the release as compared to previously disclosed ocular implants, and which are suitable for repeat dosing. The present invention addresses this need.

OBJECTS OF THE INVENTION

[00014] It is an object of certain examples of the present disclosure to provide a new ocular implant comprising a TKI such as axitinib that provides a sustained release of TKI such as axitinib over an extended period of time, such as at least 3 months, or at least 6 months, such as for a period of about 6 months to about 12 months.

[00015] It is an object of certain examples of the present disclosure to provide an ocular implant comprising a TKI such as axitinib that provides for a sustained release of TKI such as axitinib *in vivo* (in the vitreous) of about 1 µg/day or more over at least 3 months.

[00016] It is an object of certain examples of the present disclosure to provide an ocular implant comprising a TKI such as axitinib that provides for a sustained release of TKI such as axitinib wherein the *in vitro* or *in vivo* release of TKI from the implant is accelerated as compared to known implants.

[00017] It is an object of certain examples of the present disclosure to provide an ocular implant comprising a TKI such as axitinib that provides for a sustained release of TKI such as axitinib wherein the *in vitro* or *in vivo* release of the TKI from the implant is faster than from a comparative known implant which contains the same dose of TKI such as axitinib.

[00018] It is an object of certain examples of the present disclosure to provide an ocular implant comprising a TKI such as axitinib that provides for a sustained release of TKI such as axitinib wherein the *in vitro* release rate of the TKI from the implant per day on one or more days, or the average release rate per day over a certain period of time is higher than from a comparative known implant which contains the same dose of the TKI.

[00019] It is an object of certain examples of the present disclosure to provide an ocular implant comprising a TKI such as axitinib that provides for sustained release of the TKI, wherein therapeutically effective levels of TKI in the retina, choroid, and/or retinal pigment epithelium (RPE) are reached faster than with a comparative known implant which contains the same dose of the TKI.

[00020] It is an object of certain examples of the present disclosure to provide an ocular implant comprising a TKI such as axitinib that provides for sustained release of the TKI, wherein the *in vitro* release rate per day on one or more days, and/or the average release rate per day over a certain period of time, and/or the amount of the TKI released on one or more days, and/or the cumulative amount of the TKI released over a certain period of time, and/or the percentage of the TKI (based on the total amount of the TKI contained in the implant, or based on the total amount of the TKI released in the *in vitro* test), is higher than from a comparative known implant which contains the same dose of the TKI.

[00021] It is an object of certain examples of the present disclosure to provide an ocular implant fulfilling one or more of the objects stated above for use in the treatment of ocular diseases, including (wet) AMD, DR, DME, and RVO.

[00022] It is an object of certain examples of the present disclosure to provide an ocular implant fulfilling one or more of the objects stated above for use in the treatment of ocular diseases, including (wet) AMD, DR, DME, and RVO, wherein the treatment period with one single implant is at least 3 months, such as at least 6, at least 9, at least 10 months, or at least 12 months, such as from about 6 to about 9 months, or from about 6 to about 12 months.

[00023] It is an object of certain examples of the present disclosure to provide an ocular implant fulfilling one or more of the objects stated above for use in the treatment of ocular diseases, including (wet) AMD, DR, DME, and RVO, wherein the TKI levels in ocular tissues such as the retina, the choroid, or the retinal pigment epithelium, as well as the vitreous humor are maintained at a therapeutically efficient level, in particular at a level sufficient for inhibition or deceleration of angiogenesis, over a period of at least 3 months, such as at least 6, at least 9, at least 10 months, or at least 12 months, such as from about 6 to about 9 months, or from about 6 to about 12 months.

[00024] It is a further object of certain examples of the present disclosure to provide a method of increasing the release rate of TKI such as axitinib from an ocular implant.

[00025] It is a further object of certain examples of the present disclosure to provide forms of axitinib for use in an ocular implant, wherein these forms of axitinib have a solubility of greater than 0.3 µg/mL as measured in phosphate-buffered saline (PBS) at a pH of 7.2 to 7.4 and 37 °C after five days of incubation, and ocular implants comprising such forms of axitinib.

[00026] It is a further object of certain examples of the present disclosure to provide ocular implants having an increased hydrated surface area of at least 25 mm^2 as measured in phosphate-buffered saline (PBS) at a pH of 7.2 to 7.4 and 37 °C after 24 hours of incubation.

[00027] It is a further object of certain examples of the present disclosure to provide methods of manufacturing ocular implants fulfilling one or more of the objects stated above.

[00028] It is a further object of certain examples of the present disclosure to provide a method of treating ocular diseases, the method comprising administering an ocular implant fulfilling one or more of the objects stated above.

[00029] It is a further object of certain examples of the present disclosure to provide a method of treating (wet) AMD, DR, DME, or RVO, the method comprising administering an ocular implant fulfilling one or more of the objects stated above.

[00030] It is a further object of certain examples of the present disclosure to provide a method of treating (wet) AMD, DR, DME, or RVO, the method comprising administering an ocular implant fulfilling one or more of the objects stated above to a patient, wherein the treatment period with one single implant is at least 3 months, such as at least 6, at least 9, at least 10 months, or at least 12 months, such as from about 6 to about 9 months, or from about 6 to about 12 months, wherein

rescue medication is required to be administered only rarely, such as 1, 2 or 3 times, during the treatment period.

[00031] It is a further object of certain examples of the present disclosure to provide a method of treating an ocular disease such as (wet) AMD, DR, DME, or RVO, particularly (wet) AMD, and an ocular implant for use in such method, wherein the method provides a continuous treatment by means of repeat dosing of an ocular implant.

[00032] It is a further object of certain examples of the present disclosure to provide a method of treating an ocular disease such as (wet) AMD, DR, DME, or RVO, particularly (wet) AMD, and an ocular implant for use in such method, wherein the ocular implant containing a TKI such as axitinib allows for repeat dosing of an implant, such as every 6 to 12 months, such as every 8 to 11 months, or every 6 months, or every 9 months.

