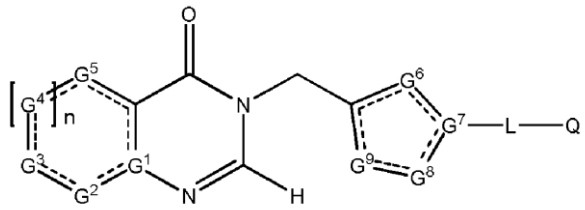
cord injury (Andrade et al., 2011) and intrathecal administration of TRPA1 antagonists attenuate cyclophosphamide-induced cystitis in rats with hyper-reflexia micturition (Chen et al., 2016).

It is therefore desirable to provide potent TRPA1 inhibitors.

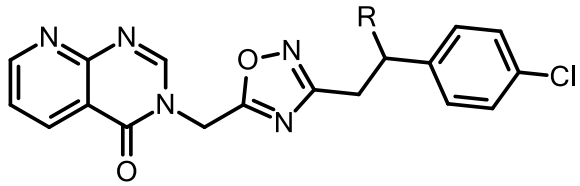
TRPA1 inhibitors of various structural classes are reviewed in S. Skerratt, Progress in Medicinal Chemistry, 2017, Volume 56, 81-115 and in D. Preti, G. Saponaro, A. Szallasi, Pharm. Pat. Anal. (2015) 4 (2), 75-94.

WO2017/060488 discloses compounds that are antagonists of TRPA1, having the generalized structural formula



The TRPA1 activity of Examples **28** and **29** bearing a tetrazolyl ring therein is not disclosed.

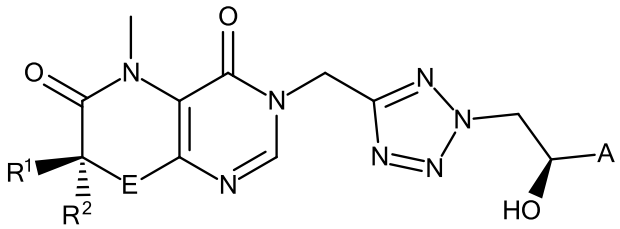
L. Schenkel, *et al*., J. Med. Chem. 2016, 59, 2794−2809 discloses quinazolinone-based TRPA1 antagonists including compounds of the generalized structural formula



of which compound **31**, wherein R is OH, is disclosed as having an antagonistic TRPA1 activity of IC_{50} 58 nM in a FLIPR assay and having an intrinsic clearance in human liver microsomes of <14 µL/min/kg.

SUMMARY

In one aspect, the present disclosure provides a compound according to formula (I)



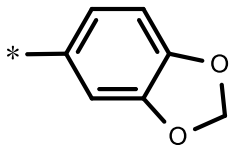
(I)

wherein

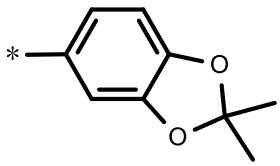
A is selected from the group consisting of phenyl, thiophenyl, benzothiophenyl or benzofuranyl, unsubstituted or substituted with one, two or three members of the group R^3 consisting of halogen, CN, C_{1-4}-alkyl, O-C_{1-4}-alkyl, C_{1-4}-fluoroalkyl, O-C_{1-4}-fluoroalkyl, C_{3-4}-cycloalkyl, O-C_{3-4}-cycloalkyl, C_{3-4}-cyclofluoroalkyl and O-C_{3-4}-cyclofluoroalkyl,

or

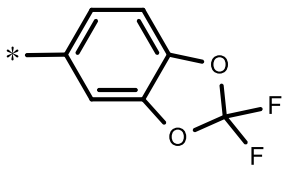
A is selected from the group consisting of



,



and



;

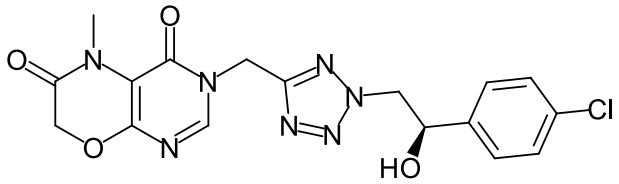
E is selected from the group consisting of O, S, SO, SO_2 and CH_2;

and

R^1 and R^2 are independently selected from the group consisting of H, C_{1-4}-alkyl, C_{1-4}-fluoroalkyl and halogen,

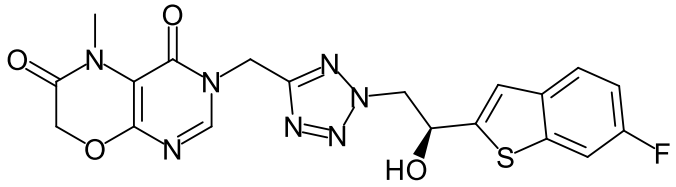
or R^1 and R^2 together with the carbon to which they are attached form a cyclopropyl or cyclobutyl ring.

