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C07D 401/14 (2006.01), **C07D 405/14** (2006.01),
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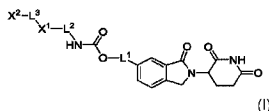
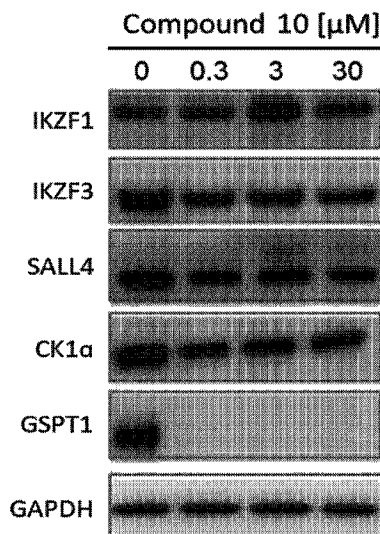
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(54) **Titre : COMPOSES D'ISOINDOLINONE**
(54) **Title: ISOINDOLINONE COMPOUNDS**

Figure 1A



(57) **Abrégé/Abstract:**

Disclosed herein are compound or pharmaceutically acceptable salts or stereoisomers thereof of formula (I). These compounds find use as modulators of cereblon, in particular in the treatment of abnormal cell growth in mammals, especially humans.

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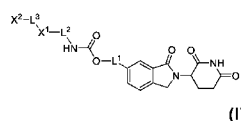
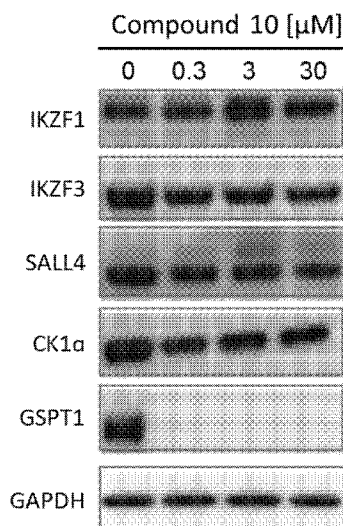
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(54) Title: ISOINDOLINONE COMPOUNDS

Figure 1A



(I)

(57) Abstract: Disclosed herein are compound or pharmaceutically acceptable salts or stereoisomers thereof of formula (I). These compounds find use as modulators of cereblon, in particular in the treatment of abnormal cell growth in mammals, especially humans.

[Continued on next page]

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DEMANDE OU BREVET VOLUMINEUX

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CECI EST LE TOME 1 DE 2
CONTENANT LES PAGES 1 À 335

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JUMBO APPLICATIONS/PATENTS

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THIS IS VOLUME 1 OF 2
CONTAINING PAGES 1 TO 335

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Isoindolinone Compounds

Cross-Reference

This application claims priority to Swiss Patent Application No. 00025/21 filed January 13, 2021, Swiss Patent Application No. 00386/21 filed April 14, 2021, Swiss Patent Application
5 No. 00655/21 filed June 4, 2021, and U.S. Provisional Application No. 63/281,049 filed November 18, 2021, the contents of each of which are incorporated herein by reference in their entireties.

Field of disclosure

The present disclosure relates to new compounds as modulators of cereblon. The disclosure
10 also relates to methods of preparation of these compounds, compositions comprising these compounds, and methods of using them in the treatment of abnormal cell growth in mammals, especially humans.

Background

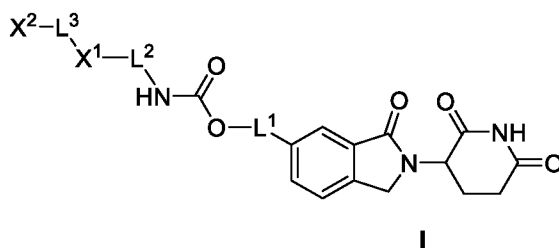
The ubiquitin proteasome system can be manipulated with different small molecules to trigger
15 targeted degradation of specific proteins of interest. Promoting the targeted degradation of pathogenic proteins using small molecule degraders is emerging as a new modality in the treatment of diseases. One such modality relies on redirecting the activity of E3 ligases such as cereblon (a phenomenon known as E3 reprogramming) using low molecular weight compounds, which have been termed molecular glues to promote the poly-ubiquitination and
20 ultimately proteasomal degradation of new protein substrates involved in the development of diseases. The molecular glues bind to both the E3 ligase and the target protein, thereby mediating an alteration of the ligase surface and enabling an interaction with the target protein. Particularly relevant compounds for the E3 ligase cereblon are the IMiD (immunomodulatory imide drugs) class including Thalidomide, Lenalidomide and
25 Pomalidomide. These IMiDs have been approved by the FDA for use in hematological cancers. However, compounds for efficiently targeting other diseases, in particular other types of cancers, are still required.

Summary of disclosure

It is therefore an object of the present disclosure to advance the state of the art of cereblon modulators and provide modulators for novel use in different diseases, in particular in different cancers.

- 5 In some embodiments, compounds are provided for use in therapy of solid tumors, such as for use in the therapy of lung cancer for example, non-small cell lung cancer (e.g., squamous cell lung cancer) and small cell lung cancer, breast cancer, and neuroendocrine cancer, e.g., neuroendocrine prostate cancer such as castration-resistant neuroendocrine prostate cancer (NEPC) and lung neuroendocrine tumors (Lu-NETs). In some embodiments,
- 10 compounds are provided for use in therapy of blood-borne (or haematological) cancers such as for use in the therapy of leukemias (e.g. acute myelogenous leukemia (AML)) and myelomas (e.g. multiple myeloma (MM)).

The present disclosure is in a first aspect directed towards a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula I:



15

wherein

- X^1 is linear or branched C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched C_{1-6} alkyl, linear or branched C_{1-6} heteroalkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-CHF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , C_{1-6} alkylamino, $-CN$, $-N(H)C(O)-C_{1-6}alkyl$, $-OC(O)-C_{1-6}alkyl$, $-OC(O)-C_{1-4}alkylamino$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , C_{1-4} alkoxy, C_{1-4} alkylhydroxy, $-CH_2F$, $-N(H)C(O)-O-C_{1-6}alkyl$, and $C(OH)(CF_3)$;
- 20

- or X^1 together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-6}alkyl$, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $C_{1-6}alkylamino$, $-CN$,
- 25

-N(H)C(O)-C₁₋₆alkyl, -OC(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy;

X² is H, C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and C₁₋₄ alkylhydroxy;

L¹ is a covalent bond, linear or branched C₁₋₆ alkyl;

L² is a covalent bond, linear or branched C₁₋₆ alkyl; and

L³ is a covalent bond, linear or branched C₁₋₆ alkyl, -O-, or -C₁₋₄ alkoxy, wherein linear or branched C₁₋₆ alkyl is unsubstituted or substituted with one or more of halogen.

In some embodiments,

X¹ is linear or branched C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, CF₃, CHF₂, CMeF₂, -O-CHF₂, -O-(CH₂)₂-OMe, OCF₃, C₁₋₆ alkylamino, -CN, -N(H)C(O)-C₁₋₆alkyl, -OC(O)-C₁₋₆alkyl, -OC(O)-C₁₋₄alkylamino, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, C₁₋₄ alkoxy and C₁₋₄ alkylhydroxy;

or X¹ together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched C₁₋₆ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, -N(H)C(O)-C₁₋₆alkyl, -OC(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy;

X² is H, C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and C₁₋₄ alkylhydroxy;

L¹ is a covalent bond, linear or branched C₁₋₆ alkyl;

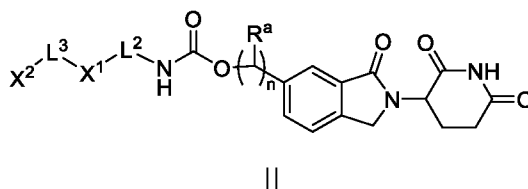
L² is a covalent bond, linear or branched C₁₋₆ alkyl; and

L³ is a covalent bond, linear or branched C₁₋₆ alkyl, -O-, -C₁₋₄ alkoxy.

In some embodiments of a compound of formula I, X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

10 In some embodiments of a compound of formula I, X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy.

15 In some embodiments, the present disclosure is directed towards a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula II:



wherein

20 X¹ is linear or branched C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, CF₃, CHF₂, CMeF₂, -O-CHF₂, -O-(CH₂)₂-OMe, OCF₃, C₁₋₆ alkylamino, -CN, -N(H)C(O)-C₁₋₆alkyl, -OC(O)-C₁₋₆alkyl, -OC(O)-C₁₋₄alkylamino, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, C₁₋₄ alkoxy and C₁₋₄ alkylhydroxy;

25 or X¹ together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₆ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, -N(H)C(O)-C₁₋

₆alkyl, -OC(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy;

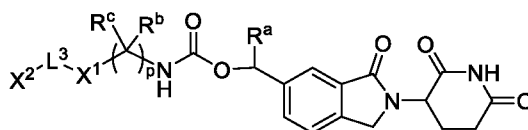
X² is H, C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and C₁₋₄ alkylhydroxy;

L² is a covalent bond, linear or branched C₁₋₆ alkyl; L³ is a covalent bond, linear or branched C₁₋₆ alkyl, -O-, -C₁₋₄ alkoxy;

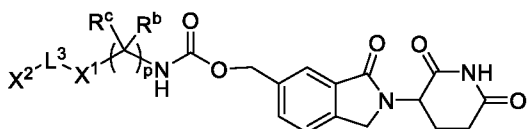
R^a is H or linear or branched C₁₋₄ alkyl, such as methyl or ethyl; and n is 1 or 2.

10 In some embodiments of a compound of formula II, n is 1.

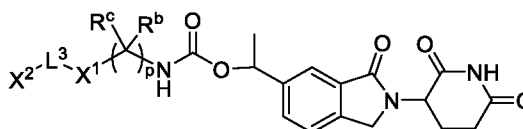
In some embodiments, the present disclosure is directed towards a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula III, such as IVa or IVb:



III



IVa



IVb

wherein

X¹ is linear or branched C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, CF₃, CHF₂, CMeF₂, -O-CHF₂, -O-(CH₂)₂-OMe, OCF₃, C₁₋₆ alkylamino, -CN, -N(H)C(O)-C₁₋₆alkyl, -OC(O)-C₁₋₆alkyl, -OC(O)-C₁₋₄alkylamino, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, C₁₋₄ alkoxy and C₁₋₄ alkylhydroxy;

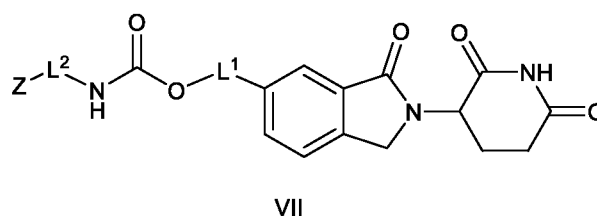
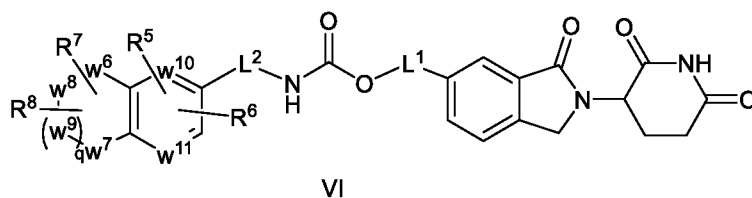
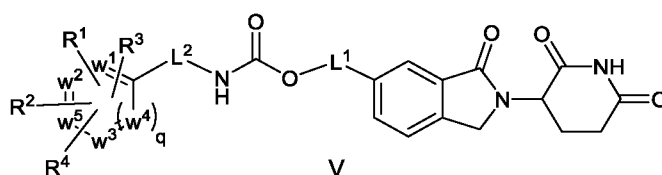
or X¹ together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₆

X² is H, C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and C₁₋₄ alkylhydroxy;

L³ is a covalent bond, linear or branched C₁₋₆ alkyl, -O-, -C₁₋₄ alkoxy;

R^a, R^b, R^c are independently of each other H, linear or branched C₁₋₄ alkyl, such as methyl; and p is 0 or 1.

In some embodiments, a compound of formula I is a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula V, VI or VII:



wherein

one or two of w^1, w^2, w^3, w^4, w^5 are independently of each other selected from C, N, S, and O, and the remaining of w^1, w^2, w^3, w^4, w^5 are C;

one or two of w^6, w^7, w^8, w^9 are selected from C and O and the remaining of w^6, w^7, w^8, w^9 are C; w^{10}, w^{11} are independently of each other selected from C and N; and q is 0 or 1;

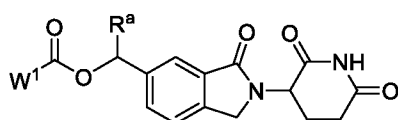
L¹ is a covalent bond, linear or branched C₁₋₆ alkyl; L² is a covalent bond, linear or branched C₁₋₆ alkyl;

R¹, R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃,
 5 OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula -L³-X², wherein L³ is a covalent bond, linear or branched C₁₋₆ alkyl, -O-, -C₁₋₄ alkoxy and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or
 10 substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and C₁₋₄ alkylhydroxy;

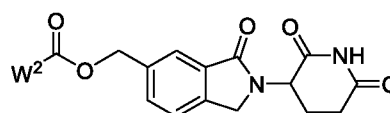
R⁵, R⁶, R⁷, R⁸ are independently of each other selected from H, linear or branched C₁₋₄ alkyl, such as methyl, and halogen, such as F or Cl, e.g. F;

Z is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, 4-8 membered heterocycloalkyl, wherein Z
 15 is unsubstituted or substituted with C₁₋₄ alkyl, C₆ aryl, C₆ aryloxy, 6 membered heteroaryl or CF₃; or Z together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with C₁₋₄ alkyl, C₆ aryl, C₆ aryloxy, 6 membered heteroaryl or CF₃; q is 0 or 1.

