[0014] Additionally, a method of the present disclosure can be carried out using an effective dose of any one of the specific compounds disclosed in the application; see, for example, Table 1.

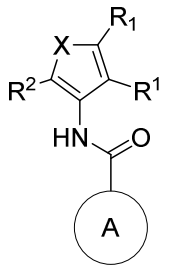
[0015] In various examples, the method of treatment of a tumor can further comprise administering an effective dose of a compound as disclosed herein via oral or intratumoral administration, or both.

[0016] In various examples, the method of treatment of a tumor can further comprise administering an effective dose of a compound as disclosed herein, wherein administering comprises administering the compound to the patient as an antibody-drug conjugate, or in a liposomal formulation.

[0017] In various examples, the method of treatment of a tumor can further comprise administering an effective dose of a compound as disclosed herein, further comprising administration of an effective dose of an immune-checkpoint targeting drug. For example, the immune-checkpoint targeting drug can be an anti-PD-L1 antibody, anti-PD-1 antibody, anti-CTLA-4 antibody, or an anti-4-1BB antibody.

[0018] In various examples, the method of treatment of a tumor can further comprise administering an effective dose of a compound as disclosed herein, further comprising administration of ionizing radiation or anticancer drugs.

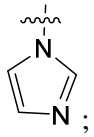
[0018a] In one aspect, the present disclosure relates to a compound of formula (IA):



(IA) ,

Wherein X is -N=C(R^1)-, or -C(R^1)=C(R^1)-; wherein each R^1 is independently H, F, Cl, or ethenyl which can be substituted; wherein at least one R^1 is ethynyl which can be substituted; R^2 is -C(O)OR; R is selected from the group consisting of H, and alkyl;

Ring A is pyridazinyl - substituted with



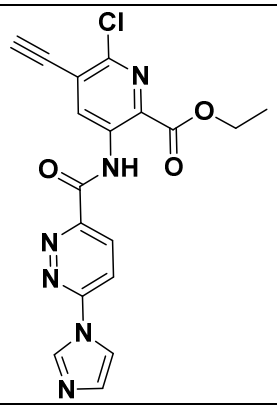
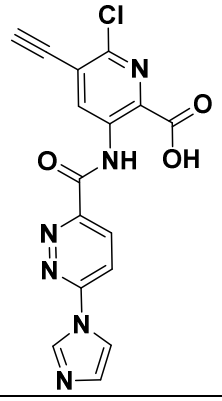
wherein a wavy line indicates a position of bonding; or a pharmaceutically acceptable salt thereof.

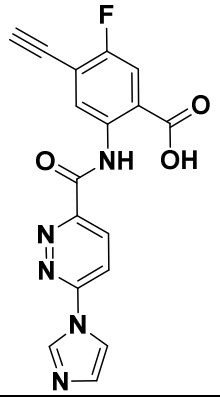
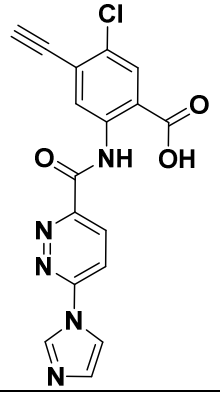
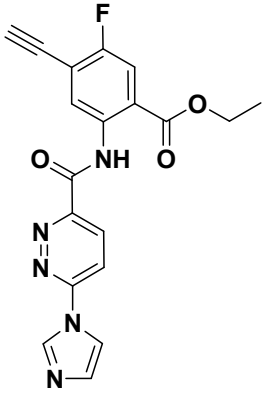
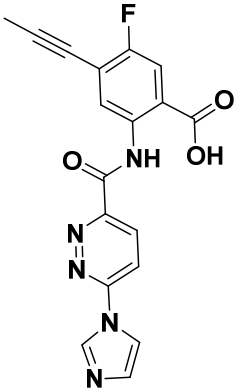
[0018b] In another aspect, the present disclosure relates to a pharmaceutical composition comprising a compound or pharmaceutically acceptable salt thereof as disclosed herein and a pharmaceutically acceptable carrier.