[00033] It is a further object of certain examples of the present disclosure to provide a method of treating an ocular disease such as (wet) AMD, DR, DME, or RVO, particularly (wet) AMD, and an ocular implant for use in such method wherein the ocular implant containing a TKI such as axitinib allows for repeat dosing of an implant, such as every 6 to 12 months, such as every 8 to 11 months, or every 6 months such that a continuous therapeutic effect is achieved without having to re-dose at a point in time when residual drug-depleted implant is still present.

[00034] It is a further object of certain examples of the present disclosure to provide a method of treating an ocular disease such as (wet) AMD, DR, DME, or RVO, particularly (wet) AMD, and an ocular implant for use in such method, wherein the ocular implant contains a TKI such as axitinib dispersed in a hydrogel, where the implant provides for a release rate of the TKI such as axitinib into the vitreous (and consequently delivery of the TKI such as axitinib to ocular tissue such as the retina or the choroid) such that the cumulative amount of TKI such as axitinib released prior to the degradation of the hydrogel (i.e., when the implant/the hydrogel is still intact) is higher than the amount of TKI such as axitinib released upon degradation of the hydrogel.

[00035] It is a further object of certain examples of the present disclosure to provide a method of treating an ocular disease such as (wet) AMD, DR, DME, or RVO, particularly (wet) AMD, and an ocular implant for use in such method, wherein the ocular implant contains a TKI such as axitinib dispersed in a hydrogel, where the implant provides for a release rate of the TKI such as axitinib into the vitreous (and consequently delivery of the TKI such as axitinib to ocular tissue such as the retina or the choroid) such that the C_{max} of TKI such as axitinib in said tissue occurs before biodegradation of the implant.

[00036] It is a further object of certain examples of the present disclosure to provide a method of treating an ocular disease such as (wet) AMD, DR, DME, or RVO, particularly (wet) AMD, and an ocular implant for use in such method, wherein the ocular implant contains a TKI such as axitinib dispersed in a hydrogel, wherein the implant provides for a release rate of the TKI such as axitinib into the vitreous humor (and consequently delivery of the TKI such as axitinib to ocular tissue such as the

retina or the choroid) such that the t_{max} of TKI such as axitinib in said tissue occurs before biodegradation of the implant and/or is shorter than the t_{max} of TKI such as axitinib as provided by known implants.

[00037] It is a further object of certain examples of the present disclosure to provide a method of treating (wet) AMD, DR, DME, or RVO, the method comprising administering an ocular implant fulfilling one or more of the objects stated above to a patient who has a history of anti-VEGF treatment, or a patient who is anti-VEGF treatment naïve.

[00038] It is a further object of certain examples of the present disclosure to provide a method of treating an ocular disease, including (wet) AMD, DR, DME, or RVO, the method comprising administering an ocular implant fulfilling one or more of the objects stated above in combination with an anti-VEGF agent.

[00039] It is a further object of certain examples of the present disclosure to provide a kit comprising one or more ocular implants fulfilling one or more of the objects stated above and optionally comprising a means for injecting the ocular implant.

[00040] One or more of these objects of the present disclosure and others are solved by one or more examples as disclosed and claimed herein.

SUMMARY

[00040a] In an aspect, there is provided a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein the implant contains axitinib polymorph IV in an amount of from 400 µg to 500 µg.

[00040b] In another aspect, there is provided a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the percentage of axitinib released from the implant in an in vitro test performed at 35°C ± 0.5 °C in 0.01N HCl with 0.25% cetyl trimethyl ammonium bromide (CTAB) in a USP apparatus 4 is:

from about 10 to about 25% after 0.5 hours,
from about 30 to about 50% after 2 hours,
from about 60 to about 90% after 6 hours,
from about 79 to about 100 % after 10 hours,
at least about 90% after 12 hours,
and/or at least about 92% after 16 hours,
or:
from about 12 to about 17% after 0.5 hours,
from about 32 to about 42% after 2 hours,
from about 62 to about 78% after 6 hours,
from about 83 to about 97% after 10 hours,
and/or at least about 94% after 16 hours

[00040c] In another aspect, there is provided a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein the percentage of axitinib released from the implant in an

in vitro test performed at 35°C ± 0.5 °C in 0.01N HCl with 0.25% cetyl trimethyl ammonium bromide (CTAB) in a USP apparatus 4 is:

at least about 10 % after 0.5 hours,

at least about 30 % after 2 hours,

at least about 58 % after 6 hours,

at least about 75 % after 10 hours,

at least about 80 % after 12 hours,

and/or at least about 90 % after 16 hours.

[00040d] In another aspect, there is provided a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the amount of axitinib released from the implant in an in vitro test performed at 35°C ± 0.5 °C in 0.01N HCl with 0.25% cetyl trimethyl ammonium bromide (CTAB) in a USP apparatus 4 is:

from about 50 to about 80 µg after 0.5 hours,

from about 140 to about 200 µg after 2 hours,

from about 270 to about 360 µg after 6 hours,

from about 350 to about 450 µg after 10 hours,

and/or at least about 410 µg after 16 hours.

[00040e] In another aspect, there is provdied a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein the implant contains about 400 µg to about 500 µg axitinib, wherein the implant has a composition on a dry basis of from about 30% to about 70% w/w axitinib and from about 20% to about 50% w/w PEG units, and wherein the solubility of the axitinib is 0.3 µg/mL or greater as measured in phosphate-buffered saline (PBS) at a pH of 7.2 to 7.4 and 37 °C at equilibrium.

[00040f] In another aspect, there is provdied the use of a sustained release biodegradable ocular implant as defined above in the manufacture of a medicament for the treatment of an ocular disease in a human patient in need thereof, the use comprising the implant to be administered to the patient's eye by intravitreal injection.

[00040g] In another aspect, there is provided a sustained release biodegradable ocular implant as defined above for use in therapy.

