the sclera and the choroid. Drug delivered in this space can go around the eye globe to the posterior segment of the eye. This route for drug delivery has been shown to be more effective for treatment of posterior segment than intravitreal injections. However, the simplicity of intravitreal injection outweighs the surgical procedure previously needed for suprachoroidal delivery. Historically, suprachoroidal delivery was achieved by creating small incision using scalpel, followed by delivery using a puncture element or cannula. More recently, a micropuncture element with a predefined, short length, which allows penetration only up to certain depth, has been used to target suprachoroidal space. Because the scleral thickness varies significantly within the patient populations, either prior mapping of eye geometry, or trial and error, is necessary while injecting with hollow micropuncture elements. If the puncture element is too long, it can easily penetrate through the thin suprachoroidal space to inject the drug in the vitreous; and, if it is too short, it delivers into the sclera. The sclera is 10 times stiffer than the choroid and 200 stiffer than the retina making it even more challenging to pierce the sclera without injecting into the vitreous. In some instances, a small volume (on the order of 100 microliters) of therapeutic needs to be injected into the suprachoroidal space, and it needs to be injected with sufficient force to displace the positive resistance of intraocular pressure pressing the choroid against the sclera to achieve a broad coverage of the posterior segment of the eye.

[6] Accordingly, there is a need for an improved system and method for suprachoroidal drug delivery that precisely, consistently and safely targets the suprachoroidal space and provides broad coverage of the posterior segment of the eye.

SUMMARY

[7] In ~~some~~ an aspect~~s~~, the present disclosure provides an injection system comprising: a syringe barrel defining a lumen between a proximal end and a distal end; a first sealing element moveably disposed within the lumen; a second sealing element moveably disposed within the lumen proximal to the first sealing element, wherein the first sealing element and the second sealing element form a seal with the lumen and define an injection chamber between them; and a puncture element extending from a distal end of the first sealing element, the puncture element being in fluid communication with the injection chamber to deliver an injection agent from the injection chamber into a space in a tissue of a patient~~,~~ ; wherein one or more of the syringe barrel, the first sealing element, and the second sealing element are configured to prevent proximal movement of the first sealing element past a pre-selected location, while allowing the second sealing element to come in contact with the first sealing element; ~~and~~ wherein the system is

configured such that, when a force is applied on the second sealing element in a distal direction, in response to a first opposing force, the first sealing element moves in the distal direction to advance the puncture element in the distal direction, without conveying the injection agent through the puncture element, and in response to a second opposing force, the first sealing element remains stationary and the injection agent is conveyed from the injection chamber through the puncture element. In some ~~embodiments~~examples, the first opposing force is due to backpressure exerted on the puncture element as the puncture element advances through the tissue; and the second opposing force is due to backpressure exerted on the puncture element as the puncture element opens into the space in the tissue. In some examples~~embodiments~~, the force applied on the second sealing element is sufficient to advance the first sealing element but is insufficient to convey the injection agent through the puncture element in response to the first opposing force; and the force applied on the second sealing element is insufficient to advance the first sealing element but is sufficient to convey the injection agent through the puncture element in response to the second opposing force.

[8] In some examples~~embodiments~~, a unidirectional stop is disposed in the syringe barrel between the first sealing element and the second sealing element, the unidirectional stop being configured to prevent a proximal movement of the first sealing element past the unidirectional stop, while allowing the second sealing element to pass through the mechanical stop to contact the first sealing element. The unidirectional stop can comprise a section of the syringe barrel having a reduced diameter, wherein the first sealing element has a diameter sufficiently larger than the reduced diameter such that the first sealing element cannot pass through the section while the second sealing element is configured to pass through the section to contact the first sealing element. In some examples~~embodiments~~, the unidirectional stop comprises a portion of an inner surface of the syringe barrel having a friction coefficient sufficient to prevent a proximal movement of the first sealing element. In some examples~~embodiments~~, the unidirectional stop comprises a mechanical stop. In some examples~~embodiments~~, the unidirectional stop comprises a foldable stop disposed between the first sealing element and the second sealing element, the foldable stop being configured to prevent a proximal movement of the first sealing element past the foldable stop and being configured to fold upon application of a force in a distal direction on the foldable stop to allow the second sealing element to pass through the foldable stop to contact the first sealing element. In some examples~~embodiments~~, the first sealing element is shaped such that a frictional or sliding force on the first sealing element in the proximal direction is higher than a frictional or sliding force on the first sealing element in the distal direction and is higher than a force of insertion of the puncture element into the tissue.