In some embodiments, the present disclosure is directed towards a compound or
 20 pharmaceutically acceptable salts or stereoisomers thereof of formula VIII, e.g. VIIIa

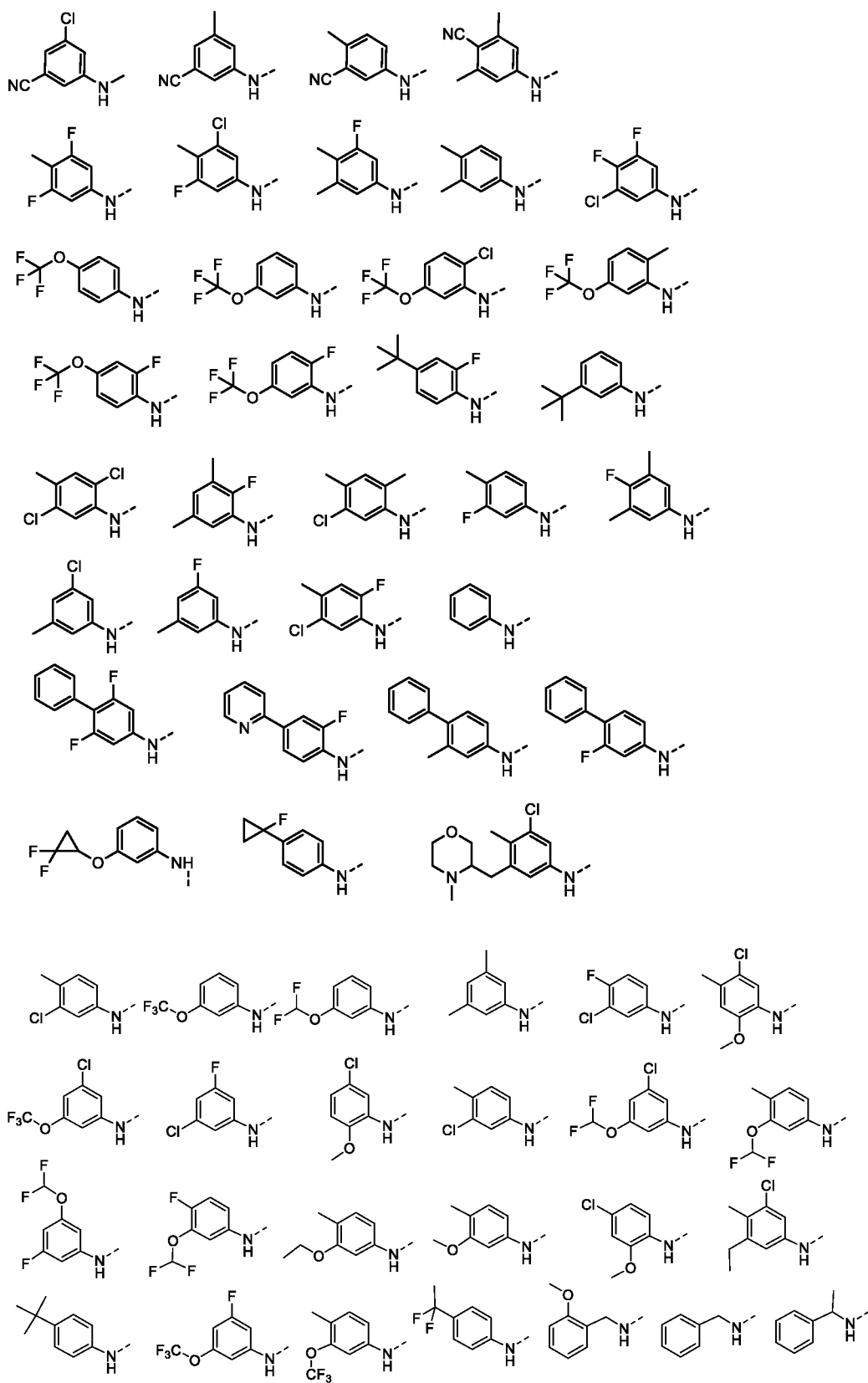


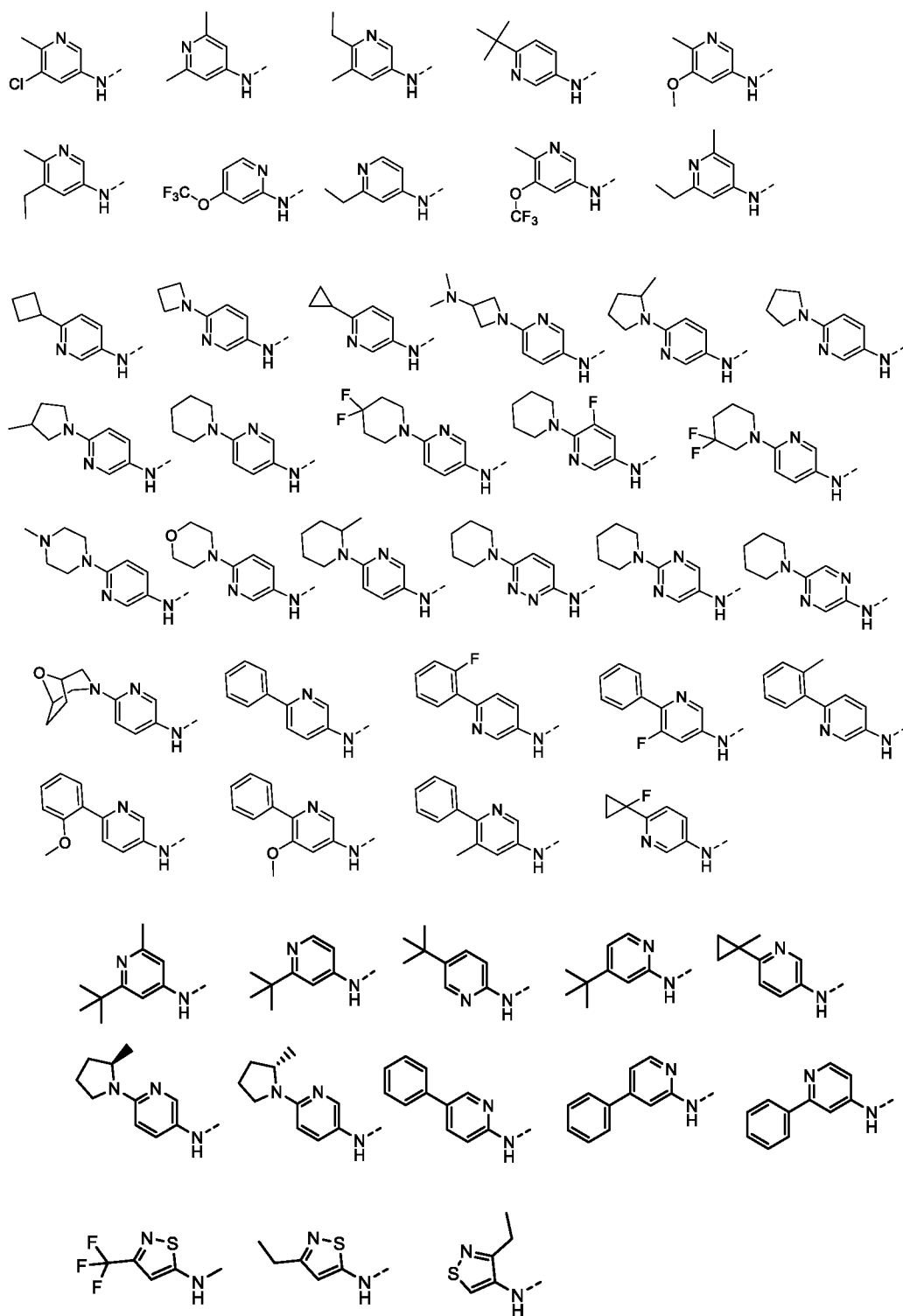
VIII



VIIIa

wherein R^a is H or methyl and W¹ and W² are selected from





- 5 In a second aspect, the disclosure is directed to a composition comprising a compound according to any one of the embodiments or pharmaceutically acceptable salts or stereoisomers thereof described herein.

In some embodiments, the composition further comprises a pharmaceutically acceptable carrier.

In some embodiments, the composition further comprises a second therapeutically active agent.

In a third aspect, the disclosure is directed to a composition according to any of the embodiments described herein, for use in therapy.

5 In a fourth aspect, some embodiments comprise a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula I-VIII, a pharmaceutical acceptable salt thereof or a composition described herein for use in the treatment of diseases associated or caused by GSPT1, in particular the treatment of cancer associated with GSPT1, such as solid cancers including but not limited to cancers of the bladder, bone, brain, breast, cervix, chest, colon,
 10 endometrium, esophagus, eye, head, kidney, liver, lymph nodes, lung, upper aerodigestive tract (including nasal cavity and paranasal sinuses, nasopharynx or cavum, oral cavity, oropharynx, larynx, hypopharynx and salivary glands), neck, ovaries, pancreas, prostate, rectum, skin, stomach, testis, throat, uterus, amyloidosis, neuroblastoma, meningioma, hemangiopericytoma, multiple brain metastase, glioblastoma multiforms, glioblastoma,
 15 brain stem glioma, poor prognosis malignant brain tumor, malignant glioma, recurrent malignant glioma, anaplastic astrocytoma, anaplastic oligodendroglioma, neuroendocrine tumor, e.g., neuroendocrine prostate cancer such as castration-resistant neuroendocrine prostate cancer (NEPC) and lung neuroendocrine tumors (Lu-NETs), rectal adenocarcinoma, colorectal cancer, including stage 3 and stage 4 colorectal cancer, unresectable colorectal
 20 carcinoma, metastatic hepatocellular carcinoma, Kaposi's sarcoma, malignant melanoma, malignant mesothelioma, malignant pleural effusion mesothelioma syndrome, peritoneal carcinoma, papillary serous carcinoma, gynecologic sarcoma, soft tissue sarcoma, scleroderma, cutaneous vasculitis, Langerhans cell histiocytosis, leiomyosarcoma, fibrodysplasia ossificans progressive, hormone refractory prostate cancer, resected high-risk
 25 soft tissue sarcoma, unrescectable hepatocellular carcinoma, fallopian tube cancer, androgen independent prostate cancer, androgen dependent stage IV non-metastatic prostate cancer, hormone-insensitive prostate cancer, chemotherapy -insensitive prostate cancer, papillary thyroid carcinoma, follicular thyroid carcinoma, medullary thyroid carcinoma, and leiomyoma; and blood bourne (liquid) or hematological cancers, including but not limited to
 30 leukemias, lymphomas, and myelomas, such as diffuse large B-cell lymphoma (DLBCL), B-cell immunoblastic lymphoma, small non-cleaved cell lymphoma, human lymphotropic virus-type 1 (HTLV-1) leukemia/lymphoma, adult T-cell lymphoma, peripheral T-cell lymphoma (PTCL), cutaneous T-cell lymphoma (CTCL), mantle cell lymphoma (MCL), Hodgkin's

lymphoma (HL), non-Hodgkin's lymphoma (NHL), AIDS-related lymphoma, follicular lymphoma, small lymphocytic lymphoma, T-cell/histiocyte rich large B-cell lymphoma, transformed lymphoma, primary mediastinal (thymic) large B-cell lymphoma, splenic marginal zone lymphoma, Richter's transformation, nodal marginal zone lymphoma, ALK-positive large B-cell lymphoma, indolent lymphoma (for example, DLBCL, follicular lymphoma, or marginal zone lymphoma), acute myelogenous leukemia (AML), acute lymphocytic leukemia (ALL), adult T-cell leukemia, chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), hairy cell leukemia, myelodysplasia, myeloproliferative disorders, chronic myelogenous leukemia (CML), acute monocytic leukemia (AMoL), myelodysplastic syndrome (MDS), human lymphotropic virus- type 1 (HTLV-1) leukemia, mastocytosis, B-cell acute lymphoblastic leukemia, Non-Hodgkin's Lymphoma, Hodgkin's Lymphoma, and multiple myeloma (MM).

Some embodiments comprise the compound or the composition according to any of the embodiments described herein for use in the treatment of breast cancer.

Some embodiments comprise the compound or the composition according to any of the embodiments described herein for use in the treatment of lung cancer, for example, non-small cell lung cancer (e.g., squamous cell lung cancer) and small cell lung cancer.

Some embodiments comprise the use of a compound or a composition according to any of the embodiments described herein for treating neuroendocrine prostate cancer, for example, castration-resistant neuroendocrine prostate cancer (NEPC).

Some embodiments comprise the use of a compound or a composition according to any of the embodiments described herein for treating lung neuroendocrine tumors (Lu-NETs).

Some embodiments comprise the compound or the composition according to any of the embodiments described herein for use in the treatment of acute myelogenous leukemia (AML) and multiple myeloma (MM).

In a fifth aspect, the disclosure is directed to a use of a compound or the composition according to any of the embodiments described herein for binding to cereblon comprising administering to a subject a therapeutically-effective amount of the composition.

Some embodiments comprise the use of a composition according to any of the embodiments described herein for treating cancer associated with GSPT1, such as solid cancers including but

not limited to cancers of the bladder, bone, brain, breast, cervix, chest, colon, endometrium, esophagus, eye, head, kidney, liver, lymph nodes, lung, upper aerodigestive tract (including nasal cavity and paranasal sinuses, nasopharynx or cavum, oral cavity, oropharynx, larynx, hypopharynx and salivary glands), neck, ovaries, pancreas, prostate, rectum, skin, stomach, testis, throat, uterus, amyloidosis, neuroblastoma, meningioma, hemangiopericytoma, multiple brain metastase, glioblastoma multiforms, glioblastoma, brain stem glioma, poor prognosis malignant brain tumor, malignant glioma, recurrent malignant glioma, anaplastic astrocytoma, anaplastic oligodendroglioma, neuroendocrine tumor, e.g., neuroendocrine prostate cancer such as castration-resistant neuroendocrine prostate cancer (NEPC) and lung neuroendocrine tumors (Lu-NETs), rectal adenocarcinoma, colorectal cancer, including stage 3 and stage 4 colorectal cancer, unresectable colorectal carcinoma, metastatic hepatocellular carcinoma, Kaposi's sarcoma, malignant melanoma, malignant mesothelioma, malignant pleural effusion mesothelioma syndrome, peritoneal carcinoma, papillary serous carcinoma, gynecologic sarcoma, soft tissue sarcoma, scleroderma, cutaneous vasculitis, Langerhans cell histiocytosis, leiomyosarcoma, fibrodysplasia ossificans progressive, hormone refractory prostate cancer, resected high-risk soft tissue sarcoma, unresectable hepatocellular carcinoma, fallopian tube cancer, androgen independent prostate cancer, androgen dependent stage IV non-metastatic prostate cancer, hormone-insensitive prostate cancer, chemotherapy -insensitive prostate cancer, papillary thyroid carcinoma, follicular thyroid carcinoma, medullary thyroid carcinoma, and leiomyoma, and blood bourne (liquid) or hematological cancers, including but not limited to leukemias, lymphomas, and myelomas, such as diffuse large B-cell lymphoma (DLBCL), B-cell immunoblastic lymphoma, small non-cleaved cell lymphoma, human lymphotropic virus-type 1 (HTLV-1) leukemia/lymphoma, adult T-cell lymphoma, peripheral T-cell lymphoma (PTCL), cutaneous T-cell lymphoma (CTCL), mantle cell lymphoma (MCL), Hodgkin's lymphoma (HL), non-Hodgkin's lymphoma (NHL), AIDS-related lymphoma, follicular lymphoma, small lymphocytic lymphoma, T-cell/histiocyte rich large B-cell lymphoma, transformed lymphoma, primary mediastinal (thymic) large B-cell lymphoma, splenic marginal zone lymphoma, Richter's transformation, nodal marginal zone lymphoma, ALK-positive large B-cell lymphoma, indolent lymphoma (for example, DLBCL, follicular lymphoma, or marginal zone lymphoma), acute myelogenous leukemia (AML), acute lymphocytic leukemia (ALL), adult T-cell leukemia, chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), hairy cell leukemia, myelodysplasia, myeloproliferative disorders, chronic myelogenous leukemia (CML), acute monocytic leukemia (AMoL), myelodysplastic syndrome (MDS), human lymphotropic virus-

type 1 (HTLV-1) leukemia, mastocytosis, B-cell acute lymphoblastic leukemia, Non-Hodgkin's Lymphoma, Hodgkin's Lymphoma, and multiple myeloma (MM).