[00040h] In another aspect, there is provided a kit comprising one or more sustained release biodegradable ocular implant(s) as defined above and one or more needles for injection, wherein each implant is loaded in a needle having a gauge size of 25 or thinner, wherein each needle is pre-connected to an injection device.

[00041] In one general example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and a tyrosine kinase inhibitor (TKI), wherein tyrosine kinase inhibitor particles are dispersed within the hydrogel, characterized in that the solubility of the tyrosine kinase inhibitor is greater than 0.3 µg/mL as measured in phosphate-buffered saline (PBS) at a pH of 7.2 to 7.4 and 37 °C after five days of incubation.

[00042] For example, in certain examples the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib polymorph IV in an amount of from about 400 µg to about 500 µg, wherein axitinib particles are dispersed within the hydrogel.

[00043] In another general example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and a tyrosine kinase inhibitor, wherein tyrosine kinase inhibitor particles are dispersed within the hydrogel, characterized in that the hydrated surface area of the implant is at least 25 mm^2 as measured in phosphate-buffered saline (PBS) at a pH of 7.2 to 7.4 and 37 °C after 24 hours of incubation.

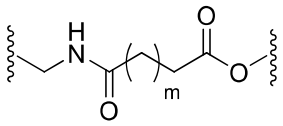
[00044] In a further general example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and a tyrosine kinase inhibitor, wherein tyrosine kinase inhibitor particles are dispersed within the hydrogel, wherein the cumulative amount of tyrosine kinase inhibitor released from the implant over a period defined by any initial number of days up to the day when 80% of the tyrosine kinase inhibitor contained in the implant is released is higher than the cumulative amount of tyrosine kinase inhibitor released over the same period of time from a comparative implant, wherein the comparative implant differs from the sustained release biodegradable ocular

implant only in that the solubility of the tyrosine kinase inhibitor in the comparative implant is lower as measured in PBS at a pH of 7.2 to 7.4 and 37 °C after five days of incubation, and wherein the release of tyrosine kinase inhibitor from both implants is measured under identical conditions.

[00045] In a further general example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and a tyrosine kinase inhibitor, wherein tyrosine kinase inhibitor particles are dispersed within the hydrogel, wherein the average release rate of tyrosine kinase inhibitor per day from the implant over a period defined by any initial number of days up to the day when 80% of the tyrosine kinase inhibitor contained in the implant is released is higher than the average release rate of tyrosine kinase inhibitor per day from a comparative implant over the same period of time, wherein the comparative implant differs from the sustained release biodegradable ocular implant only in that the solubility of the tyrosine kinase inhibitor in the comparative implant is lower as measured in PBS at a pH of 7.2 to 7.4 and 37 °C after five days of incubation, and wherein the release of tyrosine kinase inhibitor from both implants is measured under identical conditions.

[00046] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the implant comprises axitinib polymorph IV and the implant contains axitinib in an amount corresponding to about 250 to about 700 µg axitinib free base, such as about 400 to about 500 µg axitinib free base, wherein the hydrogel comprises crosslinked PEG units.

[00047] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the implant comprises axitinib polymorph IV in an amount of from about 360 µg to about 562.5 µg, or from about 405 µg to about 495 µg, such as about 450 µg, wherein the hydrogel comprises crosslinked multi-armed PEG units having a number average molecular weight of about 20,000 Daltons, wherein the crosslinks between the PEG units include a group represented by the following formula

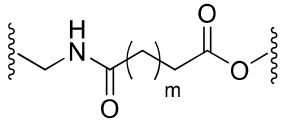


wherein m is 6,

wherein the implant is cylindrical and in its dried state has a length of 10 mm or less, such as from 6 to 9 mm, and a diameter of from 0.25 to 0.45 mm and/or in its hydrated state (after 24 hours in PBS at a pH of 7.2 to 7.4 at 37 °C) has a length of 12 mm or less, 10 mm or less, such as from 8 to 9 mm and a diameter of from 0.5 to 0.9 mm, and wherein the axitinib particles have a d90 particle size of less than 8 µm and a d50 particle size of less than 3 µm.

[00048] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the implant comprises axitinib polymorph IV in an amount of from about 480 µg to about 750 µg, or from about 540 µg to about 660 µg, such as about 600 µg, wherein the hydrogel

comprises crosslinked multi-armed PEG units having a number average molecular weight of about 20,000 Daltons, wherein the crosslinks between the PEG units include a group represented by the following formula



wherein m is 6,

wherein the implant is cylindrical and in its dried state has a length of 10 mm or less, such as from 6 to 9 mm, and a diameter of from 0.25 to 0.45 mm and/or in its hydrated state (after 24 hours in PBS at a pH of 7.2 to 7.4 at 37 °C) has a length of 10 mm or less, such as from 8 to 9 mm and a diameter of from 0.5 to 0.9 mm, and wherein the axitinib particles have a d90 particle size of less than 8 μm and a d50 particle size of less than 3 μm.

[00049] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the implant comprises axitinib polymorph IV and the implant contains axitinib in an amount corresponding to from about 360 μg to about 562.5 μg, or from about 405 μg to about 495 μg, such as about 450 μg axitinib free base, and releases at least about 60 μg axitinib over the initial day, and/or at least about 100 μg axitinib over the initial 2 days, and/or at least about 130 μg axitinib over the initial 3 days, and/or at least about 220 μg axitinib over the initial 7 days and/or at least about 275 μg axitinib over the initial 10 days in an *in vitro* test performed at 37°C in an 25%/75% (v/v) ethanol/water mixture under 2x sink conditions.