[9] In some examples~~embodiments~~, in a relaxed state, the first sealing element has a size that is between 1.01 to 2 times larger than a size of the lumen of the syringe barrel. In some examples~~embodiments~~, in a relaxed state, the first sealing element has a size that is between 1.01 to 1.10 times larger than a size of the lumen of the syringe barrel. In some examples~~embodiments~~, in a relaxed state, the first sealing element has a size that is between 1.01 to 1.4 times larger than a size of the lumen of the syringe barrel. An inner surface of the syringe barrel can be modified to increase friction between the inner surface of the syringe barrel and the first sealing element. In some examples~~embodiments~~, a lock is disposed distally of the first sealing element and configured to selectively lock the first sealing element in place. The lock can include a sealed compartment defined in the lumen of the syringe barrel distal to the first sealing element, an incompressible substance inside the compartment, and a valve to release the incompressible substance from the compartment, such that when the valve is closed, a distal movement of the first sealing element is prevented and, when the valve is open, the distal movement of the first sealing element is allowed.

[10] In some examples~~embodiments~~, a touch trigger mechanism is disposed between the first sealing element and the second sealing element, the touch trigger mechanism is configured to deploy when the first sealing element comes in contact with the second sealing element to prevent a distal movement of the first sealing element. In some examples~~embodiments~~, a fill port is disposed on a surface of the syringe barrel and being in fluid communication with the injection chamber. In some examples~~embodiments~~, such fill port can comprise a receptacle disposed on an outside surface of the syringe barrel and configured to receive a vial; a flowpath connecting the receptacle and the injection chamber; a self-sealing member configured to seal the flowpath; and a puncture element disposed in the receptacle, the puncture element being configured to pierce through the self-sealing member to fluidly connect a vial received in the receptacle with the injection chamber. In some examples~~embodiments~~, the puncture element is moveable relative to the receptacle such that, when the vial is received in the receptacle, the puncture element is moved toward the injection chamber to pierce the self-sealing member and to fluidly connect the vial with the injection chamber, when the medicament container removed from the receptacle, the puncture element is moved away from the injection chamber, thereby allowing the self-sealing member to seal the flowpath.

[11] In some examples~~embodiments~~, a support element is disposed about a distal portion of the puncture element, the support element being moveable in relation to the puncture element and the syringe barrel. The injection chamber can comprise a first chamber and a second chamber, wherein a chamber sealing portion of the second sealing element fluidly isolates the first

chamber from the second chamber, such that a movement of the chamber sealing portion fluidly connects the first and second chambers. In some examples~~embodiments~~, the injection chamber comprises a first chamber and a second chamber, wherein the first chamber and the second chamber are fluidly isolated from one another when the second sealing element is in an initial position and wherein a movement of the second sealing element fluidly connects the first and second chambers. In some examples~~embodiments~~, the second sealing element is configured to engage the first sealing element and to withdraw the first sealing element and the puncture element into the syringe barrel.

[12] In some examples~~aspects~~, the present disclosure provides a method for treatment of an eye disease, the method comprises: pre-inserting into a sclera of a patient a puncture element of an injection system, the injection system comprising: a syringe barrel defining a lumen between a proximal end and a distal end; a first sealing element moveably disposed within the lumen; a second sealing element moveably disposed within the lumen proximal to the first sealing element, wherein the first sealing element and the second sealing element form a seal with the lumen and define an injection chamber between them; the puncture element extending from a distal end of the first sealing element, the puncture element being in fluid communication with the injection chamber to deliver an injection agent from the injection chamber into a space in a tissue of a patient; and wherein one or more of the syringe barrel, the first sealing element, and the second sealing element are configured to prevent proximal movement of the first sealing element past a pre-selected location, while allowing the second sealing element to come in contact with the first sealing element; advancing the puncture element through the sclera by applying a force onto the second sealing element, the force being sufficient to move the first sealing element in the distal direction to advance the puncture element in the distal direction, without conveying the injection agent through the puncture element; and maintaining the force onto the second sliding element as the puncture element passes through the sclera and opens into a suprachoroidal space (SCS) such that the injection agent is conveyed from the injection chamber through the puncture element into the SCS, without further distal movement of the first sealing element. In some examples~~embodiments~~, the eye disease is age-related macular degeneration (AMD), diabetic macular edema (DME), glaucoma, retinal vein occlusion (RVO), uveitis, endophthalmitis, Stargardt disease, Leber Congenital Amaurosis (LCA), Retinitis Pigmentosa, or Choroideremia. In some examples~~embodiments~~, the injection fluid comprises one or more injection agent formulations comprising a viral delivery vector comprising a gene of interest and a promoter selected to promote the gene of interest. The gene of interest can be an anti-VEGFR2 gene, the delivery vector can be an AAV vector, a promoter for the anti-