Some embodiments comprise the use of a compound or a composition according to any of the embodiments described herein for treating breast cancer.

- 5 Some embodiments comprise the use of a compound or a composition according to any of the embodiments described herein for treating lung cancer, for example, non-small cell lung cancer (e.g., squamous cell lung cancer) and small cell lung cancer.

Some embodiments comprise the use of a compound or a composition according to any of the embodiments described herein for treating neuroendocrine prostate cancer, for example,
10 castration-resistant neuroendocrine prostate cancer (NEPC).

Some embodiments comprise the use of a compound or a composition according to any of the embodiments described herein for treating lung neuroendocrine tumors (Lu-NETs).

Some embodiments comprise the use of a compound or a composition according to any of the embodiments described herein for treating acute myelogenous leukemia (AML) and
15 multiple myeloma (MM).

In a sixth aspect, the disclosure is directed to a method of treating cancer in a subject, comprising administering to a subject a therapeutically effective amount of the compound or the composition of any of the embodiments as described herein.

In some embodiments, the method comprises a compound according to any of the
20 embodiments as described herein or pharmaceutically acceptable salts or stereoisomers thereof that binds to cereblon.

In a seventh aspect, the disclosure is directed to a method of treating a Myc-driven cancer in a subject in need thereof, comprising administering the subject a therapeutically effective amount of the compound or a composition as described herein. In an eighth aspect, the
25 disclosure is directed to a method of degrading GSPT1 in a subject suffering from cancer, comprising administering the subject a therapeutically effective amount of a compound or a composition as described herein.

In a ninth aspect, the disclosure is directed to a method of reducing the level of GSPT1 in a subject suffering from cancer, comprising administering the subject a therapeutically effective amount of a compound or a composition as described herein.

Brief description of the figures

5 Figure 1: Figure 1A shows that cells treated with 0.3 μ M compound 10 induces complete degradation of GSPT1, while no induction of degradation of IKZF1, IKZF3, SALL4, CK1alpha was observed at concentrations up to 30 μ M. Figure 1B shows that based on a mass spectrometry-based proteomics analysis of a cancer cell line treated with compound 10, GSPT1 was the most statistically significant downregulated protein (x-axis represents the
10 protein fold-change ($\log_2$); y-axis represents the p-value, which is an assessment of whether the observation is a result of change or the result of a random occurrence, with smaller p-values suggesting stronger evidence of an actual change).

Figure 2: Figure 2A shows that NSCLC cell lines expressing high levels of N-Myc (NCI-H1155 represented as filled triangles, ABC-1 represented as filled rhombi) were highly sensitive to
15 treatment with compound 10, when compared to the cell lines expressing low levels of N-Myc (EBC-1 represented as empty triangles, NCI-H2023 represented as empty circles). GSPT1 was degraded by compound 10 after six hours of treatment in high N-Myc NCI-H1155 and ABC-1 cells with a DC50 of 3 nM and 22 nM, respectively (x-axis represents μ M concentration of compound 10; y-axis represents the viability in %). In both cell lines, we
20 observed complete degradation of GSPT1, Figure 2B illustrates that compound 10 degrades GSPT1 in a concentration dependent manner (x-axis represents μ M concentration of compound 10; y-axis represents relative levels of GSPT1)

Figure 3: Figure 3A shows that oral administration of compound 10 in a N-Myc-driven mouse xenograft model using the human cell line NCI-H1155 led to tumor growth inhibition (with
25 no body weight loss observed). At a dose of 1 mg/kg once daily, tumor growth was suppressed for two weeks. At a dose of 3 mg/kg once daily or 6 mg/kg dosed for five days on and nine days off, tumor size decreased, became undetectable by day eight and remained so until the end of the study at day 21 (x-axis represents days post treatment initiation [days]; y-axis represents tumor volume [mm^3], mean $\pm$ SEM; empty circles O: vehicle, PO, QD; filled
30 squares, 1 mg/kg, PO, QD; filled triangles, 3 mg/kg PO, QD; filled triangles inverted, 6 mg/kg, PO, 5 on – 9 off; filled rhombi, gemcitabine 40 mg/kg IP, Q4Dx5).

Figure 3B shows complete degradation of GSPT1 in tumors of mice treated with compound 10 at all three dose levels as compared to mice treated with vehicle control (from left to right: vehicle, 1 mg/kg, 3 mg/kg, 6 mg/kg).

Figures 3C and 3D show that oral administration of compound 10 in a N-Myc-driven mouse xenograft model using the human cell line NCI-H1770 and NCI-H526, respectively, led to tumor growth inhibition (with no body weight loss observed). At a dose of 3 mg/kg once daily or 6 mg/kg dosed for five days on and nine days off, tumor size decreased and remained so until the end of the study (x-axis represents days post treatment initiation [days]; y-axis represents tumor volume [mm³], mean $\pm$ SEM; empty circle O: vehicle, PO, QD; filled triangles, 3 mg/kg PO, QD; filled triangles inverted, 6 mg/kg, PO, 5 on – 9 off; filled rhombi, cisplatin 6 mg/kg IP, QWx3).

Detailed description of the disclosure

Unless specified otherwise the following general definitions apply to all compounds of the disclosure according to the description.

The term "compound of the disclosure" as used herein, refers to compounds represented by formulae I to VIII (including pharmaceutically acceptable salts and stereoisomers thereof) and any of the specific examples disclosed herein. References to any compound of any formula herein includes also pharmaceutically acceptable salts or stereoisomers thereof.

A "subject" to which administration is contemplated includes, but is not limited to, humans (*e.g.*, a pediatric subject (*e.g.*, infant, child, adolescent) or adult subject (*e.g.*, a young adult, a middle-aged adult, or a senior adult)) and/or a non-human animal, *e.g.*, a mammal such as primates (*e.g.*, cynomolgus monkeys, rhesus monkeys), cattle, pigs, horses, sheep, goats, rodents, cats, and/or dogs. In certain embodiments, the subject is a human. In certain embodiments, the subject is a non-human animal. The terms "patient" and "subject" are used interchangeably herein.

It is understood that "independently of each other" means that when a group is occurring more than one time in any compound, its definition on each occurrence is independent from any other occurrence.

It is further understood that a dashed line (or a wave being transverse to a bond) or a solid line without attachment, such as $-C_{1-4}$ alkyl, depicts the site of attachment of a residue (i.e. a partial formula).

It is further understood that the abbreviations "C" and "N" are representative for all possible degrees of saturation, which typically do not result in radicals, nitrenes or carbenes, i.e. N includes $-NH-$ and $-N=$, C includes $-CH_2-$ and $=CH-$. In addition, "C" as an atom in an aromatic or heteroaromatic ring which has a substituent R^x at any suitable position, includes $=CH-$ as well as $=CR^x-$.

The term "saturated" in reference to ring systems refers to a ring having no double or triple bonds. The term "partially unsaturated" in reference to ring systems refers to a ring that includes at least one double or triple bond, but does not include aromatic systems.

The term "aromatic" refers to monocyclic or polycyclic (e.g. bicyclic) ring systems, which show some or complete conjugation or delocalization of their electrons. Aromatic monocyclic rings, such as aryl or heteroaryl rings as defined herein, include phenyl, pyridinyl, furyl and the like. Aromatic polycyclic rings, such as aryl or heteroaryl rings as defined herein, refer to ring systems, wherein at least one ring is an aromatic ring, and thus include (i) aromatic ring systems, wherein an aromatic ring is fused to one or more aromatic rings, such as in e.g. naphthyl, indolyl, benzimidazolyl, and the like (also referred to as fully aromatic ring systems), and (ii) aromatic ring systems, wherein an aromatic ring is fused to one or more non-aromatic rings, such as in e.g. indanyl, indenyl, phthalimidyl, naphthimidyl, phenanthridinyl, tetrahydronaphthyl, 1,4-dihydronaphthyl, and the like (also referred to as partially aromatic ring systems).

The term "non-aromatic" refers to (i) fully saturated rings such as monocyclic rings, e.g. cyclohexyl, and bicyclic rings, e.g. tetrahydronaphthyl, and (ii) partially unsaturated rings such as monocyclic rings, e.g. cyclohexenyl, and bicyclic rings, e.g. 1,4-dihydronaphthyl.

The term " C_{6-10} aryl" includes both fully aromatic C_{6-10} aryl and partially aromatic C_{6-10} aryl having 6, 7, 8, 9, or 10 ring atoms and includes monocycles and fused bicycles. Examples of fully aromatic C_{6-10} aryl include e.g. phenyl (fully aromatic C_6 aryl), naphthyl (fully aromatic C_{10} aryl). Examples of partially aromatic C_{6-10} aryl include e.g. indenyl (partially aromatic C_9 aryl), 2,3-dihydroindenyl (partially aromatic C_9 aryl), 1, 2, 3, 4-tetrahydronaphthyl (partially aromatic C_{10} aryl). In some embodiments for group X^1 , C_{6-10} aryl is phenyl, 2,3-

dihydroindenyl. In some embodiments for group X^2 , C_{6-10} aryl is phenyl. The term “- C_{1-6} alkyl- C_{6-10} aryl” refers to $-L^2-X^1-$ or L^3-X^2- with L^2 , L^3 being a C_{1-6} alkyl group and X^1 , X^2 being a C_{6-10} aryl, and thus refers to a C_{6-10} aryl, which is linked through a C_{1-6} alkyl group as defined herein to its neighbouring group. The term “- C_{1-6} alkoxy- C_{6-10} aryl” refers to $-L^2-X^1-$ or L^3-X^2- with L^2 , L^3 being a C_{1-6} alkoxy group and X^1 , X^2 being a C_{6-10} aryl, and thus refers to a C_{6-10} aryl, which is linked through a C_{1-6} alkoxy group as defined herein to its neighbouring group. The term “-O- C_{6-10} aryl” or “ C_{6-10} aryloxy” refers to $-L^2-X^1-$ or L^3-X^2- with L^2 , L^3 being -O- and X^1 , X^2 being a C_{6-10} aryl, and thus refers to a C_{6-10} aryl, which is linked through a -O- group to its neighbouring group. The C_{6-10} aryl group may be unsubstituted or substituted with C_{1-4} alkyl, such as methyl, ethyl, t-butyl, fluorinated C_{1-4} alkyl, such as $-CF_3$, $-C(CH_3)_2$, C_{1-4} alkoxy, such as methoxy, ethoxy, fluorinated C_{1-4} alkoxy, such as $-OCF_3$, $-OCHF_2$, CN, $-N(Me)_2$, halogen, such as F, Cl, or Br, such as F or Cl.

In some embodiments for X^1 , a C_{6-10} aryl group refers to a fully aromatic ring system, e.g. phenyl, which is unsubstituted or substituted with C_{1-4} alkyl, such as methyl, ethyl, t-butyl, fluorinated C_{1-4} alkyl, such as $-C(CH_3)_2$, C_{1-4} alkoxy, such as methoxy, ethoxy, fluorinated C_{1-4} alkoxy, such as $-OCF_3$, $-OCHF_2$, CN, halogen, such as F or Cl, In some embodiments for X^1 , a C_{6-10} aryl group refers to a partially aromatic ring system, e.g. 2,3-dihydroindenyl, which is unsubstituted or substituted with C_{1-4} alkyl, such as methyl, ethyl, t-butyl, or halogen, such as F or Cl,

In some embodiments for X^2 , a C_{6-10} aryl group refers to a fully aromatic ring system, e.g. phenyl, which is unsubstituted or substituted with C_{1-4} alkyl, such as methyl, ethyl, C_{1-4} alkoxy, such as methoxy, ethoxy, halogen, such as F, Cl, or Br, such as F or Cl, e.g. F.

