 9220 Aalborg Øst, DK, 101643554	2019-10-16	2015-07-01

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EP3254684B1	HUMAN PLATELET LYSATE OR FRACTION ENRICHED IN HUMAN PLATELET-DERIVED EXTRACELLULAR VESICLES, FOR USE IN MEDICINE	The present invention is related to human platelet lysate or a fraction that is enriched for human platelet lysate derived extracellular vesicles and their use in medicine, particularly for the prevention and/or treatment of inflammatory driven diseases, neurodegenerative diseases, immune/autoimmune diseases, cardiovascular diseases, dermatologic diseases, orthopedic diseases, tissue regenerative medicine, oncologic diseases, infectious diseases, transplant rejections, stroke, ischemia or Graft-versus-Host Disease. The present invention is further related to a method of manufacture of a pharmaceutical preparation or a diagnostic preparation or a cosmetic preparation comprising the step of adding human platelet lysate or a fraction that is enriched for human platelet lysate derived extracellular vesicles to the pharmaceutical preparation or a diagnostic preparation or a cosmetic preparation.	1. Pharmaceutical preparation comprising a fraction that is enriched for human platelet lysate derived extracellular vesicles for use in medicine. 2. Pharmaceutical preparation comprising a fraction that is enriched for human platelet lysate derived extracellular vesicles for use in the prevention and/or treatment of inflammatory driven diseases, neurodegenerative diseases, immune/autoimmune diseases, cardiovascular diseases, dermatologic diseases, infectious diseases, transplant rejections, stroke, ischemia or Graft-versus-Host Disease.	Lysatpharma GmbH, 07745 Jena, DE, 101839164	2019-10-23	2016-06-08