VEGFR2 gene can be a CAG promoter. In some examples~~embodiments~~, the injection fluid comprises one or more injection agent formulations comprising an anti-VEGFR2 compound selected from a group consisting of bevacizumab, ranibizumab, aflibercept, Ramucirumab, disintegrins, anti-prostaglandins, tryptophanyl-tRNAsynthetase-derived polypeptides, Inosine monophosphate dehydrogenase (IMPDH) inhibitors and anti-PDGF to treat AMD; and corticosteroids to treat uveitis, chorioretinitis, or other inflammatory eye diseases; botulinum toxin for various ocular applications; tyrosine kinase inhibitors.

[13] In ~~some~~ an aspect~~s~~, the present disclosure provides a kit for injection of an injection agent into a tissue comprising: an injection system comprising: a syringe barrel defining a lumen between a proximal end and a distal end; a first sealing element moveably disposed within the lumen; a second sealing element moveably disposed within the lumen proximal to the first sealing element, wherein the first sealing element and the second sealing element form a seal with the lumen and define an injection chamber between them; a puncture element extending from a distal end of the first sealing element, the puncture element being in fluid communication with the injection chamber to deliver an injection agent from the injection chamber into a space in a tissue of a patient;~~ and~~ wherein one or more of the syringe barrel, the first sealing element, and the second sealing element are configured to prevent proximal movement of the first sealing element past a pre-selected location, while allowing the second sealing element to come in contact with the first sealing element;~~ and~~ wherein the system is configured such that, when a force is applied on the second sealing element in a distal direction, in response to a first opposing force, the first sealing element moves in the distal direction to advance the puncture element in the distal direction, without conveying the injection agent through the puncture element,~~ and~~ in response to a second opposing force, the first sealing element remains stationary and the injection agent is conveyed from the injection chamber through the puncture element; and a volume of the injection fluid comprising one or more injection agent formulations. In some examples~~embodiments~~, the eye disease is age-related macular degeneration (AMD), diabetic macular edema (DME), glaucoma, retinal vein occlusion (RVO), uveitis, endophthalmitis, Stargardt disease, Leber Congenital Amaurosis (LCA), Retinitis Pigmentosa, or Choroideremia. In some examples~~embodiments~~, the injection fluid comprises one or more injection agent formulations comprising a viral delivery vector comprising a gene of interest and a promoter selected to promote the gene of interest. The gene of interest can be an anti-VEGFR2 gene, the delivery vector can be an AAV vector, a promoter for the anti-VEGFR2 gene can be CAG promoter. In some examples~~embodiments~~, the injection fluid comprises one or more injection agent formulations comprising an anti-VEGFR2 compound selected

Claims

What is claimed is:

1. An injection system comprising:

a syringe barrel defining a lumen between a proximal end and a distal end;

a first sealing element moveably disposed within the lumen;

a second sealing element moveably disposed within the lumen proximal to the first sealing element, wherein the first sealing element and the second sealing element form a seal with the lumen and define an injection chamber between them; and

a puncture element extending from a distal end of the first sealing element, the puncture element being in fluid communication with the injection chamber to deliver an injection agent from the injection chamber into a space in a tissue of a patient~~,~~;

wherein one or more of the syringe barrel, the first sealing element, and the second sealing element are configured to prevent proximal movement of the first sealing element past a pre-selected location, while allowing the second sealing element to come in contact with the first sealing element;~~, and~~

wherein the system is configured such that, when a force is applied on the second sealing element in a distal direction,

in response to a first opposing force, the first sealing element moves in the distal direction to advance the puncture element in the distal direction, without conveying the injection agent through the puncture element, and

in response to a second opposing force, the first sealing element remains stationary and the injection agent is conveyed from the injection chamber through the puncture element.