The term “5-10 membered heteroaryl” refers to a fully or partially aromatic ring system in form of monocycles or fused bicycles having 5, 6, 7, 8, 9, 10 ring atoms selected from C, N, O, and S, such as C, N, and O, or C, N, and S, with the number of N atoms being e.g. 0, 1, 2 or 3 and the number of O and S atoms each being 0, 1 or 2. In some embodiments a 5-10 membered heteroaryl refers to a fully aromatic ring system having 5, 6, 7, 8, 9, 10, such as 5 or 6, e.g. 6 ring atoms selected from C and N, with the number of N atoms being 1, 2 or 3, such as 1 or 2. In some embodiments a 5-10 membered heteroaryl refers to a fully aromatic ring system having 5, 6, 7, 8, 9, 10, such as 5 or 6, e.g. 5 ring atoms selected from C, N, O, S with the number of N, S and O atoms each being independently 0, 1 or 2. In some embodiments the total number of N, S and O atoms is 2. In some embodiments a 5-10

membered heteroaryl refers to a fully aromatic ring system having 5 ring atoms selected from C, N, S with the number of N and S atoms each being independently 0 or 1. In some embodiments the total number of N and S atoms is 2. In some embodiments a 5-10 membered heteroaryl refers to a fully aromatic ring system having 6 ring atoms selected from C and N, with the number of N atoms being 1 or 2. In other embodiments a 5-10 membered heteroaryl refers to a partially aromatic ring system having 9 or 10 ring atoms selected from C, N and O, with the number of O atoms being 1, 2 or 3, such as 1 or 2, and the number of N atoms being 1 or 2, such as 1. In some embodiments, examples of "5-10 membered heteroaryl" include furyl, imidazolyl, isoxazolyl, oxazolyl, pyrazinyl, pyrazolyl (pyrazyl), pyridazinyl, pyridinyl, pyrimidinyl, pyrrolyl, thiophenyl, thiazolyl, thienyl, indolyl, quinazolinyl, oxazoliny, isoxazoliny, indazoliny, isothiazolyl, 1,3-benzodioxolyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, benzodihydropyrane, 1,2,3,4-tetrahydronaphthyl, 2,3-dihydroindenyl and the like. In some embodiments, examples of "5-10 membered heteroaryl" include 5-membered heteroaryl, such as isothiazole, 6-membered heteroaryl, such as pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, 9-membered heteroaryl, such as 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, and 10-membered heteroaryl, such as benzodihydropyrane (chromane), dihydropyrano-pyridine. The term "-C₁₋₆ alkyl 5-10 membered heteroaryl" refers to -L²-X¹- or L³-X²- with L², L³ being a C₁₋₆ alkyl group and X¹, X² being a 5-10 membered heteroaryl, and thus refers to a 5-10 membered heteroaryl, which is linked through a C₁₋₆ alkyl group as defined herein to its neighbouring group. The term "-C₁₋₆ alkoxy 5-10 membered heteroaryl" refers to -L²-X¹- or L³-X²- with L², L³ being a C₁₋₆ alkoxy group and X¹, X² being a 5-10 membered heteroaryl, and thus refers to a 5-10 membered heteroaryl, which is linked through a C₁₋₆ alkoxy group as defined herein to its neighbouring group. The term "-O-5-10 membered heteroaryl" refers to -L²-X¹- or L³-X²- with L², L³ being -O- and X¹, X² being a 5-10 membered heteroaryl, and thus refers to a 5-10 membered heteroaryl, which is linked through a -O- group to its neighbouring group. The 5-10 membered heteroaryl group may be unsubstituted or substituted with C₁₋₄ alkyl, such as methyl, ethyl, t-butyl, fluorinated C₁₋₄ alkyl, such as -CF₃, -C(CH₃)F₂, C₁₋₄ alkoxy, such as methoxy, ethoxy, fluorinated C₁₋₄ alkoxy, such as -OCF₃, -OCHF₂, CN, -N(Me)₂, halogen, such as F, Cl, or Br, such as F or Cl. In some embodiments, the 5-10 membered heteroaryl

group may be unsubstituted or substituted with C₁₋₄ alkyl, such as methyl, ethyl, t-butyl, fluorinated C₁₋₄ alkyl, such as -CF₃, C₁₋₄ alkoxy, such as methoxy, ethoxy, halogen, such as F or Cl.

In some embodiments for X¹, a 5-10 membered heteroaryl refers to a fully aromatic ring system having 5 ring atoms selected from C, N and S with the number of N and S atoms being independently of each other 0 or 1, e.g. 1 or a fully aromatic ring system having 6 ring atoms selected from C and N, with the number of N atoms being 1 or 2 or a partially aromatic ring system having 9 or 10 ring atoms selected from C, N and O, with the number of O atoms being 1 or 2 and the number of N atoms being 1. In some embodiments for X¹, a 5-10 membered heteroaryl refers to isothiazole, phenyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine.

In some embodiments for X² a 5-10 membered heteroaryl refers to a fully aromatic ring system having 6 ring atoms selected from C and N, with the number of N atoms being 1 or 2, such as 1. In some embodiments for X² a 5-10 membered heteroaryl refers to pyridinyl.

The term "C₃₋₈ cycloalkyl" refers to a non-aromatic, i.e. saturated or partially unsaturated alkyl ring system, such as monocycles, fused bicycles, bridged bicycles or spirobicycles, containing 3, 4, 5, 6, 7, or 8 carbon atoms. The term "C₃₋₆ cycloalkyl" refers to a non-aromatic, i.e. saturated or partially unsaturated alkyl ring system, such as monocycles, fused bicycles, bridged bicycles or spirobicycles, containing 3, 4, 5, or 6 carbon atoms. Examples of "C₃₋₈ cycloalkyl" include monocycles, such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bridged bicycles, such as bicyclo[1.1.1]pentyl, bicyclo[2.1.1]hexyl, fused bicycles, such as bicyclo[3.1.0]hexyl. The C₃₋₆ cycloalkyl group may be unsubstituted or substituted with C₁₋₄ alkyl, such as methyl, ethyl, t-butyl, fluorinated C₁₋₄ alkyl, such as -CF₃, -C(CH₃)F₂, C₁₋₄ alkoxy, such as methoxy, ethoxy, fluorinated C₁₋₄ alkoxy, such as -OCF₃, -OCHF₂, CN, -N(Me)₂, halogen, such as F, Cl, or Br, such as F or Cl. In some embodiments the C₃₋₆ cycloalkyl group may be unsubstituted or substituted by e.g. one or more of C₁₋₄ alkyl, such as methyl and halogen, such as F. The term "-C₁₋₄ alkyl-C₃₋₆ cycloalkyl" refers to -L²-X¹- or L³-X²- with L², L³ being a C₁₋₄ alkyl group and X¹, X² being C₃₋₆ cycloalkyl as defined herein and refers to a C₃₋₆ cycloalkyl, which is linked through a C₁₋₆ alkyl group as defined herein to its neighbouring

group. The term “-O-C₃₋₆ cycloalkyl” refers to -L²-X¹- or L³-X²- with L², L³ being -O- and X¹, X² being C₃₋₆ cycloalkyl as defined herein and refers to a C₃₋₆ cycloalkyl, which is linked through -O- to its neighbouring group. The term “-C₁₋₄ alkoxy-C₃₋₆ cycloalkyl” refers to -L²-X¹- or L³-X²- with L², L³ being a C₁₋₄ alkoxy group and X¹, X² being C₃₋₆ cycloalkyl as defined herein and refers to a C₃₋₆ cycloalkyl, which is linked through a C₁₋₆ alkoxy group as defined herein to its neighbouring group. In some embodiments for X¹, a C₃₋₆ cycloalkyl refers to cyclopropyl, cyclopentyl, cyclohexyl. In some embodiments for X², a C₃₋₆ cycloalkyl refers to cyclopropyl, cyclobutyl.

The term “4-8 membered heterocycloalkyl” refers to a non-aromatic, i.e. saturated or partially unsaturated ring system having 4, 5, 6, 7 or 8 ring atoms (of which at least one is a heteroatom), which ring atoms are selected from C, N, O, and S, such as C, N, and O, the number of N atoms being 0, 1, or 2 and the number of O and S atoms each being 0, 1, or 2. In some embodiments the term “4-8 membered heterocycloalkyl” comprises saturated or partially unsaturated monocycles, fused bicycles, bridged bicycles or spirobicycles. In some embodiments the term “4-8 membered heterocycloalkyl” comprises fully saturated or partially unsaturated monocycles and bridged bicycles. Examples of 4-8 membered heterocycloalkyl groups include azetidiny, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydrothiopyranyl, dihydropyranyl, tetrahydropyranyl, 1,3-dioxolanyl, 1,4-dioxanyl, 1,4-oxathianyl, 1,4-dithianyl, 1,3-dioxanyl, 1,3-dithianyl, piperazinyl, thiomorpholinyl, piperidinyl, morpholinyl, azabicyclo[2.2.1]heptan-5-yl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl and the like.. The 4-8 membered heterocycloalkyl group may be unsubstituted or substituted with C₁₋₄ alkyl, such as methyl, ethyl, C₁₋₄ alkoxy, such as methoxy, ethoxy, halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments, the 4-8 membered heterocycloalkyl representing group X¹ is a non-aromatic ring system having 5 or 6 ring atoms of which at least one is a heteroatom selected from N and O, the number of N atoms being 1 or 2 and the number of O being 0, 1, or 2, such as a non-aromatic 6 membered ring system having 1 or 2 N-atoms, such as piperidine. In some embodiments, the 4-8 membered heterocycloalkyl formed by groups X¹ together with the N atom of the carbamate forms is a non-aromatic ring system having 5 or 6 ring atoms of which at least one is a heteroatom selected from N and O, the number of N atoms being 1 or 2 and the number of O being 0, 1, or 2, e.g. a non-aromatic ring system having 5 or 6 ring atoms comprising one or two N-atoms. Examples include pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl. In some embodiments, the 4-8 membered

heterocycloalkyl representing X^2 is a non-aromatic ring system having 4, 5, 6, 7 or 8 ring atoms of which at least one is a heteroatom selected from N and O, the number of N atoms being 1 or 2 and the number of O being 0, 1, or 2. In some embodiments, 4-8 membered heterocycloalkyl include 4-membered heterocycloalkyl having at least one heteroatom selected from N and O, the number of N atoms being 1 or 2 and the number of O being 0 or 1, such as azetidiny, oxetanyl, unsubstituted or substituted by e.g. C_{1-4} alkyl, such as methyl; 5-membered heterocycloalkyl having 1 or 2 N-atoms, such as pyrrolidinyl, unsubstituted or substituted by e.g. one or more of C_{1-4} alkyl, such as methyl; 6-membered heterocycloalkyl having N and O-atoms, such as morpholinyl, piperazinyl, piperidinyl, dioxanyl, unsubstituted or substituted by e.g. one or more of C_{1-4} alkyl, such as methyl, halogen, e.g. F; 7-membered heterocycloalkyl having N and O-atoms, such as 1 N- and 1 O-atom, such as 2-oxa-5-azabicyclo[2.2.1]heptan-5-yl, 1,4-diazabicyclo[3.2.1]octan-4-yl, 3-methyl-3-azabicyclo[3.1.0]hexan-1-yl; 8-membered heterocycloalkyl having N and O-atoms, such as 1 N- and 1 O-atom, such as 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

The term " C_{1-4} alkyl 4-8 membered heterocycloalkyl" refers to $-L^2-X^1-$ or L^3-X^2- with L^2 , L^3 being C_{1-4} alkyl and X^1 , X^2 being 4-8 membered heterocycloalkyl as defined herein. Thus, the 4-8 membered heterocycloalkyl is linked through a C_{1-4} alkyl group as defined to the neighbouring group. In some embodiments, the alkyl may be C_1 , resulting in $-(CH_2)-(4-8$ membered heterocycloalkyl) or C_2 , resulting in $-(CH_2)_2-(4-8$ membered heterocycloalkyl) or C_3 , resulting in $-(CH_2)_3-(4-8$ membered heterocycloalkyl) or C_4 , resulting in $-(CH_2)_4-(4-8$ membered heterocycloalkyl). Examples include $-(CH_2)$ -morpholinyl, $-(CH_2)_2$ -morpholinyl, $-(CH_2)_3$ -morpholinyl, $-(CH_2)_4$ -morpholinyl, $-(CH_2)$ -piperazinyl, $-(CH_2)_2$ -N-methyl-piperazinyl, $-(CH_2)_3$ -piperazinyl or $-(CH_2)_4$ -piperazinyl.

The term " $-C_{1-4}$ alkoxy 4-8 membered heterocycloalkyl" refers to $-L^2-X^1-$ or L^3-X^2- with L^2 , L^3 being C_{1-4} alkoxy and X^1 , X^2 being 4-8 membered heterocycloalkyl as defined herein. Thus, the 4-8 membered heterocycloalkyl is linked via a C_{1-4} alkoxy group as defined herein to its neighbouring group. In some embodiments, the C_{1-4} alkoxy may be C_1 , resulting in $-(O-CH_2)-(4-8$ membered heterocycloalkyl) or C_2 , resulting in $-(O-CH_2)_2-(4-8$ membered heterocycloalkyl) or C_3 , resulting in $-(O-CH_2)_3-(4-8$ membered heterocycloalkyl). Examples include $-(O-CH_2)-(N$ -morpholinyl), $-(O-CH_2)_2-(N$ -morpholinyl).

The term " $-O-(4-8$ membered heterocycloalkyl)" refers to $-L^2-X^1-$ or L^3-X^2- with L^2 , L^3 being $-O-$ and X^1 , X^2 being 4-8 membered heterocycloalkyl as defined herein. Thus, the 4-8

membered heterocycloalkyl is linked through an –O-atom to the neighbouring group. Examples include –O-morpholinyl, –O-piperazinyl, –O-pyrrolidinyl and the like.

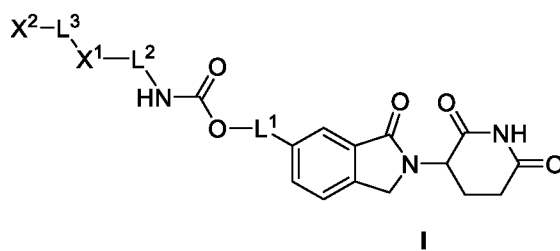
The term "halogen" or "hal" as used herein may be fluoro, chloro, bromo or iodo such as fluoro, chloro or bromo, e.g. fluoro or chloro.

- 5 The term "C₁₋₄ alkyl" and "C₁₋₆alkyl" refer to a fully saturated branched or unbranched hydrocarbon moiety having 1, 2, 3 or 4 and 1, 2, 3, 4, 5 or 6 carbon atoms, respectively. Representative examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, iso-butyl, tert-butyl, n-pentyl, iso-pentyl, neopentyl, n-hexyl, isohexyl or neohexyl.
- 10 The term "C₁₋₆ heteroalkyl" refers to an alkyl as defined with 1, 2, 3, 4, 5 or 6 carbon atoms in which at least one carbon atom is replaced with a heteroatom, such as N, O, or S, e.g. N, O. It is understood that the heteroatom may further be substituted with one or two C₁₋₆ alkyl. Examples include –(CH₂)₂-O-Me, –(CH₂)₃-O-Me, –(CH₂)₂-O-CH₂Me, –(CH₂)₂-NMe₂, –(CH₂)-NMe₂, –(CH₂)₂-NEt₂, –(CH₂)-NEt₂ and the like.
- 15 The term "C₁₋₄alkylamino" refers to a fully saturated branched or unbranched C₁₋₄ alkyl, which is substituted with at least one, such as only one, amino group, alkylamino group or dialkylaminogroup, such as NH₂, HN(C₁₋₄alkyl) or N(C₁₋₄alkyl)₂. Thus, a C₁₋₄alkylamino refers to C₁₋₄alkylamino, C₁₋₄alkyl-(C₁₋₄alkyl)amino, C₁₋₄alkyl-(C₁₋₄dialkyl)amino. Examples include but are not limited to methylaminomethyl, dimethylamonimethyl, aminomethyl, 20 dimethylaminoethyl, aminoethyl, methylaminoethyl, n-propylamino, iso-propylamino, n-butylamino, sec-butylamino, iso-butylamino, tert-butylamino.

The term "C₁₋₄ alkoxy" refers to an unsubstituted or substituted alkyl chain linked to the remainder of the molecule through an oxygen atom, and in particular to methoxy, ethoxy, n-propoxy, iso-propoxy, n-butoxy, iso-butoxy, and t-butoxy.