[00050] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the implant comprises axitinib polymorph IV and the implant contains axitinib in an amount corresponding to from about 360 μg to about 562.5 μg, or from about 405 μg to about 495 μg, such as about 450 μg axitinib free base, and releases at least about 35 μg axitinib over the initial day, and/or at least about 60 μg axitinib over the initial 2 days, and/or at least about 100 μg axitinib over the initial 4 days, and/or at least about 180 μg axitinib over the initial 7 days and/or at least about 200 μg axitinib over the initial 9 days in an *in vitro* test performed at 37°C in an 25%/75% (v/v) ethanol/water mixture under 3x sink conditions

[00051] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the implant comprises axitinib polymorph IV and the implant contains axitinib in an amount corresponding to from about 480 μg to about 750 μg, or from about 540 μg to about 660 μg, such as about 600 μg axitinib free base, and releases at least about 70 μg axitinib over the initial day, and/or at least about 130 μg axitinib over the initial 2 days, and/or at least about 180 μg axitinib over the initial 3 days, and/or at least about 300 μg axitinib over the initial 7 days and/or at least about 375

µg axitinib over the initial 10 days in an *in vitro* test performed at 37°C in an 25%/75% (v/v) ethanol/water mixture under 2x sink conditions.

[00052] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the implant comprises axitinib polymorph IV and the implant contains axitinib in an amount corresponding to from about 480 µg to about 750 µg, or from about 540 µg to about 660 µg, such as about 600 µg axitinib free base, and releases at least about 50 µg axitinib over the initial day, and/or at least about 100 µg axitinib over the initial 2 days, and/or at least about 180 µg axitinib over the initial 4 days, and/or at least about 280 µg axitinib over the initial 7 days and/or at least about 300 µg axitinib over the initial 9 days in an *in vitro* test performed at 37°C in an 25%/75% (v/v) ethanol/water mixture under 3x sink conditions.

[00053] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the implant comprises axitinib polymorph IV and the implant contains axitinib in an amount corresponding to from about 360 µg to about 562.5 µg, or from about 405 µg to about 495 µg, such as about 450 µg axitinib free base, and releases at least 50% of the total released amount of axitinib over the initial 3 days in an in vitro test, and/or releases at least 80% of the total released amount of axitinib over the initial 7 days in an in vitro test, and/or releases at least 92% of the total released amount of axitinib over the initial 10 days in an in vitro test performed at 37°C in an 25%/75% (v/v) ethanol/water mixture under 2x sink conditions.

[00054] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the implant comprises axitinib polymorph IV and the implant contains axitinib in an amount corresponding to from about 360 µg to about 562.5 µg, or from about 405 µg to about 495 µg, such as about 450 µg axitinib free base, and releases at least 30% of the total released amount of axitinib over the initial 3 days in an in vitro test, and/or releases at least 60% of the total released amount of axitinib over the initial 7 days in an in vitro test, and/or releases at least 80% of the total released amount of axitinib over the initial 10 days in an in vitro test performed at 37°C in an 25%/75% (v/v) ethanol/water mixture under 2x sink conditions.

[00055] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the implant comprises axitinib polymorph IV and the implant contains axitinib in an amount corresponding to from about 360 µg to about 562.5 µg, or from about 405 µg to about 495 µg, such as about 450 µg axitinib free base, and releases at least 15% of the total released amount of axitinib over the initial 2 days in an in vitro test, and/or releases at least 30% of the total released amount of axitinib over the initial 4 days in an in vitro test, and/or releases at least 50% of the total released amount of axitinib over the initial 7 days in an in vitro test, wherein the in vitro test is performed at 37°C in an 25%/75% (v/v) ethanol/water mixture under 3x sink conditions.

[00056] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the implant comprises axitinib polymorph IV and the implant contains axitinib in an amount corresponding to from about 480 µg to about 750 µg, or from about 540 µg to about 660 µg, such as about 600 µg axitinib free base, and releases at least 50% of the total released amount of axitinib over the initial 3 days in an in vitro test, and/or releases at least 80% of the total released amount of axitinib over the initial 7 days in an in vitro test, and/or releases at least 92% of the total released amount of axitinib over the initial 10 days in an in vitro test performed at 37°C in an 25%/75% (v/v) ethanol/water mixture under 2x sink conditions.

[00057] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the implant comprises axitinib polymorph IV and the implant contains axitinib in an amount corresponding to from about 480 µg to about 750 µg, or from about 540 µg to about 660 µg, such as about 600 µg axitinib free base, and releases at least 30% of the total released amount of axitinib over the initial 3 days in an in vitro test, and/or releases at least 60% of the total released amount of axitinib over the initial 7 days in an in vitro test, and/or releases at least 80% of the total released amount of axitinib over the initial 10 days in an in vitro test performed at 37°C in an 25%/75% (v/v) ethanol/water mixture under 2x sink conditions.

[00058] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the implant comprises axitinib polymorph IV and the implant contains axitinib in an amount corresponding to from about 480 µg to about 750 µg, or from about 540 µg to about 660 µg, such as about 600 µg axitinib free base, and releases at least 15% or at least 20% of the total released amount of axitinib over the initial 2 days in an in vitro test, and/or releases at least 35% of the total released amount of axitinib over the initial 4 days in an in vitro test, and/or releases at least 55% of the total released amount of axitinib over the initial 7 days in an in vitro test, wherein the in vitro test is performed at 37°C in an 25%/75% (v/v) ethanol/water mixture under 3x sink conditions.

[00059] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib polymorph IV in an amount of from about 400 µg to about 500 µg, wherein axitinib particles are dispersed within the hydrogel, wherein the implant is an intravitreal implant and has a composition on a dry basis (in % w/w) of about 30 to about 75% axitinib, about 20 to about 50% PEG units, and about 0.5 to about 15 % sodium phosphate salt and on a wet basis (in % w/w) of about 5 to about 17% axitinib, about 4 to about 12% PEG units, and about 0.2 to about 5 % sodium phosphate salt, wherein the hydrogel comprises a PEG hydrogel network formed by crosslinking 4a20kPEG-SAZ and 8a20kPEG-NH_2 units, wherein the implant has a length that is greater than its width, and in its dried state has a length of 11 mm or less, such as from 5 to 11 mm, and a width of from 0.2 to 0.4 mm, such as 0.28 to 0.38 mm and/or in its hydrated state (after 24 hours in PBS at a pH of 7.4 at 37 °C) has a length of 11 mm or less, such as from 5 to 11 mm and a width of

from 0.4 to 2 mm, and wherein the axitinib particles have a d90 particle size of less than 8 μm and a d50 particle size of less than 3 μm.