2. The system of claim 1, wherein:

the first opposing force is due to backpressure exerted on the puncture element as the puncture element advances through the tissue; and

the second opposing force is due to backpressure exerted on the puncture element as the puncture element opens into the space in the tissue.

3. The system of claim 1, wherein:

the force applied on the second sealing element is sufficient to advance the first sealing element but is insufficient to convey the injection agent through the puncture element in response to the first opposing force; and

the force applied on the second sealing element is insufficient to advance the first sealing element but is sufficient to convey the injection agent through the puncture element in response to the second opposing force.

4. The system of claim 1, wherein a unidirectional stop is disposed in the syringe barrel between the first sealing element and the second sealing element, the unidirectional stop being configured to prevent a proximal movement of the first sealing element past the unidirectional stop, while allowing the second sealing element to pass through ~~the~~ a mechanical stop to contact the first sealing element.

5. The system of claim 4, wherein the unidirectional stop comprises a section of the syringe barrel having a reduced diameter, wherein the first sealing element has a diameter sufficiently larger than the reduced diameter such that the first sealing element cannot pass through the section while the second sealing element is configured to pass through the section to contact the first sealing element.

6. The system of claim 4, wherein the unidirectional stop comprises a portion of an inner surface of the syringe barrel having a friction coefficient sufficient to prevent ~~a~~ the proximal movement of the first sealing element.

7. The system of claim 4, wherein the unidirectional stop comprises ~~a~~ the mechanical stop.

8. The system of claim 4, wherein the unidirectional stop comprises a foldable stop is disposed between the first sealing element and the second sealing element, the foldable stop being configured to prevent ~~a~~ the proximal movement of the first sealing element past the foldable stop and being configured to fold upon application of a force in ~~a~~ the distal direction on the foldable stop to allow the second sealing element to pass through the foldable stop to contact the first sealing element.

9. The system of claim 1, wherein the first sealing element is shaped such that a first frictional or sliding force on the first sealing element in the proximal direction is higher than a second frictional or sliding force on the first sealing element in the distal direction and is higher than a force of insertion of the puncture element into the tissue.

10. The system of any one of claims 1-9, wherein, in a relaxed state, the first sealing element has a size that is between 1.01 to 2 times larger than a size of the lumen of the syringe barrel.

11. The system of any one of claims 1-9, wherein, in a relaxed state, the first sealing element has a size that is between 1.01 to 1.10 times larger than a size of the lumen of the syringe barrel.

12. The system of any one of claims 1-9, wherein an inner surface of the syringe barrel is modified to increase friction between the inner surface of the syringe barrel and the first sealing element.

13. The system of any one of claims 1-9, further comprising a lock disposed distally of the first sealing element and configured to selectively lock the first sealing element in place.

14. The system of claim 13, wherein the lock comprises a sealed compartment defined in the lumen of the syringe barrel distal to the first sealing element, an incompressible substance inside the compartment, and a valve to release the incompressible substance from the

compartment, such that when the valve is closed, a distal movement of the first sealing element is prevented and, when the valve is open, the distal movement of the first sealing element is allowed.

15. The system of any one of claims 1-9, further comprising a touch trigger mechanism between the first sealing element and the second sealing element, the touch trigger mechanism is configured to deploy when the first sealing element comes in contact with the second sealing element to prevent a distal movement of the first sealing element.

16. The system of any one of claims 1-9, further comprising a fill port disposed on a surface of the syringe barrel and being in fluid communication with the injection chamber.

17. The system of claim 16, wherein the fill port comprises:

a receptacle disposed on an outside surface of the syringe barrel and configured to receive a vial;

a flowpath connecting the receptacle and the injection chamber;

a self-sealing member configured to seal the flowpath; and

a puncture element disposed in the receptacle, the puncture element being configured to pierce through the self-sealing member to fluidly connect a vial comprising the injection agent and received in the receptacle with the injection chamber.