- 25 Based on the definitions given throughout the application the skilled person knows which combinations are synthetically feasible and realistic, e.g. typically combinations of groups leading to some heteroatoms directly linked to each other, e.g. –O–O–, are not contemplated, however synthetically feasible combinations, such as –S–N= in isothiazole are contemplated.

In a first aspect the disclosure provides a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula I:



wherein

- 5 X^1 is linear or branched C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched C_{1-6} alkyl, linear or branched C_{1-6} heteroalkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-CHF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , C_{1-6} alkylamino, $-CN$, $-N(H)C(O)-C_{1-6}alkyl$, $-OC(O)-C_{1-6}alkyl$, $-OC(O)-C_{1-4}alkylamino$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , C_{1-4} alkoxy, C_{1-4} alkylhydroxy, $-CH_2F$, $-N(H)C(O)-O-C_{1-6}alkyl$, and $C(OH)(CF_3)$;

or X^1 together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-6}alkyl$, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $C_{1-6}alkylamino$, $-CN$, $-N(H)C(O)-C_{1-6}alkyl$, $-OC(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , $C_{1-4}alkylhydroxy$, and $C_{1-4}alkoxy$;

X^2 is H, C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched $C_{1-6}alkyl$, $-C_{1-4}alkoxy$, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $C_{1-4}alkylhydroxy$;

L^1 is a covalent bond, linear or branched $C_{1-6}alkyl$;

L^2 is a covalent bond, linear or branched $C_{1-6}alkyl$; and

L^3 is a covalent bond, linear or branched $C_{1-6}alkyl$, $-O-$, or $-C_{1-4}alkoxy$, wherein linear or branched $C_{1-6}alkyl$ is unsubstituted or substituted with one or more of halogen.

In some embodiments, X^1 is linear or branched C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched C_{1-6} alkyl, linear or branched C_{1-6} heteroalkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-CHF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , C_{1-6} alkylamino, $-CN$, $-N(H)C(O)-C_{1-6}alkyl$, $-OC(O)-C_{1-6}alkyl$, $-OC(O)-C_{1-4}alkylamino$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , C_{1-4} alkoxy and C_{1-4} alkylhydroxy;

or X^1 together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched C_{1-6} alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, $-N(H)C(O)-C_{1-6}alkyl$, $-OC(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy;

X^2 is H, C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and C_{1-4} alkylhydroxy;

L^1 is a covalent bond, linear or branched C_{1-6} alkyl;

L^2 is a covalent bond, linear or branched C_{1-6} alkyl;

L^3 is a covalent bond, linear or branched C_{1-6} alkyl, $-O-$, $-C_{1-4}$ alkoxy.

In some embodiments of a compound of formula I, L^1 is a linear or branched C_{1-6} alkyl. In some embodiments of a compound of formula I, L^1 is linear or branched C_{1-4} alkyl, such as $-CH_2-$ or $-CH(CH_3)-$.

In some embodiments of a compound of formula I, L^2 is a covalent bond. In some embodiments of a compound of formula I, L^2 is linear or branched C_{1-6} alkyl, such as linear or branched C_{1-4} alkyl, e.g. $-CH_2-$ or $-CH(CH_3)-$.

In some embodiments of a compound of formula I, L^3 is a covalent bond. In some embodiments L^3 is linear or branched C_{1-4} alkyl. In some embodiments of a compound of formula I, L^3 is $-O-$. In some embodiments of a compound of formula I, L^3 is linear or branched C_{1-4} alkoxy, such as $-O-CH_2-$, $-O-CH_2-CH_2-$.

In some embodiments of a compound of formula I, L^1 is $-\text{CH}_2-$ and L^2 is a covalent bond. In some embodiments of a compound of formula I, L^1 is $-\text{CH}_2-$ and L^2 is $-\text{CH}_2-$. In some embodiments of a compound of formula I, L^1 is $-\text{CH}_2-$ and L^2 is $-\text{CH}(\text{CH}_2)-$.

In some embodiments of a compound of formula I, L^1 is $-\text{CH}_2-$, L^2 is a covalent bond and L^3 is a covalent bond. In some embodiments of a compound of formula I, L^1 is $-\text{CH}_2-$, L^2 is a covalent bond and L^3 is $-\text{CH}_2-$. In some embodiments of a compound of formula I, L^1 is $-\text{CH}_2-$, L^2 is a covalent bond and L^3 is $-\text{O}-$. In some embodiments of a compound of formula I, L^1 is $-\text{CH}_2-$, L^2 is a covalent bond and L^3 is $-\text{O}-\text{CH}_2-$. In some embodiments of a compound of formula I, L^1 is $-\text{CH}_2-$, L^2 is a covalent bond and L^3 is $-\text{O}-\text{CH}_2-\text{CH}_2-$.

In some embodiments of a compound of formula I, X^1 is linear or branched $-\text{C}_{1-6}$ alkyl, $-\text{C}_{3-6}$ cycloalkyl, $-\text{C}_{6-10}$ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , C_{1-6} alkylamino, $-\text{CN}$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , C_{1-6} alkylamino, $-\text{CN}$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy.

In some embodiments of a compound of formula I, X^1 is linear or branched $-\text{C}_{1-6}$ alkyl, $-\text{C}_{3-6}$ cycloalkyl, $-\text{C}_{6-10}$ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , OCHF_2 , CN and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , OCF_3 , OCHF_2 , and C_{1-4} alkoxy.

In some embodiments of a compound of formula I, X^1 is linear or branched $-\text{C}_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , C_{1-6} alkylamino, -

CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdiny, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula I, X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdiny, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I, X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy.

In some embodiments of a compound of formula I, X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, and halogen, e.g. F.

In some embodiments of a compound of formula I, X² is H, cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdiny, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NMe₂ and halogen, e.g. F.

In some embodiments of a compound of formula I, X² is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl,

methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula I L¹ is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -

C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl,

pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of
 5 halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdiny, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆
 10 alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of
 15 halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdiny, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.
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In some embodiments of a compound of formula I L¹ is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen,
 25 linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

30 In some embodiments of a compound of formula I L¹ is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen,

linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

- 5 In some embodiments of a compound of formula I L¹ is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

- In some embodiments of a compound of formula I L¹ is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

- In some embodiments of a compound of formula I L¹ is -CH(CH₃)- and X¹ is phenyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, such as methyl, fluorinated C₁₋₄ alkoxy, such as -OCF₃.

In some embodiments of a compound of formula I L^2 is a covalent bond and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy.

In some embodiments of a compound of formula I L^2 is a covalent bond and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy.

In some embodiments of a compound of formula I L^2 is a covalent bond and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, or C_{1-4} alkoxy.

In some embodiments of a compound of formula I L^2 is a covalent bond and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-

2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN, and C_{1-4} alkoxy.

In some embodiments of a compound of formula I L^2 is linear or branched C_{1-4} alkyl and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy.

In some embodiments of a compound of formula I L^2 is linear or branched C_{1-4} alkyl and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy.

In some embodiments of a compound of formula I L^2 is linear or branched C_{1-4} alkyl and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a

pyrrolidinyl, piperdinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

- 5 In some embodiments of a compound of formula I L² is linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl,
 10 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, piperazinyl, which is unsubstituted or
 15 substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen,
 20 linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

- 25 In some embodiments of a compound of formula I L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is
 30 unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L^2 is $-CH_2-$ and X^1 is linear or branched - C_{1-6} alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, or C_{1-4} alkoxy.

In some embodiments of a compound of formula I L^2 is $-CH_2-$ and X^1 is linear or branched - C_{1-6} alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN , and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, , piperazinyl, , which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN , and C_{1-4} alkoxy.

In some embodiments of a compound of formula I, L^2 is $-CH_2-$ and X^1 is phenyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, and C_{1-4} alkoxy, preferably unsubstituted or substituted $-OMe$.

In some embodiments of a compound of formula I L^2 is $-CH(CH_3)-$ and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of

the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, piperidinyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl,

piperdiny, piperaziny, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is H, L² is -CH(CH₃)- and X¹ is phenyl.

- 5 In some embodiments of a compound of formula I L¹ is -CH₂-, L² is a covalent bond and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

- In some embodiments of a compound of formula I L¹ is -CH₂-, L² is a covalent bond and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

- 20 In some embodiments of a compound of formula I L¹ is -CH₂-, L² is a covalent bond and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxany, phenyl, dihydroindenyl, isothiazolyl, pyridiny, pyraziny, pyridaziny, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdiny, morpholinyl, piperaziny, N-methyl piperaziny, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -

C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂-, L² is a covalent bond and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂-, L² is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂-, L² is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂-, L² is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl,

bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂-, L² is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂-, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂-, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂-, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂-, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂-, L² is -CH₂- and X¹ is phenyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, and C₁₋₄ alkoxy, preferably unsubstituted or substituted -OMe.

In some embodiments of a compound of formula I L¹ is -CH₂-, L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂-, L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH₂-, L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L^1 is $-CH_2-$, L^2 is $-CH(CH_3)-$ and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN , and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN , and C_{1-4} alkoxy.

In some embodiments of a compound of formula I L^1 is $-CH_2-$, L^2 is $-CH(CH_3)-$ and X^1 is phenyl.

In some embodiments of a compound of formula I L^1 is $-CH(CH_3)-$, L^2 is a covalent bond and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy.

In some embodiments of a compound of formula I L^1 is $-CH(CH_3)-$, L^2 is a covalent bond and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy.

In some embodiments of a compound of formula I L^1 is $-CH(CH_3)-$, L^2 is a covalent bond and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-

dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -
 5 C_{1-4} alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -
 10 C_{1-4} alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, or C_{1-4} alkoxy.

In some embodiments of a compound of formula I L^1 is $-CH(CH_3)-$, L^2 is a covalent bond and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-
 15 dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -
 20 C_{1-4} alkyl, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN , and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN , and C_{1-4} alkoxy.

In some embodiments of a compound of formula I L^1 is $-CH(CH_3)-$, L^2 is a covalent bond and X^1 is phenyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F,
 25 linear or branched $-C_{1-4}$ alkyl, such as methyl, fluorinated C_{1-4} alkoxy, such as $-OCF_3$

In some embodiments of a compound of formula I L^1 is $-CH(CH_3)-$, L^2 is a linear or branched C_{1-4} alkyl and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$,
 30 OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 ,

CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH(CH₃)-, L² is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH(CH₃)-, L² is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH(CH₃)-, L² is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together

with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH(CH₃)-, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH(CH₃)-, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH(CH₃)-, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH(CH₃)-, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-
 5 2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a
 10 pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH(CH₃)-, L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of
 15 halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH(CH₃)-, L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of
 20 halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which
 25 is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula I L¹ is -CH(CH₃)-, L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl,
 30 pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl,

cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched - C_{1-4} alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched - C_{1-4} alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, or C_{1-4} alkoxy.

In some embodiments of a compound of formula I L^1 is $-CH(CH_3)-$, L^2 is $-CH(CH_3)-$ and X^1 is linear or branched - C_{1-6} alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched - C_{1-4} alkyl, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN , and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched - C_{1-4} alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN , and C_{1-4} alkoxy.

In some embodiments of a compound of formula I, L^2 is a covalent bond and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

In some embodiments of a compound of formula I, L^2 is a covalent bond and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

In some embodiments of a compound of formula I, L^2 is a covalent bond and X^2 is H, cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidyl, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-

azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 and halogen.

In some embodiments of a compound of formula I, L^2 is a covalent bond and X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

10 In some embodiments of a compound of formula I, L^2 is $-CH_2-$ and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

15 In some embodiments of a compound of formula I, L^2 is $-CH_2-$ and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

In some embodiments of a compound of formula I, L^2 is $-CH_2-$ and X^2 is C_6 aryl, which is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, 20 such as unsubstituted or substituted with $-OMe$.

In some embodiments of a compound of formula I, L^2 is $-CH(CH_3)-$ and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ 25 alkylhydroxy.

In some embodiments of a compound of formula I, L^2 is $-CH(CH_3)-$ and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

In some embodiments of a compound of formula I, L^2 is $-\text{CH}(\text{CH}_3)-$ and X^2 is C_6 aryl, which is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-\text{C}_{1-4}$ alkoxy, e.g. unsubstituted.

5 In some embodiments of a compound of formula I, L^3 is a covalent bond and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-\text{C}_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , and $-\text{C}_{1-4}$ alkylhydroxy.

10 In some embodiments of a compound of formula I, L^3 is a covalent bond and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-\text{C}_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

15 In some embodiments of a compound of formula I, L^3 is a covalent bond and X^2 is H, cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-\text{C}_{1-4}$ alkoxy, NH_2 , NMe_2 and halogen.

20 In some embodiments of a compound of formula I, L^3 is a covalent bond and X^2 is cyclopropyl, cyclobutyl, azetidiny, oxetanyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, C_6 aryl, pyridinyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, e.g. methyl, $-\text{C}_{1-4}$ alkoxy, e.g. $-\text{OMe}$, NMe_2 and halogen, e.g. F.

25 In some embodiments of a compound of formula I, L^3 is a covalent bond and X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

30 In some embodiments of a compound of formula I, L^3 is a covalent bond and X^2 is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, azetidiny, NMe_2 -

azetidiny, oxetanyl, methyl-oxetanyl, pyrrolidiny, methyl-pyrrolidiny, piperidiny, Me-piperidiny, Di-F-piperidiny, N-Me-piperaziny, morpholiny, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, C₆ aryl, methoxy-C₆ aryl, pyridiny.

In some embodiments of a compound of formula I, L³ is a linear or branched C₁₋₄ alkyl, such as -CH₂-, and X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy.

In some embodiments of a compound of formula I, L³ is a linear or branched C₁₋₄ alkyl, such as -CH₂-, and X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, and halogen, e.g. F.

In some embodiments of a compound of formula I, L³ is a linear or branched C₁₋₄ alkyl, such as -CH₂-, and X² is H, cyclopropyl, cyclobutyl, C₆ aryl, pyridiny, pyrrolidiny, piperdiny, morpholiny, oxetanyl, piperaziny, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂ and halogen.

In some embodiments of a compound of formula I, L³ is a linear or branched C₁₋₄ alkyl, such as -CH₂-, and X² is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridiny, pyrrolidiny, N-methyl-pyrrolidiny, methyl-pyrrolidiny, piperdiny, N-methyl piperdiny, methyl-piperdiny, difluoro-piperidiny, morpholiny, N-methyl-morpholiny, oxetanyl, methyl-oxetanyl, piperaziny, N-methyl-piperaziny, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula I, L³ is linear or branched C₁₋₄ alkyl, such as -CH₂-, and X² is morpholiny, N-methyl-morpholiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula I, L³ is -O- and X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted

or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy.

In some embodiments of a compound of formula I, L³ is -O- and X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, and halogen, e.g. F.