[00060] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib polymorph IV in an amount of from about 400 μg to about 500 μg, wherein axitinib particles are dispersed within the hydrogel, wherein the implant is an intravitreal implant and has a composition on a dry basis (in % w/w) of about 30 to about 75% axitinib, about 20 to about 50% PEG units, and about 0.5 to about 15 % sodium phosphate salt and on a wet basis (in % w/w) of from about 5 to about 17% axitinib, about 4 to about 12% PEG units, and about 0.2 to about 5 % sodium phosphate salt, wherein the hydrogel comprises a PEG hydrogel network formed by crosslinking 4a20kPEG-SAZ and 8a20kPEG-NH_2 precursors, wherein the implant in its dried state has a width of from 0.20 to 0.40 mm, and in its hydrated state (after 24 hours in PBS at a pH of 7.4 at 37 °C) has a length of 11 mm or less, and wherein the implant has a hydrated surface area (after 24 hours incubation in PBS at a pH of 7.2 to 7.4 at 37 °C) of from 10 to 30 mm^2.

[00061] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib polymorph IV in an amount of from about 400 μg to about 500 μg, wherein axitinib particles are dispersed within the hydrogel, wherein the implant is an intravitreal implant and has a composition on a dry basis (in % w/w) of about 30 to about 75% axitinib, about 20 to about 50% PEG units, and about 0.5 to about 15 % sodium phosphate salt and on a wet basis (in % w/w) of about 5 to about 17% axitinib, about 4 to about 12% PEG units, and about 0.2 to about 5 % sodium phosphate salt, wherein the hydrogel comprises a PEG hydrogel network formed by crosslinking 4a20kPEG-SAZ and 8a20kPEG-NH_2 units, wherein the implant in its dried state has a length of from 5 to 11 mm and a width of from 0.28 to 0.38 mm and/or in its hydrated state (after 24 hours in PBS at a pH of 7.4 at 37 °C) has a length of from 5 to 11 mm and a width of from 0.4 to 2 mm.

[00062] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib polymorph IV in an amount of from about 400 μg to about 500 μg, wherein axitinib particles are dispersed within the hydrogel, wherein the implant is an intravitreal implant and has a composition on a dry basis (in % w/w) of about 54 to about 69% axitinib, a PEG hydrogel network formed by crosslinking about 17 to 26% 4a20kPEG-SAZ with about 8 to about 13% 8a20kPEG-NH_2, about 3 to about 5% dibasic sodium phosphate, and about 1 to about 3% monobasic sodium phosphate.

[00063] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib polymorph IV in an amount of from about 400 μg to about 500 μg, such as about 450 μg, wherein axitinib particles are dispersed within the hydrogel, wherein the hydrogel comprises a PEG hydrogel, wherein the implant in its dry state has a width of from 0.30 to 0.36 mm, and wherein the implant provides for a release of axitinib in an *in vitro* test performed at 35°C ± 0.5 °C in 0.01N HCl with 0.25% cetyl trimethyl ammonium bromide (CTAB) in a USP apparatus 4 that is characterized in that the percentage of axitinib released from the implant (wherein the

percentage of released axitinib is based on the maximum amount of axitinib released from the implant representing 100%) is:
at least about 10 % after 0.5 hours,
at least about 30 % after 2 hours,
at least about 58 % after 6 hours,
at least about 75 % after 10 hours,
at least about 80 % after 12 hours,
and/or at least about 90 % after 16 hours;
such as:
at least about 10 % after 0.5 hours,
at least about 19 % after 1 hour,
at least about 30 % after 2 hours,
at least about 45 % after 4 hours,
at least about 58 % after 6 hours,
at least about 70 % after 8 hours,
at least about 75 % after 10 hours,
at least about 80 % after 12 hours,
and/or at least about 90 % after 16 hours.

[00064] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib polymorph IV in an amount of from about 400 µg to about 500 µg, such as about 450 µg, wherein axitinib particles are dispersed within the hydrogel, wherein the hydrogel comprises a hydrogel network formed by crosslinking 4a20kPEG-SAZ and 8a20kPEG-NH_2 units, wherein the implant has a composition (dry basis; in % w/w) as follows: from about 60% to about 70% axitinib and from about 25% to about 35% PEG units, wherein the implant in its dry state has a width of from 0.30 to 0.36 mm and a total weight of from about 0.6 mg to about 1 mg, and wherein the implant provides for a release of axitinib in an *in vitro* test performed at 35°C ± 0.5 °C in 0.01N HCl with 0.25% cetyl trimethyl ammonium bromide (CTAB) in a USP apparatus 4 that is characterized in that the percentage of axitinib released from the implant (wherein the percentage of released axitinib is based on the maximum amount of axitinib released from the implant representing 100%) is:
from about 10 to about 20% after 0.5 hours,
from about 30 to about 45% after 2 hours,
from about 58 to about 81% after 6 hours,
from about 75 to about 98 % after 10 hours,
at least about 80% after 12 hours,
and/or at least about 90% after 16 hours,
such as:
from about 10 to about 20% after 0.5 hours,

from about 19 to about 30% after 1 hour,
from about 30 to about 45% after 2 hours,
from about 45 to about 65% after 4 hours,
from about 58 to about 81% after 6 hours,
form about 70 to about 90% after 8 hours,
from about 75 to about 98 % after 10 hours,
at least about 80% after 12 hours,
and/or at least about 90% after 16 hours.