18. The system of claim 17, wherein the puncture element is moveable relative to the receptacle such that,

when the vial is received in the receptacle, the puncture element is moved toward the injection chamber to pierce the self-sealing member and to fluidly connect the vial with the injection chamber, and

when the vial is ~~medicament container~~ removed from the receptacle, the puncture element is moved away from the injection chamber, thereby allowing the self-sealing member to seal the flowpath.

19. The system of any one of claims 1-9, wherein a support element is disposed about a distal portion of the puncture element, the support element being moveable in relation to the puncture element and the syringe barrel.

20. The system of any one of claims 1-9, wherein the injection chamber comprises a first chamber and a second chamber, wherein a chamber sealing portion of the second sealing element fluidly isolates the first chamber from the second chamber, such that a movement of the chamber sealing portion fluidly connects the first and second chambers.

21. The system of any one of claims 1-9, wherein the injection chamber comprises a first chamber and a second chamber, wherein the first chamber and the second chamber are fluidly isolated from one another when the second sealing element is in an initial position and wherein a movement of the second sealing element fluidly connects the first and second chambers.

22. The system of any one of claims 1-9, wherein the second sealing element is configured to engage the first sealing element and to withdraw the first sealing element and the puncture element into the syringe barrel.

~~23. A method for treatment of an eye disease, the method comprises:~~

~~pre-inserting, into a sclera of a patient, a puncture element of an injection system, the injection system comprising:~~

~~a syringe barrel defining a lumen between a proximal end and a distal end;~~

~~a first sealing element moveably disposed within the lumen;~~

a second sealing element moveably disposed within the lumen proximal to the first sealing element, wherein the first sealing element and the second sealing element form a seal with the lumen and define an injection chamber between them;

the puncture element extending from a distal end of the first sealing element, the puncture element being in fluid communication with the injection chamber to deliver an injection agent from the injection chamber into a space in a tissue of a the patient; and

wherein one or more of the syringe barrel, the first sealing element, and the second sealing element are configured to prevent proximal movement of the first sealing element past a pre-selected location, while allowing the second sealing element to come in contact with the first sealing element;

advancing the puncture element through the sclera by applying a force onto the second sealing element, the force being sufficient to move the first sealing element in the a distal direction to advance the puncture element in the distal direction, without conveying the injection agent through the puncture element; and

maintaining the force onto the second sealing sliding element as the puncture element passes through the sclera and opens into a suprachoroidal space (SCS) such that the injection agent is conveyed from the injection chamber through the puncture element into the SCS, without further distal movement of the first sealing element.

24. The method of claim 23, wherein:

the first opposing force is due to backpressure exerted on the puncture element as the puncture element advances through the tissue; and

the second opposing force is due to backpressure exerted on the puncture element as the puncture element opens into the space in the tissue.

25. The method of claim 23, wherein:

the force applied on the second sealing element is sufficient to advance the first sealing element but is insufficient to convey the injection agent through the puncture element in response to the first opposing force; and

the force applied on the second sealing element is insufficient to advance the first sealing element but is sufficient to convey the injection agent through the puncture element in response to the second opposing force.

26. The method of claim 23, wherein the injection system comprises a unidirectional stop is disposed in the syringe barrel between the first sealing element and the second sealing element, the unidirectional stop being configured to prevent a proximal movement of the first sealing element past the unidirectional stop, while allowing the second sealing element to pass through the mechanical stop to contact the first sealing element.

27. The method of claim 26, wherein the unidirectional stop comprises a section of the syringe barrel having a reduced diameter, wherein the first sealing element has a diameter sufficiently larger than the reduced diameter such that the first sealing element cannot pass through the section while the second sealing element is configured to pass through the section to contact the first sealing element.

28. The method of claim 26, wherein the unidirectional stop comprises a portion of an inner surface of the syringe barrel having a friction coefficient sufficient to prevent a proximal movement of the first sealing element.

29. The method of claim 26, wherein the unidirectional stop comprises a mechanical stop.

30. The method of claim 26, wherein the unidirectional stop comprises a foldable stop is disposed between the first sealing element and the second sealing element, the foldable stop being configured to prevent a proximal movement of the first sealing element past the foldable stop and being configured to fold upon application of a force in a distal direction on the foldable stop to allow the second sealing element to pass through the foldable stop to contact the first sealing element.