In some embodiments of a compound of formula I, L³ is -O- and X² is H, cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂ and halogen.

In some embodiments of a compound of formula I, L³ is -O- and X² is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula I, L³ is -O- and X² is cyclopropyl, pyrrolidinyl, N-methyl-pyrrolidinyl,

In some embodiments of a compound of formula I, L³ is -O-CH₂- and X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy.

In some embodiments of a compound of formula I, L³ is -O-CH₂- and X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, and halogen, e.g. F.

In some embodiments of a compound of formula I, L^3 is $-O-CH_2-$ and X^2 is H, cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, -
 5 C_{1-4} alkoxy, NH_2 , NMe_2 and halogen.

In some embodiments of a compound of formula I, L^3 is $-O-CH_2-$ and X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl,
 10 morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula I, L^3 is $-O-CH_2-$ and X^2 is pyrrolidinyl, N-methyl-pyrrolidinyl.

15 In some embodiments of a compound of formula I, L^3 is $-O-CH_2-CH_2-$ and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

20 In some embodiments of a compound of formula I, L^3 is $-O-CH_2-CH_2-$ and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

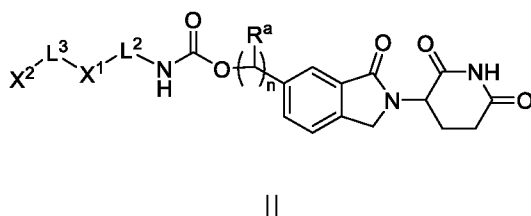
In some embodiments of a compound of formula I, L^3 is $-O-CH_2-CH_2-$ and X^2 is H,
 25 cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 and halogen.

In some embodiments of a compound of formula I, L^3 is $-O-CH_2-CH_2-$ and X^2 is H,
 30 cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl,

methyl-pyrrolidinyl, piperdiny, N-methyl piperdiny, methyl-piperdiny, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

- 5 In some embodiments of a compound of formula I, L^3 is $-O-CH_2-CH_2-$ and X^2 is morpholinyl.

In specific embodiments the compound of formula I is a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula II:



- 10 wherein

X^1 is linear or branched C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched C_{1-6} alkyl, linear or branched C_{1-6} heteroalkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-CHF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , C_{1-6} alkylamino, $-CN$, $-N(H)C(O)-C_{1-6}alkyl$, $-OC(O)-C_{1-6}alkyl$, $-OC(O)-C_{1-4}alkylamino$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , C_{1-4} alkoxy and C_{1-4} alkylhydroxy;

15

or X^1 together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-6}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, $-N(H)C(O)-C_{1-6}alkyl$, $-OC(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy;

20

X^2 is H, C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and C_{1-4} alkylhydroxy;

25

L^2 is a covalent bond, linear or branched C_{1-6} alkyl; L^3 is a covalent bond, linear or branched C_{1-6} alkyl, $-O-$, $-C_{1-4}$ alkoxy;

R^a is H or linear or branched C₁₋₄ alkyl, such as methyl or ethyl; and n is 1 or 2.

In some embodiments of a compound of formula II, R^a is H. In some embodiments of a compound of formula II, R^a is linear or branched C₁₋₄ alkyl, such as methyl.

In some embodiments of a compound of formula II, n is 1.

- 5 In some embodiments of a compound of formula II, L² is a covalent bond. In some embodiments of a compound of formula II, L² is linear or branched C₁₋₆ alkyl. In some embodiments of a compound of formula II, L² is linear or branched C₁₋₄ alkyl, such as -CH₂- or -CH(CH₃)-.

- 10 In some embodiments of a compound of formula II, L³ is a covalent bond. In some embodiments of a compound of formula II, L³ is linear or branched C₁₋₄ alkyl. In some embodiments of a compound of formula II, L³ is -O-. In some embodiments L³ is linear or branched C₁₋₄ alkoxy, such as -O-CH₂-, -O-CH₂-CH₂-, O-CH₂-CH₂-CH₂-.

- 15 In some embodiments of a compound of formula II, L¹ is -CH₂- and L² is a covalent bond. In some embodiments of a compound of formula II, L¹ is -CH₂- and L² is -CH₂-. In some embodiments L¹ is -CH₂- and L² is -CH(CH₃)-.

- In some embodiments of a compound of formula II, L¹ is -CH₂-, L² is a covalent bond and L³ is a covalent bond. In some embodiments of a compound of formula II, L¹ is -CH₂-, L² is a covalent bond and L³ is -CH₂-. In some embodiments of a compound of formula II, L¹ is -CH₂-, L² is a covalent bond and L³ is -O-. In some embodiments of a compound of formula II, L¹ is -CH₂-, L² is a covalent bond and L³ is -O-CH₂-. In some embodiments of a compound of formula II, L¹ is -CH₂-, L² is a covalent bond and L³ is -O-CH₂-CH₂-.
- 20

- In some embodiments of a compound of formula II, X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.
- 25

In some embodiments of a compound of formula II, X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II, X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula II, X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II, X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

- 5 In some embodiments of a compound of formula II, X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

- 10 In some embodiments of a compound of formula II, X^2 is H, cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 and halogen.

- 15 In some embodiments of a compound of formula II, X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.
- 20

- In some embodiments of a compound of formula II n is 1, R^a is H and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy.
- 25

- In some embodiments of a compound of formula II n is 1, R^a is H and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen,
- 30

linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

- 5 In some embodiments of a compound of formula II n is 1, R^a is H and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

- In some embodiments of a compound of formula II n is 1, R^a is H and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

- In some embodiments of a compound of formula II n is 1, R^a is -CH₃ and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆

alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

- 5 In some embodiments of a compound of formula II n is 1, R^a is -CH₃ and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is
10 unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃ and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl,
15 pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -
20 O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdiny, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

- 25 In some embodiments of a compound of formula II n is 1, R^a is -CH₃ and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl,
30 dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -

OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdiny, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃ and X¹ is phenyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, such as methyl, fluorinated C₁₋₄ alkoxy, such as -OCF₃.

In some embodiments of a compound of formula II L² is a covalent bond and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II L² is a covalent bond and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II L² is a covalent bond and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdiny, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of

halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, or C_{1-4} alkoxy.

In some embodiments of a compound of formula II L^2 is a covalent bond and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN , and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN , and C_{1-4} alkoxy.

In some embodiments of a compound of formula II L^2 is linear or branched C_{1-4} alkyl and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy.

In some embodiments of a compound of formula II L^2 is linear or branched C_{1-4} alkyl and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy.

In some embodiments of a compound of formula II L^2 is linear or branched C_{1-4} alkyl and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-

dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -
 5 C_{1-4} alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -
 10 C_{1-4} alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, or C_{1-4} alkoxy.

In some embodiments of a compound of formula II L^2 is linear or branched C_{1-4} alkyl and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-
 15 dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -
 20 C_{1-4} alkyl, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN , and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN , and C_{1-4} alkoxy.

In some embodiments of a compound of formula II L^2 is $-CH_2-$ and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 5-6 membered
 25 heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-$
 30 OMe , OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy.

In some embodiments of a compound of formula II L^2 is $-CH_2-$ and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 6 membered

heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula II L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, , piperazinyl, , which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II, L² is -CH₂- and X¹ is phenyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, and C₁₋₄ alkoxy, preferably -OMe.

In some embodiments of a compound of formula II L^2 is $-\text{CH}(\text{CH}_3)-$ and X^1 is linear or branched $-\text{C}_{1-6}$ alkyl, $-\text{C}_{3-6}$ cycloalkyl, $-\text{C}_{6-10}$ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , C_{1-6} alkylamino, $-\text{CN}$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , C_{1-6} alkylamino, $-\text{CN}$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy.

In some embodiments of a compound of formula II L^2 is $-\text{CH}(\text{CH}_3)-$ and X^1 is linear or branched $-\text{C}_{1-6}$ alkyl, $-\text{C}_{3-6}$ cycloalkyl, $-\text{C}_{6-10}$ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , OCF_3 , OCHF_2 , CN and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , OCF_3 , OCHF_2 , CN and C_{1-4} alkoxy.

In some embodiments of a compound of formula II L^2 is $-\text{CH}(\text{CH}_3)-$ and X^1 is linear or branched $-\text{C}_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , C_{1-6} alkylamino, $-\text{CN}$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , C_{1-6} alkylamino, $-\text{CN}$, NH_2 , C_{1-4} alkylhydroxy, or C_{1-4} alkoxy.

In some embodiments of a compound of formula II L^2 is $-\text{CH}(\text{CH}_3)-$ and X^1 is linear or branched $-\text{C}_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-

2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN, and C_{1-4} alkoxy.

In some embodiments of a compound of formula II, L^2 is $-CH(CH_3)-$ and X^1 is phenyl.

In some embodiments of a compound of formula II n is 1, R^a is H, L^2 is a covalent bond and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is H, L^2 is a covalent bond and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is H, L^2 is a covalent bond and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4}

alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched - C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is H, L² is a covalent bond and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched - C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is H, L² is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is H, L² is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered

heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is H, L² is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is H, L² is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is H, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋

₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

- 5 In some embodiments of a compound of formula II n is 1, R^a is H, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is
10 unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

- In some embodiments of a compound of formula II n is 1, R^a is H, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl,
15 pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -
20 O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdiny, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

- 25 In some embodiments of a compound of formula II n is 1, R^a is H, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl,
30 dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -

OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is H, L² is -CH₂- and X¹ is phenyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, and C₁₋₄ alkoxy, preferably unsubstituted or substituted -OMe.

In some embodiments of a compound of formula II n is 1, R^a is H, L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is H, L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is H, L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is

unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is H, L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is H, L² is -CH(CH₃)- and X¹ is phenyl.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is a covalent bond and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is a covalent bond and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is a covalent bond and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is a covalent bond and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II, n is 1, R^a is -CH₃, L² is a covalent bond and X¹ is phenyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, and C₁₋₄ alkoxy, fluorinated C₁₋₄ alkyl, such as -CF₃.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with

one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is a linear or branched C₁₋₄ alkyl and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-

dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdiny, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a

pyrrolidinyl, piperdiny, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

- 5 In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is -CH₂- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl,
 10 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdiny, piperazinyl, which is unsubstituted or
 15 substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of
 20 halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

- 25 In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which
 30 is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula II n is 1, R^a is -CH₃, L² is -CH(CH₃)- and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula II, L³ is a covalent bond and X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy.

In some embodiments of a compound of formula II, L^3 is a covalent bond and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

- 5 In some embodiments of a compound of formula II, L^3 is a covalent bond and X^2 is H, cyclopropyl, cyclobutyl, azetidiny, oxetanyl, pyrrolidiny, piperidiny, piperaziny, morpholiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, C_6 aryl, pyridiny, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, e.g. methyl, $-C_{1-4}$ alkoxy, e.g. $-OMe$, NMe_2 and halogen, e.g. F.
- 10 In some embodiments of a compound of formula II, L^3 is a covalent bond and X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridiny, pyrrolidiny, N-methyl-pyrrolidiny, methyl-pyrrolidiny, piperdiny, N-methyl piperdiny, methyl-piperdiny, difluoro-piperidiny, morpholiny, N-methyl-morpholiny, oxetanyl, methyl-oxetanyl, piperaziny, N-methyl-
- 15 piperaziny, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula II, L^3 is a covalent bond and X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, azetidiny, NMe_2 -azetidiny, oxetanyl, methyl-oxetanyl, pyrrolidiny, methyl-pyrrolidiny, 20 piperidiny, Me-piperidiny, Di-F-piperidiny, N-Me-piperaziny, morpholiny, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, C_6 aryl, methoxy- C_6 aryl, pyridiny.

In some embodiments of a compound of formula II, L^3 is a linear or branched C_{1-4} alkyl, such as $-CH_2-$, and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or 25 branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

In some embodiments of a compound of formula II, L^3 is a linear or branched C_{1-4} alkyl, such as $-CH_2-$, and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or 30 branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

In some embodiments of a compound of formula II, L^3 is a linear or branched C_{1-4} alkyl, such as $-CH_2-$, and X^2 is H, cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 and halogen.

In some embodiments of a compound of formula II, L^3 is a linear or branched C_{1-4} alkyl, such as $-CH_2-$, and X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula II, L^3 is linear or branched C_{1-4} alkyl, such as $-CH_2-$, and X^2 is morpholinyl, N-methyl-morpholinyl, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula II, L^3 is $-O-$ and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

In some embodiments of a compound of formula II, L^3 is $-O-$ and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

In some embodiments of a compound of formula II, L^3 is $-O-$ and X^2 is H, cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 and halogen.

In some embodiments of a compound of formula II, L^3 is $-O-$ and X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl,

fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula II, L³ is -O- and X² is cyclopropyl, pyrrolidinyl, N-methyl-pyrrolidinyl,

In some embodiments of a compound of formula II, L³ is -O-CH₂- and X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy.

In some embodiments of a compound of formula II, L³ is -O-CH₂- and X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, and halogen, e.g. F.

In some embodiments of a compound of formula II, L³ is -O-CH₂- and X² is H, cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂ and halogen.

In some embodiments of a compound of formula II, L³ is -O-CH₂- and X² is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula II, L³ is -O-CH₂- and X² is pyrrolidinyl, N-methyl-pyrrolidinyl.

In some embodiments of a compound of formula II, L^3 is $-O-CH_2-CH_2-$ and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

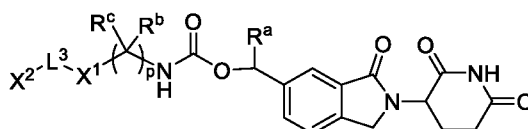
In some embodiments of a compound of formula II, L^3 is $-O-CH_2-CH_2-$ and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

In some embodiments of a compound of formula II, L^3 is $-O-CH_2-CH_2-$ and X^2 is H, cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 and halogen.

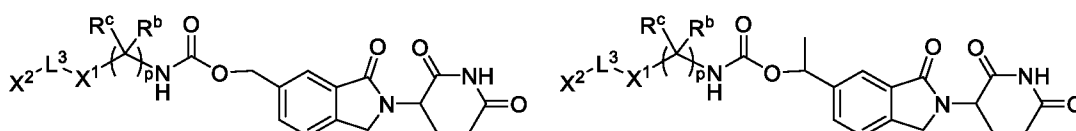
In some embodiments of a compound of formula II, L^3 is $-O-CH_2-CH_2-$ and X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula II, L^3 is $-O-CH_2-CH_2-$ and X^2 is morpholinyl.