[00065] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib polymorph IV in an amount of from about 400 µg to about 500 µg, wherein axitinib particles are dispersed within the hydrogel, wherein the hydrogel comprises a PEG hydrogel, wherein the implant in its dry state has a width of from 0.30 to 0.36 mm, and wherein the implant is characterized in that the amount of axitinib released from the implant in an *in vitro* test performed at 35°C ± 0.5 °C in 0.01N HCl with 0.25% cetyl trimethyl ammonium bromide (CTAB) in a USP apparatus 4 is:
at least about 50 µg after 0.5 hours,
at least about 140 µg after 2 hours,
at least about 270 µg after 6 hours,
at least about 350 µg after 10 hours,
at least about 400 µg after 12 hours,
and/or at least about 410 µg after 16 hours,
such as:
at least about 50 µg after 0.5 hours,
at least about 90 µg after 1 hour,
at least about 140 µg after 2 hours,
at least about 230 µg after 4 hours,
at least about 270 µg after 6 hours,
at least about 340 µg after 8 hours,
at least about 350 µg after 10 hours,
at least about 400 µg after 12 hours,
and/or at least about 410 µg after 16 hours.

[00066] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib polymorph IV in an amount of from about 400 µg to about 500 µg, wherein axitinib particles are dispersed within the hydrogel, wherein the hydrogel comprises a PEG hydrogel network formed by crosslinking 4a20kPEG-SAZ and 8a20kPEG-NH_2 units, wherein the implant has a composition (dry basis; in % w/w) as follows: from about 60% to about 70% axitinib and from about 25% to about 35% PEG units, wherein the implant in its dry state has a width of from 0.30 to 0.36 mm and a total weight of from about 0.6 mg to about 1 mg, and wherein the

implant is characterized in that the amount of axitinib released from the implant in an *in vitro* test performed at 35°C ± 0.5 °C in 0.01N HCl with 0.25% cetyl trimethyl ammonium bromide (CTAB) in a USP apparatus 4 is:

from about 50 to about 80 µg after 0.5 hours,
from about 140 to about 210 µg after 2 hours,
from about 270 to about 380 µg after 6 hours,
from about 350 to about 470 µg after 10 hours,
at least about 400 µg after 12 hours,
and/or at least about 410 µg after 16 hours,

such as:

from about 50 to about 80 µg after 0.5 hours,
from about 90 to about 130 µg after 1 hour,
from about 140 to about 210 µg after 2 hours,
from about 230 to about 290 µg after 4 hours,
from about 270 to about 380 µg after 6 hours,
from about 340 to about 440 µg after 8 hours,
from about 350 to about 470 µg after 10 hours,
at least about 400 µg after 12 hours,
and/or at least about 410 µg after 16 hours.

[00067] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant comprising a hydrogel and axitinib polymorph IV in an amount of from about 400 µg to about 500 µg, wherein axitinib particles are dispersed within the hydrogel, wherein the hydrogel comprises crosslinked PEG units, wherein the amount of axitinib being released upon final degradation of the hydrogel in the vitreous humor is less than 200 µg, wherein the implant in its dry state (prior to injection) has a width of from about 0.3 to about 0.4 mm, such as about 0.33 to about 0.36 mm, and a length of less than about 11 mm, and in its hydrated state (after 24 hours in PBS at a pH of 7.4 at 37 °C) has a length of less than about 11 mm, such as a length of from about 8 to about 10 mm.

[00068] In a further example, the present disclosure relates to a method of treating an ocular disease in a patient in need thereof, the method comprising administering to the patient's eye a sustained release biodegradable ocular implant according to one example of the disclosure, such as by means of intravitreal injection.

[00069] In a further example, the present disclosure relates to a sustained release biodegradable ocular implant as disclosed herein, for use in a method of treating an ocular disease in a patient in need thereof, the method comprising administering to the patient's eye a sustained release biodegradable ocular implant according to an example of the disclosure.

[00070] In a further example, the present disclosure relates to a use of a sustained release biodegradable ocular implant as disclosed herein, for the preparation of a medicament for use in a method of treating an ocular disease in a patient in need thereof, the method comprising administering

to the patient's eye a sustained release biodegradable ocular implant according to an example of the disclosure.

[00071] In a further example, the present disclosure relates to a method of manufacturing a sustained release biodegradable ocular implant according to the disclosure, the method comprising the steps of forming a hydrogel comprising a polymer network and axitinib particles dispersed within the hydrogel, shaping the hydrogel and drying the hydrogel.

[00072] In a further example, the present disclosure relates to another method of manufacturing a sustained release biodegradable ocular implant according to the disclosure, the method comprising melt extruding or injection molding a composition comprising polymer or polymer (such as PEG) precursors and axitinib to form the implant.

[00073] In a further example, the present disclosure relates to a kit comprising one or more sustained release biodegradable ocular implant(s) of the present disclosure and one or more needles for injection, wherein each implant is loaded in a needle, such as in a needle having a gauge size of 25 or thinner.

[00074] In a further example, the present disclosure relates to a method of increasing the release rate and/or the average release rate and/or the released amount of total TKI contained in an ocular implant and/or the released share of the total TKI contained in the implant or the total TKI released from an implant in a certain period of time.

[00075] The individual examples of the present disclosure are disclosed in the specification and claimed in the independent claims, while the dependent claims claim particular examples and variations of these aspects of the disclosure. Details of the various aspects of the present disclosure are provided in the detailed description below.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1: TKI release profile (In Vitro Method B) from implants manufactured by HME or wet casting: (A) Mass released; (B) % Release.

Figure 2: Implant manufactured by HME (3x filament).

Figure 3: Star shaped implant and example calculation of dimensions.

Figure 4: XPRD results – peaks for citric acid, fumaric acid and tartaric acid.

Figure 5: Synthetic schemes of prodrugs of **Example 5**

Figure 6: ^{1}H-NMR of the prodrug of **Example 5.1**

Figure 7: LCMS of the prodrug of **Example 5.1**

Figure 8: HPLC of the prodrug of **Example 5.1**

Figure 9: ^{1}H-NMR of axitinib N-m(PEG)$_4$-oxymethyl prodrug of **Example 5.2**

CLAIMS

1. A sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein the implant contains axitinib polymorph IV in an amount of from 400 µg to 500 µg.