~~31. The method of claim 23, wherein the first sealing element is shaped such that a frictional or sliding force on the first sealing element in the proximal direction is higher than a frictional or sliding force on the first sealing element in the distal direction and is higher that a force of insertion of the puncture element into the tissue.~~

~~32. The method of any one of claims 23-31, wherein, in a relaxed state, the first sealing element has a size that is between 1.01 to 2 times larger than a size of the lumen of the syringe barrel.~~

~~33. The method of any one of claims 23-31, wherein, in a relaxed state, the first sealing element has a size that is between 1.01 to 1.10 times larger than a size of the lumen of the syringe barrel.~~

~~34. The method of any one of claims 23-31, wherein an inner surface of the syringe barrel is modified to increase friction between the inner surface of the syringe barrel and the first sealing element.~~

~~35. The method of any one of claims 23-31, wherein the injection system further comprises a lock disposed distally of the first sealing element and configured to selectively lock the first sealing element in place.~~

~~36. The method of claim 35, wherein the lock comprises a sealed compartment defined in the lumen of the syringe barrel distal to the first sealing element, an incompressible substance inside the compartment, and a valve to release the incompressible substance from the compartment, such that when the valve is closed, a distal movement of the first sealing element is prevented and, when the valve is open, the distal movement of the first sealing element is allowed.~~

~~37. The method of any one of claims 23-31, wherein the injection system further comprises a touch trigger mechanism between the first sealing element and the second sealing element, the touch trigger mechanism is configured to deploy when the first sealing element comes in contact with the second sealing element to prevent a distal movement of the first sealing element.~~

38. The method of any one of claims 23-31, wherein the injection system further comprises a fill port disposed on a surface of the syringe barrel and being in fluid communication with the injection chamber.

39. The method of claim 2638, wherein the fill port comprises:

a receptacle disposed on an outside surface of the syringe barrel and configured to receive a vial;

a flowpath connecting the receptacle and the injection chamber;

a self-sealing member configured to seal the flowpath; and

a the puncture element disposed in the receptacle, the puncture element being configured to pierce through the self-sealing member to fluidly connect a vial received in the receptacle with the injection chamber.

40. The method of claim 39, wherein the puncture element is moveable relative to the receptacle such that,

when the vial is received in the receptacle, the puncture element is moved toward the injection chamber to pierce the self-sealing member and to fluidly connect the vial with the injection chamber,

when the medicament container removed from the receptacle, the puncture element is moved away from the injection chamber, thereby allowing the self-sealing member to seal the flowpath.

41. The method of any one of claims 23-31, wherein a support element is disposed about a distal portion of the puncture element, the support element being moveable in relation to the puncture element and the syringe barrel.

42. The method of any one of claims 23-31, wherein the injection chamber comprises a first chamber and a second chamber, wherein a chamber sealing portion of the second sealing element fluidly isolates the first chamber from the second chamber, such that a movement of the chamber sealing portion fluidly connects the first and second chambers.

~~43. The method of any one of claims 23-31, wherein the injection chamber comprises a first chamber and a second chamber, wherein the first chamber and the second chamber are fluidly isolated from one another when the second sealing element is in an initial position and wherein a movement of the second sealing element fluidly connects the first and second chambers.~~

~~44. The method of any one of claims 23-31, wherein the eye disease is age-related macular degeneration (AMD), diabetic macular edema (DME), glaucoma, retinal vein occlusion (RVO), uveitis, endophthalmitis, Stargardt disease, Leber Congenital Amaurosis (LCA), Retinitis Pigmentosa, or Choroideremia.~~

~~45. The method of claim 44, wherein the injection fluid comprises one or more injection agent formulations comprising a viral delivery vector comprising a gene of interest and a promoter selected to promote the gene of interest.~~

~~46. The method of claim 45, wherein the gene of interest is an anti-VEGFR2 gene.~~

~~47. The method of claim 46, wherein the delivery vector is an AAV vector.~~

~~48. The method of claim 47, wherein the promoter is a CAG promoter for the anti-VEGFR2 gene.~~