In another aspect, the present disclosure provides the compound of formula



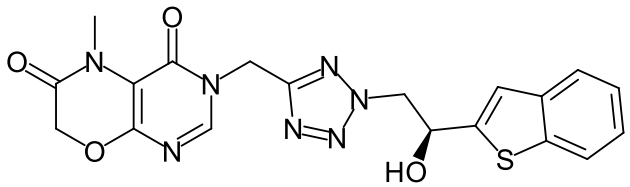
.

In another aspect, the present disclosure provides the compound of formula



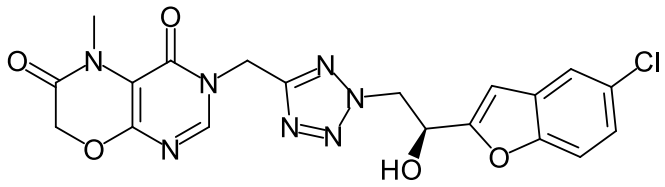
.

In another aspect, the present disclosure provides the compound of formula



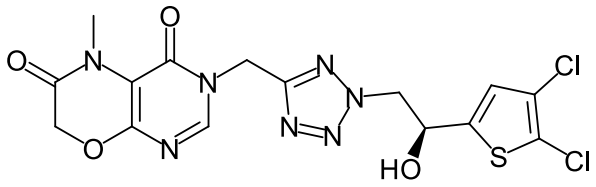
.

In another aspect, the present disclosure provides the compound of formula



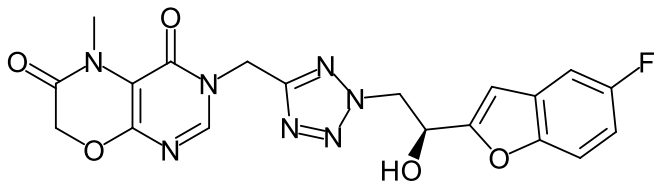
.

In another aspect, the present disclosure provides the compound of formula



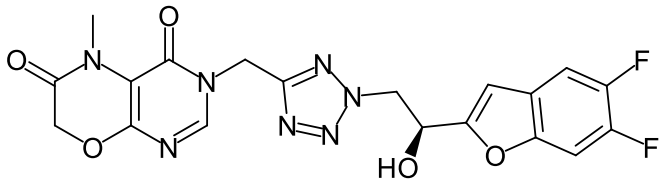
.

In another aspect, the present disclosure provides the compound of formula



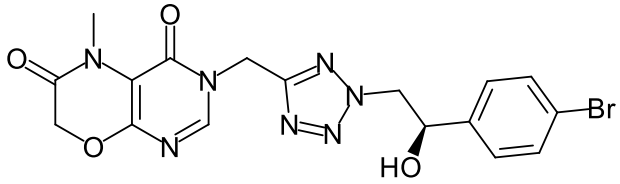
.

In another aspect, the present disclosure provides the compound of formula



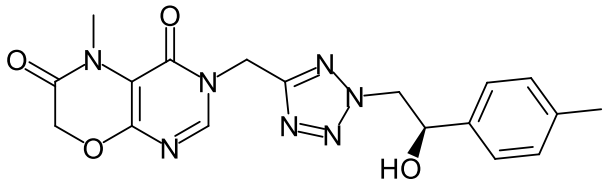
.

In another aspect, the present disclosure provides the compound of formula



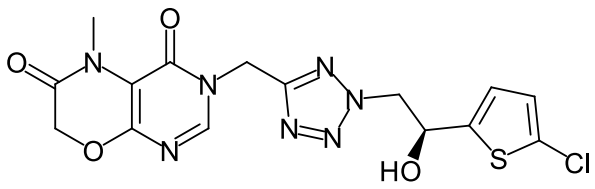
.

In another aspect, the present disclosure provides the compound of formula



.

In another aspect, the present disclosure provides the compound of formula



.

In another aspect, the present disclosure provides a salt, particularly a pharmaceutically acceptable salt, of a compound as described herein.

In another aspect, the present disclosure provides a pharmaceutical composition comprising at least one compound of formula I as described herein or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable excipients.

In another aspect, the present disclosure provides the compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, for use as a medicament.

In another aspect, the present disclosure provides the compound as described herein, or a pharmaceutically acceptable salt thereof, for use in the treatment or prevention of inflammatory airway diseases or fibrotic diseases or cough.

In another aspect, the present disclosure provides the compound as described herein, or a pharmaceutically acceptable salt thereof, for use in the treatment or prevention of idiopathic lung disease (IPF) or cough.

In another aspect, the present disclosure provides use of the compound as described herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prevention of inflammatory airway diseases or fibrotic diseases or cough.

In another aspect, the present disclosure provides use of the compound as described herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prevention of idiopathic lung disease (IPF) or cough.

DETAILED DESCRIPTION OF THE INVENTION