2. The sustained release biodegradable ocular implant of claim 1, wherein axitinib particles are dispersed within the hydrogel.

3. The sustained release biodegradable ocular implant of claim 1 or 2, wherein the implant is an intravitreal implant.

4. The sustained release biodegradable ocular implant of any of the preceding claims, wherein the implant contains axitinib polymorph IV in an amount of from 405 µg to 495 µg.

5. The sustained release biodegradable ocular implant of any of the preceding claims, wherein the implant is a single stranded implant which is cylindrical and has a hydrated surface area of from 10 mm^2 to 30 mm^2, such as from 16.0 mm^2 to 25.0 mm^2, as measured in phosphate-buffered saline (PBS) at a pH of 7.2 to 7.4 and 37 °C after 24 hours of incubation.

6. The sustained release biodegradable ocular implant of claim 1 or 2, wherein the implant is a single-stranded implant which is cylindrical and has a hydrated surface area of from 15 mm^2 to 40 mm^2, as measured in phosphate-buffered saline (PBS) at a pH of 7.2 to 7.4 and 37 °C after 24 hours of incubation.

7. The sustained release biodegradable ocular implant of any of the preceding claims, wherein the implant in its hydrated state (after 24 hours in PBS at a pH of 7.2 to 7.4 at 37 °C) has a length of from 7 to 10 mm and a width of from 0.5 to 0.9 mm.

8. The sustained release biodegradable ocular implant of any of the preceding claims, wherein the implant in its dry state has a length of from 6 mm to 10 mm and has a width of from 0.2 mm to 0.5 mm.

9. The sustained release biodegradable implant of claim 2, wherein the implant is an intravitreal implant, and wherein the implant has a composition on a dry basis (in % w/w) of 30 to 75% axitinib, 20 to 50% polyethylene glycol (PEG) units, and 0.5 to 15 % sodium phosphate salt, and on a wet basis (in % w/w) of from 5 to 17% axitinib, 4 to 12% PEG units, and 0.2 to 5 % sodium phosphate salt,
wherein the hydrogel comprises a PEG hydrogel network formed by crosslinking 4a20kPEG-SAZ and 8a20kPEG-NH_2 precursors,

wherein the implant in its dried state has a width of from 0.20 to 0.40 mm, and in its hydrated state (after 24 hours in PBS at a pH of 7.4 at 37 °C) has a length of 11 mm or less,
and wherein the implant has a hydrated surface area of from 10 to 30 mm^2.

10. The sustained release biodegradable implant of claim 2, wherein the implant is an intravitreal implant, and wherein the hydrogel comprises a PEG hydrogel network formed by crosslinking 4a20kPEG-SAZ and 8a20kPEG-NH_2 units,
wherein the implant in its dried state has a width of from 0.20 to 0.40 mm, and in its hydrated state (after 24 hours in PBS at a pH of 7.4 at 37 °C) has a length of 11 mm or less,
and wherein the implant provides for a release of axitinib in an in vitro test performed at 35°C ± 0.5 °C in 0.01N HCl with 0.25% cetyl trimethyl ammonium bromide (CTAB) in a USP apparatus 4 that is characterized in that the percentage of axitinib released from the implant is:
from 10 to 18% after 0.5 hours,
from 30 to 45% after 2 hours,
from 60 to 80% after 6 hours,
from 79 to 98 % after 10 hours,
at least 90% after 12 hours,
and at least 92% after 16 hours,
wherein the percentage of released axitinib is based on 450 µg axitinib representing 100%.

11. A sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the percentage of axitinib released from the implant in an in vitro test performed at 35°C ± 0.5 °C in 0.01N HCl with 0.25% cetyl trimethyl ammonium bromide (CTAB) in a USP apparatus 4 is:
from about 10 to about 25% after 0.5 hours,
from about 30 to about 50% after 2 hours,
from about 60 to about 90% after 6 hours,
from about 79 to about 100 % after 10 hours,
at least about 90% after 12 hours,
and/or at least about 92% after 16 hours,
or:
from about 12 to about 17% after 0.5 hours,
from about 32 to about 42% after 2 hours,
from about 62 to about 78% after 6 hours,
from about 83 to about 97% after 10 hours,
and/or at least about 94% after 16 hours

12. A sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein the percentage of axitinib released from the implant in an in vitro test performed at 35°C ± 0.5 °C in 0.01N HCl with 0.25% cetyl trimethyl ammonium bromide (CTAB) in a USP apparatus 4 is:

at least about 10 % after 0.5 hours,

at least about 30 % after 2 hours,

at least about 58 % after 6 hours,

at least about 75 % after 10 hours,

at least about 80 % after 12 hours,

and/or at least about 90 % after 16 hours.

13. A sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein axitinib particles are dispersed within the hydrogel, wherein the amount of axitinib released from the implant in an in vitro test performed at 35°C ± 0.5 °C in 0.01N HCl with 0.25% cetyl trimethyl ammonium bromide (CTAB) in a USP apparatus 4 is:

from about 50 to about 80 µg after 0.5 hours,

from about 140 to about 200 µg after 2 hours,

from about 270 to about 360 µg after 6 hours,

from about 350 to about 450 µg after 10 hours,

and/or at least about 410 µg after 16 hours.

14. The sustained release biodegradable ocular implant according to any one of claims 11 to 13, wherein the in vitro test is performed at 35°C ± 0.5 °C in 100 mL 0.01N HCl with 0.25% cetyl trimethyl ammonium bromide (CTAB) in a USP apparatus 4 in a 22.6 mm diameter cell with a laminar flow rate of 8 mL/min, wherein the implant is located between glass beads.

15. The sustained release biodegradable ocular implant according to any of claims 11 to 14, wherein the solubility of the axitinib is 0.3 µg/mL or greater, such as 0.35 µg/mL or greater, such as 0.4 µg/mL or greater, as measured in phosphate-buffered saline (PBS) at a pH of 7.2 to 7.4 and 37 °C at equilibrium.