~~49. The method of claim 44, wherein the injection fluid comprises one or more injection agent formulations comprising an anti-VEGFR2 compound selected from a group consisting of bevacizumab, ranibizumab, aflibercept, Ramucirumab, disintegrins, anti-prostaglandins, tryptophanyl-tRNAsynthetase-derived polypeptides, Inosine monophosphate dehydrogenase (IMPDH) inhibitors and anti-PDGF to treat AMD; and corticosteroids to treat uveitis, chorioretinitis, or other inflammatory eye diseases; botulinum toxin for various ocular applications; tyrosine kinase inhibitors.~~

~~50.~~23. A kit for injection of an injection agent into a tissue comprising:

an injection system comprising:

a syringe barrel defining a lumen between a proximal end and a distal end;

a first sealing element moveably disposed within the lumen;

a second sealing element moveably disposed within the lumen proximal to the first sealing element, wherein the first sealing element and the second sealing element form a seal with the lumen and define an injection chamber between them;

a puncture element extending from a distal end of the first sealing element, the puncture element being in fluid communication with the injection chamber to deliver an injection agent from the injection chamber into a space in a tissue of a patient; ~~and~~

wherein one or more of the syringe barrel, the first sealing element, and the second sealing element are configured to prevent proximal movement of the first sealing element past a pre-selected location, while allowing the second sealing element to come in contact with the first sealing element~~,~~; ~~and~~

wherein the system is configured such that, when a force is applied on the second sealing element in a distal direction,

in response to a first opposing force, the first sealing element moves in the distal direction to advance the puncture element in the distal direction, without conveying the injection agent through the puncture element, ~~and~~

in response to a second opposing force, the first sealing element remains stationary and the injection agent is conveyed from the injection chamber through the puncture element; and

a volume of the injection fluid comprising one or more injection agent formulations.

~~51. The kit of claim 50, wherein:~~

~~the first opposing force is due to backpressure exerted on the puncture element as the puncture element advances through the tissue; and~~

~~the second opposing force is due to backpressure exerted on the puncture element as the puncture element opens into the space in the tissue.~~

52. The kit of claim 50, wherein:

the force applied on the second sealing element is sufficient to advance the first sealing element but is insufficient to convey the injection agent through the puncture element in response to the first opposing force; and

the force applied on the second sealing element is insufficient to advance the first sealing element but is sufficient to convey the injection agent through the puncture element in response to the second opposing force.

53. The kit of claim 50, wherein the injection system further comprises a unidirectional stop is disposed in the syringe barrel between the first sealing element and the second sealing element, the unidirectional stop being configured to prevent a proximal movement of the first sealing element past the unidirectional stop, while allowing the second sealing element to pass through the mechanical stop to contact the first sealing element.

54. The kit of claim 53, wherein the unidirectional stop comprises a section of the syringe barrel having a reduced diameter, wherein the first sealing element has a diameter sufficiently larger than the reduced diameter such that the first sealing element cannot pass through the section while the second sealing element is configured to pass through the section to contact the first sealing element.

55. The kit of claim 53, wherein the unidirectional stop comprises a portion of an inner surface of the syringe barrel having a friction coefficient sufficient to prevent a proximal movement of the first sealing element.

56. The kit of claim 53, wherein the unidirectional stop comprises a mechanical stop.

57. The kit of claim 53, wherein the unidirectional stop comprises a foldable stop is disposed between the first sealing element and the second sealing element, the foldable stop being configured to prevent a proximal movement of the first sealing element past the foldable stop

~~and being configured to fold upon application of a force in a distal direction on the foldable stop to allow the second sealing element to pass through the foldable stop to contact the first sealing element.~~

~~58. The kit of claim 50, wherein the first sealing element is shaped such that a frictional or sliding force on the first sealing element in the proximal direction is higher than a frictional or sliding force on the first sealing element in the distal direction and is higher that a force of insertion of the puncture element into the tissue.~~

~~59. The kit of any one of claims 50-58, wherein, in a relaxed state, the first sealing element has a size that is between 1.01 to 2 times larger than a size of the lumen of the syringe barrel.~~

~~60. The kit of any one of claims 50-58, wherein, in a relaxed state, the first sealing element has a size that is between 1.01 to 1.10 times larger than a size of the lumen of the syringe barrel.~~

~~61. The kit of any one of claims 50-58, wherein an inner surface of the syringe barrel is modified to increase friction between the inner surface of the syringe barrel and the first sealing element.~~

~~62.~~24. The kit of ~~any one of~~ claim~~s~~ 23~~50-58~~, wherein the injection system further comprises a lock disposed distally of the first sealing element and configured to selectively lock the first sealing element in place.