In specific embodiments the compound of formula I or II is a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula III, such as IVa or IVb:



III



IVa

IVb

wherein

X¹ is linear or branched C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more
 5 of halogen, linear or branched C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, CF₃, CHF₂, CMeF₂, -O-CHF₂, -O-(CH₂)₂-OMe, OCF₃, C₁₋₆ alkylamino, -CN, -N(H)C(O)-C₁₋₆alkyl, -OC(O)-C₁₋₆alkyl, -OC(O)-C₁₋₄alkylamino, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, C₁₋₄ alkoxy and C₁₋₄ alkylhydroxy;

or X¹ together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl,
 10 which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₆ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, -N(H)C(O)-C₁₋₆alkyl, -OC(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy;

X² is H, C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered
 15 heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and C₁₋₄ alkylhydroxy;

L³ is a covalent bond, linear or branched C₁₋₆ alkyl, -O-, -C₁₋₄ alkoxy;

R^a, R^b, R^c are independently of each other H, linear or branched C₁₋₄ alkyl, such as methyl;

20 p is 0 or 1.

In some embodiments of a compound of formula III, R^a is H. In some embodiments of a compound of formula III, R^a is linear or branched C₁₋₄ alkyl, such as methyl.

In some embodiments of a compound of formula III, IVa or IVb, p is 0. In some embodiments of a compound of formula III, IVa or IVb, p is 1. In some embodiments of a compound of
 25 formula III, IVa or IVb, p is 1 and R^b and R^c are H. In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b is linear or branched C₁₋₄ alkyl, such as methyl and R^c is H.

In some embodiments of a compound of formula III, IVa or IVb, L³ is a covalent bond. In some embodiments of a compound of formula III, IVa or IVb, L³ is linear or branched C₁₋₄ alkyl, such

as $-\text{CH}_2-$. In some embodiments of a compound of formula III, IVa or IVb, L^3 is $-\text{O}-$. In some embodiments L^3 is linear or branched C_{1-4} alkoxy, such as $-\text{O}-\text{CH}_2-$, $-\text{O}-(\text{CH}_2)_2-$.

In some embodiments of a compound of formula III, IVa or IVb, X^1 is linear or branched $-\text{C}_{1-6}$ alkyl, $-\text{C}_{3-6}$ cycloalkyl, $-\text{C}_{6-10}$ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , C_{1-6} alkylamino, $-\text{CN}$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-$ OMe, OCF_3 , OCHF_2 , C_{1-6} alkylamino, $-\text{CN}$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy.

In some embodiments of a compound of formula III, IVa or IVb, X^1 is linear or branched $-\text{C}_{1-6}$ alkyl, $-\text{C}_{3-6}$ cycloalkyl, $-\text{C}_{6-10}$ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , OCF_3 , OCHF_2 , CN and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , OCF_3 , OCHF_2 , CN and C_{1-4} alkoxy.

In some embodiments of a compound of formula III, IVa or IVb, X^1 is linear or branched $-\text{C}_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , C_{1-6} alkylamino, $-\text{CN}$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-\text{C}_{1-4}$ alkyl, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , C_{1-6} alkylamino, $-\text{CN}$, NH_2 , C_{1-4} alkylhydroxy, or C_{1-4} alkoxy.

In some embodiments of a compound of formula III, IVa or IVb, X^1 is linear or branched $-\text{C}_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-

dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, IVa or IVb, X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy.

In some embodiments of a compound of formula III, IVa or IVb, X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, and halogen, e.g. F.

In some embodiments of a compound of formula II, L³ is -O-CH₂-CH₂- and X² is H, cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂ and halogen.

In some embodiments of a compound of formula III, IVa or IVb, X² is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula III, R^a is H and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered

heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is H and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is H and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is H and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine,

wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is -CH₃ and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is -CH₃ and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is -CH₃ and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such

as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is -CH₃ and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is -CH₃ and X¹ is phenyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, such as methyl, fluorinated C₁₋₄ alkoxy, such as -OCF₃.

In some embodiments of a compound of formula III, IVa, or IVb, p is 0 and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, IVa, or IVb, p is 0 and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, IVa, or IVb, p is 0 and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, IVa, or IVb, p is 0 and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b, R^c are H and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b, R^c are H and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b, R^c are H and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b, R^c are H and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, , piperazinyl, , which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b, R^c are H and X¹ is phenyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, and C₁₋₄ alkoxy, preferably unsubstituted or substituted with -OMe.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b is -CH₃, R^c is H and
 5 X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted
 10 with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b is -CH₃, R^c is H and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy;
 15 or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b is -CH₃, R^c is H and
 20 X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl,
 25 cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is
 30 unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b is -CH₃, R^c is H and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b is -CH₃, R^c is H and X¹ is phenyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, and C₁₋₄ alkoxy preferably unsubstituted or substituted -OMe.

In some embodiments of a compound of formula III, IVa or IVb, p is 0 and X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy.

In some embodiments of a compound of formula III, IVa or IVb, p is 0 and X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, and halogen, e.g. F.

In some embodiments of a compound of formula III, IVa or IVb, p is 0 and X² is H, cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperidinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, e.g. Me, -C₁₋₄ alkoxy, e.g. -OMe, NH₂, NMe₂ and halogen, e.g. F.

In some embodiments of a compound of formula III, IVa or IVb, p is 0 and X² is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆

aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula III, IVa or IVb, p is 0 and X² is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, azetidiny, NMe₂-azetidiny, oxetanyl, methyl-oxetanyl, pyrrolidinyl, methyl-pyrrolidinyl, piperidinyl, Me-piperidinyl, Di-F-piperidinyl, N-Me-piperazinyl, morpholinyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, C₆ aryl, methoxy-C₆ aryl, pyridinyl

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b and R^c are H, and X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b and R^c are H, and X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, and halogen, e.g. F.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b and R^c are H, and X² is H, cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂ and halogen.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b and R^c are H, and X² is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b and R^c are H, and X² is phenyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, and C₁₋₄ alkoxy, preferably unsubstituted or substituted -OMe.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b is CH₃, R^c are H, and
 5 X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b is CH₃, R^c are H, and
 10 X² is H, C₃₋₆ cycloalkyl, C₆ aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, and halogen, e.g. F.

In some embodiments of a compound of formula II, L³ is -O-CH₂-CH₂- and X² is H, cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl,
 15 piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂ and halogen.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b is CH₃, R^c are H, and X² is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl,
 20 C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

25 In some embodiments of a compound of formula III, IVa or IVb, p is 1, R^b is CH₃, R^c are H, and X² is phenyl.

In some embodiments of a compound of formula III, R^a is H, p is 0 and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen,
 30 linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of

the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy.

In some embodiments of a compound of formula III, R^a is H, p is 0 and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy.

In some embodiments of a compound of formula III, R^a is H, p is 0 and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, or C_{1-4} alkoxy.

In some embodiments of a compound of formula III, R^a is H, p is 0 and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN , and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl,

piperdiny, piperaziny, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is H, p is 1, R^b and R^c are H, and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is H, p is 1, R^b and R^c are H, and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is H, p is 1, R^b and R^c are H, and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxany, phenyl, dihydroindenyl, isothiazolyl, pyridiny, pyraziny, pyridaziny, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidiny, piperdiny, morpholiny, piperaziny, N-methyl piperaziny, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is H, p is 1, R^b and R^c are H, and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN, and C_{1-4} alkoxy.

In some embodiments of a compound of formula III, R^a is H, p is 1, R^b and R^c are H, and X^1 is phenyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, and C_{1-4} alkoxy, preferably unsubstituted or substituted $-OMe$.

In some embodiments of a compound of formula III, R^a is H, p is 1, R^b is CH_3 , R^c are H, and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy.

In some embodiments of a compound of formula III, R^a is H, p is 1, R^b is CH_3 , R^c are H, and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy.

In some embodiments of a compound of formula III, R^a is H, p is 1, R^b is CH_3 , R^c are H, and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl,

bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is H, p is 1, R^b is CH₃, R^c are H, and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is H, p is 1, R^b is CH₃, R^c are H, and X¹ is phenyl.

In some embodiments of a compound of formula III, R^a is CH₃, p is 0 and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted

with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy.

In some embodiments of a compound of formula III, R^a is CH_3 , p is 0 and X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN and C_{1-4} alkoxy.

In some embodiments of a compound of formula III, R^a is CH_3 , p is 0 and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, or C_{1-4} alkoxy.

In some embodiments of a compound of formula III, R^a is CH_3 , p is 0 and X^1 is linear or branched $-C_{1-6}$ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN , and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a

pyrrolidinyl, piperdiny, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is -CH₃, p is 0 and X¹ is phenyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, such as methyl, fluorinated C₁₋₄ alkoxy, such as -OCF₃.

In some embodiments of a compound of formula III, R^a is CH₃, p is 1, R^b and R^c are H, and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is CH₃, p is 1, R^b and R^c are H, and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is CH₃, p is 1, R^b and R^c are H, and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperdiny, morpholinyl, piperazinyl, N-methyl piperazinyl, which is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -

C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, or C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is CH₃, p is 1, R^b and R^c are H, and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X¹ is unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is CH₃, p is 1, R^b is CH₃, R^c are H, and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is CH₃, p is 1, R^b is CH₃, R^c are H, and X¹ is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, -C₆₋₁₀ aryl, 5-10 membered heteroaryl, 6 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy; or X¹ together with the N atom of the carbamate forms a 6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, CN and C₁₋₄ alkoxy.

In some embodiments of a compound of formula III, R^a is CH₃, p is 1, R^b is CH₃, R^c are H, and X¹ is linear or branched -C₁₋₆ alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl,

pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is

5 unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched - C_{1-4} alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, morpholinyl, piperazinyl, N-methyl piperazinyl, which is

10 unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched - C_{1-4} alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, or C_{1-4} alkoxy.

In some embodiments of a compound of formula III, R^a is CH_3 , p is 1, R^b is CH_3 , R^c are H, and X^1 is linear or branched - C_{1-6} alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, phenyl, dihydroindenyl, isothiazolyl,

15 pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, 2,2-difluoro-1,3-benzodioxolyl, 2,3-dihydrobenzofuryl, 2-methyl-2,3-dihydrobenzofuryl, 3-methyl-2,3-dihydrobenzofuryl, 3,3-dimethyl-2,3-dihydrobenzofuryl, 2,3-dimethyl-2,3-dihydrobenzofuryl, cyclopentenopyridine, benzodihydropyrane, dihydropyrano-pyridine, wherein X^1 is

20 unsubstituted or substituted with one or more of halogen, such as Cl, F, linear or branched - C_{1-4} alkyl, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN , and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, piperazinyl, which is unsubstituted or substituted with one or more of halogen, linear or branched - C_{1-4} alkyl, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, CN , and C_{1-4} alkoxy.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is a covalent bond and X^2

25 is H, C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, - C_{1-4} alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and - C_{1-4} alkylhydroxy.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is a covalent bond and X^2

30 is H, C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, - C_{1-4} alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is a covalent bond and X^2 is H, cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 and halogen.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is a covalent bond and X^2 is H, cyclopropyl, cyclobutyl, azetidiny, oxetanyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, C_6 aryl, pyridinyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, e.g. methyl, $-C_{1-4}$ alkoxy, e.g. $-OMe$, NMe_2 and halogen, e.g. F.

In some embodiments of a compound of formula III, IVa or IVb, p is 1, L^3 is a covalent bond and X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is a covalent bond and X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, azetidiny, NMe_2 -azetidiny, oxetanyl, methyl-oxetanyl, pyrrolidinyl, methyl-pyrrolidinyl, piperidinyl, Me-piperidinyl, Di-F-piperidinyl, N-Me-piperazinyl, morpholinyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, C_6 aryl, methoxy- C_6 aryl, pyridinyl.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is a linear or branched C_{1-4} alkyl, such as $-CH_2-$, and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is a linear or branched C_{1-4} alkyl, such as $-CH_2-$, and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is a linear or branched C_{1-4} alkyl, such as $-CH_2-$, and X^2 is H, cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is
 5 unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 and halogen.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is a linear or branched C_{1-4} alkyl, such as $-CH_2-$, and X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl,
 10 pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

15 In some embodiments of a compound of formula III, IVa or IVb, L^3 is linear or branched C_{1-4} alkyl, such as $-CH_2-$, and X^2 is morpholinyl, N-methyl-morpholinyl, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is $-O-$ and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is
 20 unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

In some embodiments of a compound of formula III, IVa or IVb L^3 is $-O-$ and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is
 25 unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

In some embodiments of a compound of formula III, IVa or IVb L^3 is $-O-$ and X^2 is H, cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-
 30 azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 and halogen.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is $-O-$ and X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is $-O-$ and X^2 is cyclopropyl, pyrrolidinyl, N-methyl-pyrrolidinyl,

10 In some embodiments of a compound of formula III, IVa or IVb, L^3 is $-O-CH_2-$ and X^2 is H, C_3 - C_6 cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

15 In some embodiments of a compound of formula III, IVa or IVb, L^3 is $-O-CH_2-$ and X^2 is H, C_3 - C_6 cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

20 In some embodiments of a compound of formula III, IVa or IVb, L^3 is $-O-CH_2-$ and X^2 is H, cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 and halogen.

25 In some embodiments of a compound of formula III, IVa or IVb, L^3 is $-O-CH_2-$ and X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

30

In some embodiments of a compound of formula III, IVa or IVb, L^3 is $-O-CH_2-$ and X^2 is pyrrolidinyl, N-methyl-pyrrolidinyl.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is $-O-CH_2-CH_2-$ and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is $-O-CH_2-CH_2-$ and X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

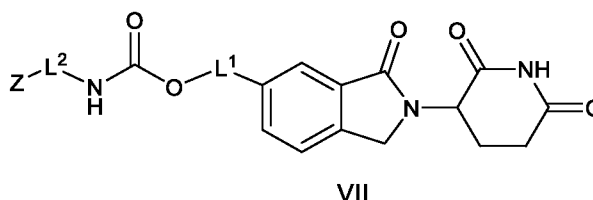
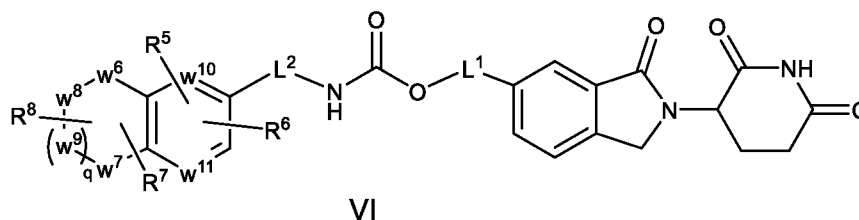
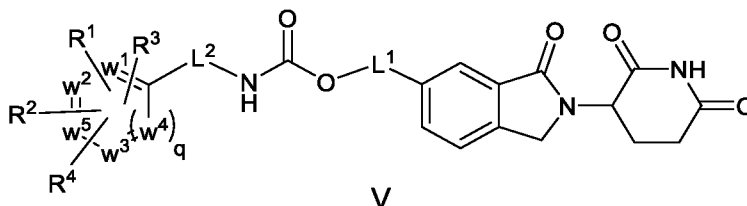
In some embodiments of a compound of formula III, IVa or IVb, L^3 is $-O-CH_2-CH_2-$ and X^2 is H, cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 and halogen.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is $-O-CH_2-CH_2-$ and X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula III, IVa or IVb, L^3 is $-O-CH_2-CH_2-$ and X^2 is morpholinyl.