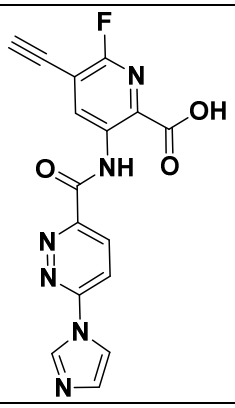
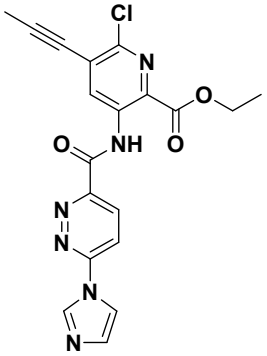
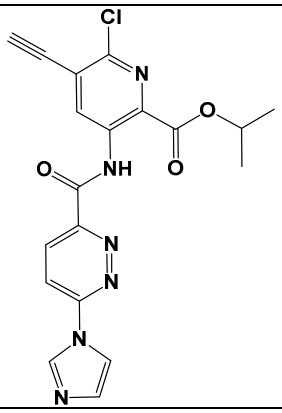
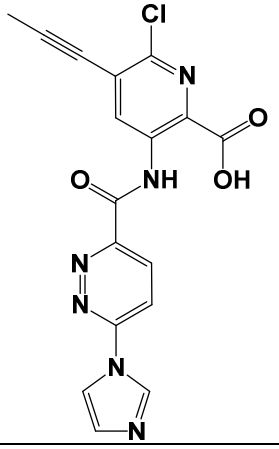
[0018c] In another aspect, the present disclosure relates to a use of a compound or pharmaceutically acceptable salt thereof as disclosed herein in the manufacture of a medicament for treating a tumor in a human patient.

[0018d] In another aspect, the present disclosure relates to a compound or pharmaceutically acceptable salt thereof as disclosed herein for use in therapy.

[0018e] In another aspect, the present disclosure relates to a compound or a pharmaceutically acceptable salt thereof selected from the following table:

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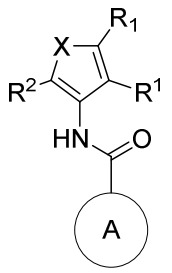
DETAILED DESCRIPTION

[0019] There is significant interest in the development of STING pathway agonists for diverse immuno-oncology applications. Most notably, STING pathway agonists have significant potential application as part of combination therapies involving immune-checkpoint targeting drugs, in patients that fail to respond to checkpoint blockade alone.

[0020] We have established a robust platform for identifying non-nucleotide small molecule STING agonists. This has been established using a primary assay involving a human THP-1 cell line carrying an IRF-inducible reporter with 5 copies of the IFN signaling response element. Counter screens, involving alternative reporter constructs, rodent cell-based assays, as well as cGAS and STING knock-out cell lines, are used to eliminate luciferase artifacts and ensure human-rodent cross species reactivity, as well as pathway selectivity.

WE CLAIM:

1. A compound of formula (IA):



(IA) ,

wherein

X is -N=C(R^1)-, or -C(R^1)=C(R^1)-;

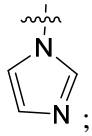
wherein each R^1 is independently H, F, Cl, or ethenyl which can be substituted;

wherein at least one R^1 is ethynyl which can be substituted;

R^2 is -C(O)OR;

R is selected from the group consisting of H, and alkyl;

Ring A is pyridazinyl, substituted with

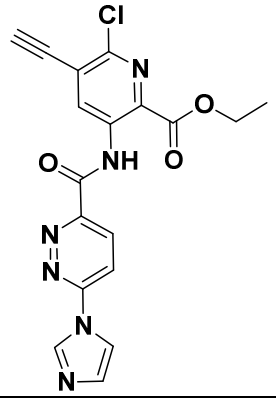
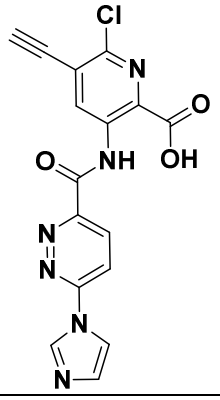
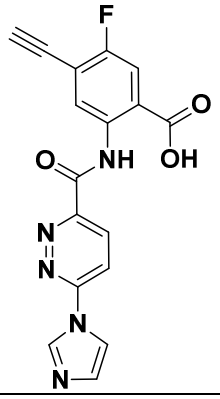
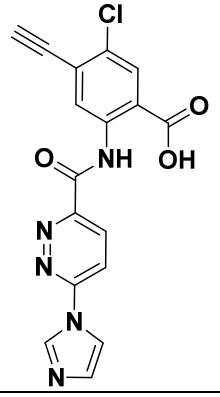