~~63. The kit of claim 62, wherein the lock comprises a sealed compartment defined in the lumen of the syringe barrel distal to the first sealing element, an incompressible substance inside the compartment, and a valve to release the incompressible substance from the compartment, such that when the valve is closed, a distal movement of the first sealing element is prevented and, when the valve is open, the distal movement of the first sealing element is allowed.~~

~~64.~~25. The kit of ~~any one of~~ claim~~s~~ 23~~50-58~~, wherein the injection system further comprises a touch trigger mechanism between the first sealing element and the second sealing element, the touch trigger mechanism is configured to deploy when the first sealing element comes in contact with the second sealing element to prevent a distal movement of the first sealing element.

~~65.~~26. The kit of ~~any one of~~ claim~~s~~ 23~~50-58~~, wherein the injection system further comprises a fill port disposed on a surface of the syringe barrel and being in fluid communication with the injection chamber.

~~66.~~27. The kit of claim 26~~65~~, wherein the fill port comprises:

a receptacle disposed on an outside surface of the syringe barrel and configured to receive a vial;

a flowpath connecting the receptacle and the injection chamber;

a self-sealing member configured to seal the flowpath; and

the~~a~~ puncture element disposed in the receptacle, the puncture element being configured to pierce through the self-sealing member to fluidly connect a vial received in the receptacle with the injection chamber.

~~67. The kit of claim 66, wherein the puncture element is moveable relative to the receptacle such that,~~

~~when the vial is received in the receptacle, the puncture element is moved toward the injection chamber to pierce the self-sealing member and to fluidly connect the vial with the injection chamber,~~

~~when the medicament container removed from the receptacle, the puncture element is moved away from the injection chamber, thereby allowing the self-sealing member to seal the flowpath.~~

~~68. The kit of any one of claims 50-58, wherein a support element is disposed about a distal portion of the puncture element, the support element being moveable in relation to the puncture element and the syringe barrel.~~

~~69.~~28. The kit of ~~any one of~~ claim~~s~~ 23~~50-58~~, wherein the injection chamber comprises a first chamber and a second chamber, wherein a chamber sealing portion of the second sealing element fluidly isolates the first chamber from the second chamber, such that a movement of the chamber sealing portion fluidly connects the first and second chambers.

~~70.~~29. The kit of ~~any one of~~ claim~~s~~ 23~~50-58~~, wherein the injection chamber comprises a first chamber and a second chamber, wherein the first chamber and the second chamber are fluidly isolated from one another when the second sealing element is in an initial position and wherein a movement of the second sealing element fluidly connects the first and second chambers.

~~71. The kit of any one of claims 50-58, wherein the injection agent is selected to treat an eye disease.~~

~~72. The kit of claim 71, wherein the eye disease is age-related macular degeneration (AMD), diabetic macular edema (DME), glaucoma, retinal vein occlusion (RVO), uveitis, endophthalmitis, Stargardt disease, Leber Congenital Amaurosis (LCA), Retinitis Pigmentosa, or Choroideremia.~~

~~73. The kit of claim 72, wherein the injection fluid comprises one or more injection agent formulations comprising a viral delivery vector comprising a gene of interest and a promoter selected to promote the gene of interest.~~

~~74. The kit of claim 73, wherein the gene of interest is an anti-VEGFR2 gene.~~

~~75. The kit of claim 74, wherein the delivery vector is an AAV vector.~~

~~76. The kit of claim 75, wherein the promoter is a CAG promoter for the anti-VEGFR2 gene.~~

~~77. The kit of claim 72, wherein the injection fluid comprises one or more injection agent formulations comprising an anti-VEGFR2 compound selected from a group consisting of~~

~~bevacizumab, ranibizumab, aflibercept, Ramucirumab, disintegrins, anti-prostaglandins, tryptophanyl-tRNAsynthetase-derived polypeptides, Inosine monophosphate dehydrogenase (IMPDH) inhibitors and anti-PDGF to treat AMD; and corticosteroids to treat uveitis, chorioretinitis, or other inflammatory eye diseases; botulinum toxin for various ocular applications; tyrosine kinase inhibitors.~~