16. A sustained release biodegradable ocular implant comprising a hydrogel and axitinib, wherein the implant contains about 400 µg to about 500 µg axitinib, wherein the implant has a composition on a dry basis of from about 30% to about 70% w/w axitinib and from about 20% to about 50% w/w PEG units, and wherein the solubility of the axitinib is 0.3 µg/mL or greater as measured in phosphate-buffered saline (PBS) at a pH of 7.2 to 7.4 and 37 °C at equilibrium.

17. The sustained release biodegradable ocular implant according to any of claims 11 to 16, wherein the implant contains about 400 µg to about 500 µg axitinib free base.

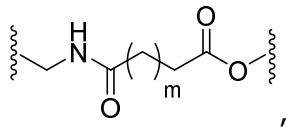
18. The sustained release biodegradable ocular implant according to any of claims 11 to 17, wherein the axitinib is an axitinib polymorph other than axitinib polymorph SAB-I.

19. The sustained release biodegradable ocular implant according to claim 18, wherein the axitinib polymorph is or comprises axitinib polymorph IV such that at least 90% by weight of the entire axitinib contained in the implant is axitinib polymorph IV.

20. The sustained release biodegradable ocular implant according to any of the preceding claims, wherein the hydrogel comprises a polymer network.

21. The sustained release biodegradable ocular implant according to claim 20, wherein the hydrogel comprises crosslinked PEG units.

22. The sustained release biodegradable ocular implant according to claim 21, wherein the PEG units are crosslinked by a hydrolyzable linker having the formula:



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wherein m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, and wherein the crosslinks within the polymer network are identical or different.

23. The sustained release biodegradable ocular implant according to claim 21 or 22, wherein the PEG units have an average molecular weight in a range from about 10,000 to about 40,000 Daltons and wherein the PEG units comprise identical or different multi-arm PEG units, such as 4-arm and/or 8-arm units.

24. The sustained release biodegradable ocular implant according to any of the preceding claims, wherein the implant has a composition on the dry basis (in % w/w) as follows: from about 30% to about 70% axitinib and from about 20% to about 50% PEG units, such as from about 50% to about 70% axitinib and from about 25% to about 45% PEG units.

25. The sustained release biodegradable ocular implant according to claim 24, wherein the implant has a composition on the dry basis (in % w/w) as follows: from about 45% to about 65% axitinib and from about 33% to about 43% PEG units.

26. The sustained release biodegradable ocular implant according to any of the preceding claims, wherein the implant has a composition on the wet basis (in % w/w) as follows: from about 5% to

about 17% axitinib and from about 4% to about 12% PEG units, such as from about 6% to about 12% axitinib and from about 5% to about 10% PEG units.

27. The sustained release biodegradable ocular implant according to claim 26, wherein the implant has a composition on the wet basis (in % w/w) as follows: from about 8% to about 10% axitinib and from about 6% to about 8% PEG units.

28. The sustained release biodegradable ocular implant according to any one of claims 21 to 27, wherein the PEG units are PEG units obtained from crosslinking 4a20kPEG-SAZ with 8a20kPEG-NH_2.

29. The sustained release biodegradable ocular implant according to claim 20, wherein the hydrogel comprises one or more of the following: polyalkylene glycol, poly(ethylene glycol)-block-poly(propylene glycol) copolymer, polyethylene imine, polyalkyl ether, such as polyethylene oxide, polypropylene oxide, polyacrylic acid, acrylate polymer, poly(electrolyte complexe), starch-graft polymer, polymaleic acid, polyvinylamine polyacrylamide, poly(hydroxyethyl-methylacrylate) (PHEMA), polybutylene terephthalate (PBT), polyvinyl alcohol, poly(vinylacetate), poly(vinylpyrrolidinone), poly(vinylpyrrolidone) (PVP), polyglycolic acid, polylactic acid (PLA), polylactic-co-glycolic acid (PLGA), water-swellable N-vinyl lactam, ester-crosslinked polyglucan, polydioxanone, polytrimethylene carbonate.

30. Use of a sustained release biodegradable ocular implant according to any one of the preceding claims in the manufacture of a medicament for the treatment of an ocular disease in a human patient in need thereof, the use comprising the implant to be administered to the patient's eye by intravitreal injection.

31. The use of claim 30, wherein the ocular disease involves angiogenesis and/or neovascularization.

32. The use of claim 30 or 31, wherein the ocular disease is neovascular age-related macular degeneration (AMD), diabetic macular edema, diabetic retinopathy, or retinal vein occlusion, particularly AMD.

33. The use of any of claims 30 to 32, wherein final biodegradation of the hydrogel occurs within 6 to 9 months after injection.

34. The use of any of claims 30 to 33, wherein the treatment period with one sustained release biodegradable ocular implant lasts for 6 to 12 months after administration, or 6 to 9 months after administration.

35. The use of any one of claims 30 to 34, wherein a new sustained release biodegradable ocular implant according to any of claims 1 to 25 is to be administered after the end of the treatment period with the first implant, wherein the re-dosing frequency is every 6 to 12 months, such as every 8 to 11 months, such as about every 6 months, every 9 months or every 12 months.

36. The use of any one of claims 30 to 35, wherein the sustained release biodegradable ocular implant is to be administered in combination with an anti-VEGF agent.

37. The use of claim 36, wherein an anti-VEGF agent is to be administered within 1 month, or 2 months, or 3 months after or prior to the administration of the sustained release biodegradable ocular implant.

38. A sustained release biodegradable ocular implant according to any one of claims 1 to 29 for use in therapy.

39. A kit comprising one or more sustained release biodegradable ocular implant(s) of any one of claims 1 to 29 and one or more needles for injection, wherein each implant is loaded in a needle having a gauge size of 25 or thinner, wherein each needle is pre-connected to an injection device.