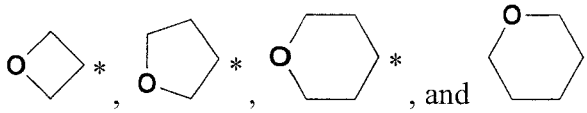
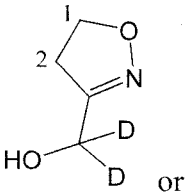
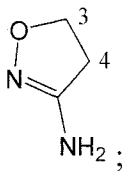
each D is independently C_1-C_6 alkyl or C_3-C_6 cycloalkyl, or two D, together with the carbon atom to which they are attached, form a C_3-C_6 carbocyclic ring or a saturated heterocycle selected from , wherein "*" denotes the position of the carbon atom to which the two D are attached;

X' is C_1-C_{10} alkyl, C_1-C_{10} alkyl substituted with C_3-C_6 cycloalkyl, C_3-C_6 cycloalkyl, aryl, aryl substituted with C_1-C_6 alkyl, or C_1-C_6 alkoxy, or X' is absent when A' and R', together with the two adjacent carbon atoms to which they are attached, form  or ;

n is 0, 1, or 2, provided that when X' is phenyl, n is not 0; and

each T is independently halogen, C_1-C_{10} alkyl, C_1-C_{10} alkyl substituted with C_3-C_6 cycloalkyl, C_3-C_6 cycloalkyl, or cyano.

In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound disclosed herein or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

In a further aspect of the present disclosure, there is provided a compound disclosed herein, or a pharmaceutically acceptable salt thereof, for use in treating, reducing a symptom of or reducing the risk of developing a retinal disease or disorder in which accumulation of A2E and/or lipofuscin in retinal tissue or VEGF signaling by RPE cells in response to oxidative stress is involved.

~~In a further aspect of the present disclosure, there is provided a compound disclosed herein, or a pharmaceutically acceptable salt thereof, for use in treating, reducing a symptom of or reducing the risk of developing a retinal disease or disorder associated with accumulation of A2E and/or lipofuscin in retinal tissue or VEGF signaling by RPE cells in response to oxidative stress.~~

In yet another aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating, reducing a symptom of or reducing the risk of developing a retinal

disease or disorder in which accumulation of A2E and/or lipofuscin in retinal tissue or VEGF signaling by RPE cells in response to oxidative stress is involved.

~~In another aspect of the present disclosure, there is provided a use of a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating, reducing a symptom of or reducing the risk of developing a retinal disease or disorder associated with accumulation of A2E and/or lipofuscin in retinal tissue or VEGF signaling by RPE cells in response to oxidative stress.~~

The present disclosure also relates to a pharmaceutical composition comprising a compound of each of the formulae described herein or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient or carrier.

The present disclosure also relates to a method of treating, reducing a symptom of or reducing the risk of developing a retinal disease or disorder in which accumulation of A2E and/or lipofuscin in retinal tissue or VEGF signaling by RPE cells in response to oxidative stress is involved.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this present disclosure belongs. In the case of conflict, the present specification, including definitions, will control. In the specification, the singular forms also include the plural unless the context clearly dictates otherwise. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present disclosure, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference. The references cited herein are not admitted to be prior art to the present disclosure. In addition, the materials, methods, and examples are illustrative only and are not intended to be limiting.

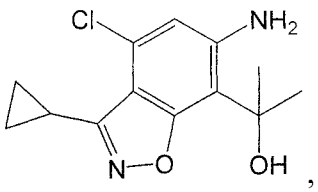
Other features and advantages of the present disclosure will be apparent from the following detailed description and claims.

BRIEF DESCRIPTION OF THE DRAWING

Figure 1 is a scheme showing the visual cycle.

DETAILED DESCRIPTION OF THE INVENTION

The invention provides heteroaryl compounds of the formulae described herein. These compounds possess desirable properties, such as improved potency (*e.g.*, more



or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

27. A compound of any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, for use in treating, reducing a symptom of or reducing the risk of developing a retinal disease or disorder in which accumulation of A2E and/or lipofuscin in retinal tissue or VEGF signaling by RPE cells in response to oxidative stress is involved.

~~28. A compound of claims 1 to 23, or a pharmaceutically acceptable salt thereof, for use in treating, reducing a symptom of or reducing the risk of developing a retinal disease or disorder associated with accumulation of A2E and/or lipofuscin in retinal tissue or VEGF signaling by RPE cells in response to oxidative stress.~~

~~29~~28. The compound of ~~any one of claims~~claim 27 ~~or 28~~, wherein the retinal disease or disorder is macular degeneration.

~~30~~29. The compound of ~~any one of claims~~claim 27 or 28, wherein the retinal disease or disorder is wet age-related macular degeneration (wet AMD), dry age-related macular degeneration (dry AMD), GA secondary to dry AMD, or Stargardt's disease.

~~31~~30. Use of a compound of any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating, reducing a symptom of or reducing the risk of developing a retinal disease or disorder in which accumulation of A2E and/or lipofuscin in retinal tissue or VEGF signaling by RPE cells in response to oxidative stress is involved.

~~32. Use of a compound of any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating, reducing a symptom of or reducing the risk of developing a retinal disease or disorder associated with accumulation of A2E and/or lipofuscin in retinal tissue or VEGF signaling by RPE cells in response to oxidative stress.~~

~~33~~31. The use of ~~any one of claims 31 or 32~~claim 30, wherein the retinal disease or disorder is macular degeneration.

~~34~~32. The use of ~~any one of claims 31 or 32~~claim 30 or 31, wherein the retinal disease or disorder is wet age-related macular degeneration (wet AMD), dry age-related macular degeneration (dry AMD), GA secondary to dry AMD, or Stargardt's disease.