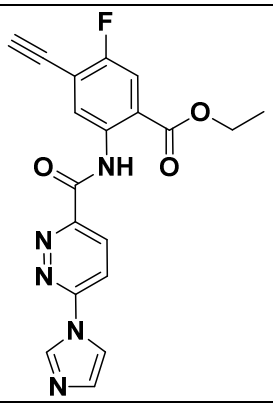
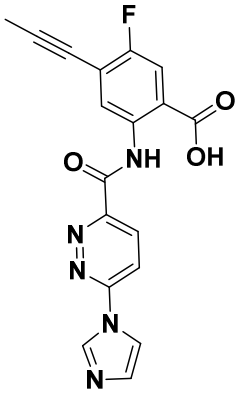
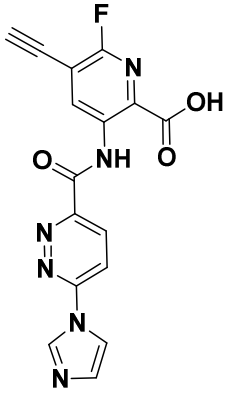
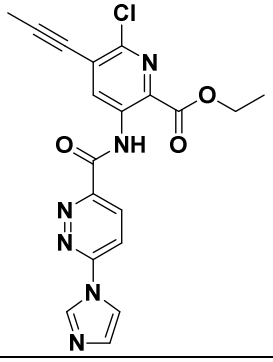
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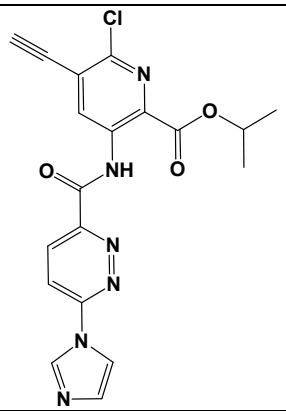
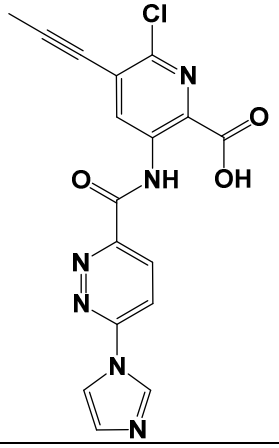
wherein a wavy line indicates a position of bonding;

or a pharmaceutically acceptable salt thereof.

2. A compound, or a pharmaceutically acceptable salt thereof, selected from the following table:

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3. A pharmaceutical composition comprising a compound or pharmaceutically acceptable salt thereof according to claim 1 or 2 and a pharmaceutically acceptable carrier.

4. Use of a compound or pharmaceutically acceptable salt thereof according to claim 1 or 2 in the manufacture of a medicament for treating a tumor in a human patient.

5. The use according to claim 4, wherein the compound stimulates expression of interferon genes in the patient.

6. The use according to claim 4 or 5, wherein the medicament is to be administered to the patient as an antibody-drug conjugate or in a liposomal formulation.

7. The use according to claim 4 or 5, wherein the medicament is to be administered in combination therapy with an immune-checkpoint targeting drug.

8. The use according to claim 7, wherein the immune-checkpoint targeting drug comprises an anti-PD-L1 antibody, anti-PD-1 antibody, anti-CTLA-4 antibody, or an anti-4-1BB antibody.

9. The use according to claim 4 or 5, wherein the medicament is to be administered in combination therapy with ionizing radiation or anticancer drugs.

10. A compound or pharmaceutically acceptable salt thereof according to claim 1 or 2 for use in therapy.