In some embodiments of a compound of formula III, IVa or IVb, X^1 is a C_6 aryl or 6-membered heteroaryl, such as a pyridine, pyridazine, pyrimidine or pyrazine. In some embodiments of a compound of formula III, IVa or IVb, X^1 is a partially aromatic 6 to 10 membered aryl or heteroaryl, such as a 5-6 or 6-6 fused ring system with a 6 membered ring being a phenyl or pyridyl group. In some embodiments of a compound of formula III, IVa or IVb, X^1 is C_{1-6} alkyl, C_{3-6} cycloalkyl, 4-8 membered heterocycloalkyl. In some embodiments of a compound of

formula III, IVa or IVb, X¹ together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl. Thus, in some embodiments a compound of formula I is a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula V, VI or VII:



wherein one or two of w¹, w², w³, w⁴, w⁵ are independently of each other selected from C, N, S, and O, and the remaining of w¹, w², w³, w⁴, w⁵ are C;

- one or two of w⁶, w⁷, w⁸, w⁹ are selected from C and O and the remaining of w⁶, w⁷, w⁸, w⁹ are C; w¹⁰, w¹¹ are independently of each other selected from C and N;

L¹ is a covalent bond, linear or branched C₁₋₆ alkyl; L² is a covalent bond, linear or branched C₁₋₆ alkyl;

- R¹, R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula -L³-X², wherein L³ is a covalent bond, linear or branched C₁₋₆ alkyl, -O-, -C₁₋₄ alkoxy; and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy;

R^5 , R^6 , R^7 , R^8 are independently of each other selected from H, linear or branched C_{1-4} alkyl, such as methyl, and halogen, such as F or Cl, e.g. F;

Z is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, 4-8 membered heterocycloalkyl, wherein Z is unsubstituted or substituted with C_{1-4} alkyl, C_6 aryl, C_6 aryloxy, 6 membered heteroaryl or CF_3 ; or Z together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with C_{1-4} alkyl, C_6 aryl, C_6 aryloxy, 6 membered heteroaryl or CF_3 ;

q is 0, 1.

In some embodiments of a compound of formula V, VI or VII, L^1 is a linear or branched C_{1-4} alkyl. In some embodiments of a compound of formula V, VI or VII, L^1 is $-CH_2-$. In some embodiments of a compound of formula V, VI or VII, L^1 is $-CH(CH_3)-$.

In some embodiments of a compound of formula V, VI or VII, L^2 is a covalent bond. In some embodiments of a compound of formula V, VI or VII, L^2 is linear or branched C_{1-4} alkyl. In some embodiments of a compound of formula V, VI or VII, L^2 is $-CH_2-$. In some embodiments of a compound of formula V, VI or VII, L^2 is $-CH(CH_3)-$.

In some embodiments of a compound of formula V, VI or VII, L^3 is a covalent bond. In some embodiments of a compound of formula V, VI or VII, L^3 is linear or branched C_{1-4} alkyl, such as $-CH_2-$. In some embodiments of a compound of formula V, VI or VII, L^3 is $-O-$. In some embodiments of a compound of formula V, VI or VII, L^3 is linear or branched C_{1-4} alkoxy, such as $-O-CH_2-$, $-O-(CH_2)_2-$.

In some embodiments of a compound of formula VI one of w^{10} and w^{11} is C and the other is N. In some embodiments of a compound of formula VI, q is 1, one of w^{10} and w^{11} is C and the other is N. In some embodiments of a compound of formula VI, q is 0, one of w^{10} and w^{11} is C and the other is N.

In some embodiments of a compound of formula VI, q is 0 and w^8 is C. In some embodiments of a compound of formula VI, q is 0, w^8 is C and w^6 , w^7 are selected from C and O. In some embodiments of a compound of formula VI, q is 0, w^8 is C and w^6 , w^7 are O. In some embodiments of a compound of formula VI, q is 0, w^8 is C and one of w^6 , w^7 is C and the other of w^6 , w^7 is O.

In some embodiments of a compound of formula VI, q is 1, and w^6, w^7, w^8, w^9 are C. In some embodiments of a compound of formula VI, q is 1, and w^6 is O and w^7, w^8, w^9 are C. In some embodiments of a compound of formula VI, q is 1, and w^7 is O and w^6, w^8, w^9 are C. In some embodiments of a compound of formula VI, q is 1, and w^8 is O and w^6, w^7, w^9 are C. In some
 5 embodiments of a compound of formula VI, q is 1, and w^9 is O and w^6, w^7, w^8 are C.

In some embodiments of a compound of formula V, q is 1 and w^1, w^2, w^3, w^4, w^5 are C. In some embodiments of a compound of formula V, q is 1 and either w^1 or w^2 or w^3 or w^4 or w^5 is N and the remaining 4 of w^1, w^2, w^3, w^4, w^5 are C. In some embodiments of a compound of formula V, q is 1 and w^1, w^2 or w^1, w^3 or w^1, w^4 or w^1, w^5 or w^2, w^3 are N and the remaining
 10 3 of w^1, w^2, w^3, w^4, w^5 are C.

In some embodiments of a compound of formula V, q is 0 and w^1, w^2, w^3, w^5 are C. In some embodiments of a compound of formula V, q is 0 and either w^1 or w^2 or w^3 or w^5 is selected from N, S and O and the remaining 4 of w^1, w^2, w^3, w^5 are C. In some embodiments of a compound of formula V, q is 0 and w^1, w^2 or w^1, w^3 or w^1, w^5 are selected from N, S and O
 15 and the remaining 2 of w^1, w^2, w^3, w^5 are C.

In some embodiments of a compound of formula V, R^1, R^2, R^3 , and R^4 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}alkyl$, $-N(H)C(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.
 20

In some embodiments of a compound of formula V, R^1, R^2, R^3 , and R^4 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, $-CN$, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, R^1 is H and R^2, R^3, R^4 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}alkyl$, $-N(H)C(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.
 25

In some embodiments of a compound of formula V, R^1 is H and R^2 , R^3 , R^4 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, $-CN$, and halogen, such as F, Cl or Br, e.g. F or Cl.

5 In some embodiments of a compound of formula V, L^1 is $-CH_2-$ and R^1 , R^2 , R^3 , and R^4 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}alkyl$, $-N(H)C(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

10 In some embodiments of a compound of formula V, L^1 is $-CH_2-$ and R^1 , R^2 , R^3 , and R^4 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, $-CN$, and halogen, such as F, Cl or Br, e.g. F or Cl.

15 In some embodiments of a compound of formula V, L^1 is $-CH(CH_3)-$ and R^1 , R^2 , R^3 , and R^4 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}alkyl$, $-N(H)C(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

20 In some embodiments of a compound of formula V, L^1 is $-CH(CH_3)-$ and R^1 , R^2 , R^3 , and R^4 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, $-CN$, and halogen, such as F, Cl or Br, e.g. F or Cl.

25 In some embodiments of a compound of formula V, L^1 is $-CH_2-$, R^1 is H and R^2 , R^3 , R^4 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}alkyl$, $-N(H)C(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

30 In some embodiments of a compound of formula V, L^1 is $-CH_2-$, R^1 is H and R^2 , R^3 , R^4 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, OCF_3 , $OCHF_2$, $-CN$, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, L^1 is $-\text{CH}(\text{CH}_3)-$, R^1 is H and R^2 , R^3 , R^4 are independently of each other selected from H, linear or branched $-\text{C}_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-\text{C}_{1-4}$ alkoxy, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , $-\text{C}_{1-6}$ alkylamino, $-\text{CN}$, $-\text{OC}(\text{O})-\text{C}_{1-6}\text{alkyl}$, $-\text{N}(\text{H})\text{C}(\text{O})-\text{C}_{1-6}\text{alkyl}$, $-\text{C}(\text{O})\text{O}-\text{C}_{1-6}\text{alkyl}$, $-\text{COOH}$, $-\text{C}_{1-6}\text{alkylC}(\text{O})\text{OH}$, $-\text{C}_{1-6}\text{alkylC}(\text{O})\text{O}-\text{C}_{1-6}\text{alkyl}$, NH_2 , $-\text{C}_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, L^1 is $-\text{CH}(\text{CH}_3)-$, R^1 is H and R^2 , R^3 , R^4 are independently of each other selected from H, linear or branched $-\text{C}_{1-6}$ alkyl, $-\text{C}_{1-4}$ alkoxy, CF_3 , CHF_2 , CMeF_2 , OCF_3 , OCHF_2 , $-\text{CN}$, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, L^2 is a covalent bond and R^1 , R^2 , R^3 , and R^4 are independently of each other selected from H, linear or branched $-\text{C}_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-\text{C}_{1-4}$ alkoxy, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , $-\text{C}_{1-6}$ alkylamino, $-\text{CN}$, $-\text{OC}(\text{O})-\text{C}_{1-6}\text{alkyl}$, $-\text{N}(\text{H})\text{C}(\text{O})-\text{C}_{1-6}\text{alkyl}$, $-\text{C}(\text{O})\text{O}-\text{C}_{1-6}\text{alkyl}$, $-\text{COOH}$, $-\text{C}_{1-6}\text{alkylC}(\text{O})\text{OH}$, $-\text{C}_{1-6}\text{alkylC}(\text{O})\text{O}-\text{C}_{1-6}\text{alkyl}$, NH_2 , $-\text{C}_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, L^2 is a covalent bond and R^1 , R^2 , R^3 , and R^4 are independently of each other selected from H, linear or branched $-\text{C}_{1-6}$ alkyl, $-\text{C}_{1-4}$ alkoxy, CF_3 , CHF_2 , CMeF_2 , OCF_3 , OCHF_2 , $-\text{CN}$, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, L^2 is a covalent bond, R^1 is H and R^2 , R^3 , R^4 are independently of each other selected from H, linear or branched $-\text{C}_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-\text{C}_{1-4}$ alkoxy, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , $-\text{C}_{1-6}$ alkylamino, $-\text{CN}$, $-\text{OC}(\text{O})-\text{C}_{1-6}\text{alkyl}$, $-\text{N}(\text{H})\text{C}(\text{O})-\text{C}_{1-6}\text{alkyl}$, $-\text{C}(\text{O})\text{O}-\text{C}_{1-6}\text{alkyl}$, $-\text{COOH}$, $-\text{C}_{1-6}\text{alkylC}(\text{O})\text{OH}$, $-\text{C}_{1-6}\text{alkylC}(\text{O})\text{O}-\text{C}_{1-6}\text{alkyl}$, NH_2 , $-\text{C}_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, L^2 is a covalent bond, R^1 is H and R^2 , R^3 , R^4 are independently of each other selected from H, linear or branched $-\text{C}_{1-6}$ alkyl, $-\text{C}_{1-4}$ alkoxy, CF_3 , CHF_2 , CMeF_2 , OCF_3 , OCHF_2 , $-\text{CN}$, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, L^2 is $-\text{CH}_2-$, and R^1 , R^2 , R^3 , and R^4 are independently of each other selected from H, linear or branched $-\text{C}_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-\text{C}_{1-4}$ alkoxy, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , $-\text{C}_{1-6}$ alkylamino, $-\text{CN}$, $-\text{OC}(\text{O})-\text{C}_{1-6}\text{alkyl}$, $-\text{N}(\text{H})\text{C}(\text{O})-\text{C}_{1-6}\text{alkyl}$, $-\text{C}(\text{O})\text{O}-\text{C}_{1-6}\text{alkyl}$, $-\text{COOH}$, $-\text{C}_{1-6}\text{alkylC}(\text{O})\text{OH}$, $-\text{C}_{1-6}\text{alkylC}(\text{O})\text{O}-\text{C}_{1-6}\text{alkyl}$, NH_2 , $-\text{C}_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, L² is -CH₂-, and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, L² is -CH(CH₃)-, and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, L² is -CH(CH₃)-, and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, L² is -CH₂-, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, L² is -CH₂-, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, L² is -CH(CH₃)-, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, L^2 is $-\text{CH}(\text{CH}_3)-$, R^c is H, R^1 is H and R^2 , R^3 , R^4 are independently of each other selected from H, linear or branched $-\text{C}_{1-6}$ alkyl, $-\text{C}_{1-4}$ alkoxy, CF_3 , CHF_2 , CMeF_2 , OCF_3 , OCHF_2 , $-\text{CN}$, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of
 5 formula $-\text{L}^3-\text{X}^2$, wherein L^3 is a covalent bond and X^2 is C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-\text{C}_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , and $-\text{C}_{1-4}$ alkylhydroxy.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of
 10 formula $-\text{L}^3-\text{X}^2$, wherein L^3 is a covalent bond and X^2 is C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-\text{C}_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of
 15 formula $-\text{L}^3-\text{X}^2$, wherein L^3 is a covalent bond and X^2 is cyclopropyl, cyclobutyl, azetidiny, oxetanyl, pyrrolidiny, piperidiny, piperaziny, morpholiny, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, C_6 aryl, pyridiny, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, e.g. methyl, $-\text{C}_{1-4}$ alkoxy, e.g. $-\text{OMe}$, NMe_2 and halogen, e.g. F.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of
 20 formula $-\text{L}^3-\text{X}^2$, wherein L^3 is a covalent bond and X^2 is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridiny, pyrrolidiny, N-methyl-pyrrolidiny, methyl-pyrrolidiny, piperdiny, N-methyl piperdiny, methyl-piperdiny, difluoro-piperidiny, morpholiny, N-methyl-morpholiny, oxetanyl, methyl-oxetanyl, piperaziny, N-methyl-piperaziny, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-
 25 oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of
 formula $-\text{L}^3-\text{X}^2$, wherein L^3 is a covalent bond and X^2 is H, cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, azetidiny, NMe_2 -azetidiny, oxetanyl, methyl-oxetanyl, pyrrolidiny, methyl-pyrrolidiny, piperidiny, Me-piperidiny, Di-F-
 30 piperidiny, N-Me-piperaziny, morpholiny, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, C_6 aryl, methoxy- C_6 aryl, pyridiny.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is a linear or branched C_{1-4} alkyl, such as $-CH_2-$, and X^2 is C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is a linear or branched C_{1-4} alkyl, such as $-CH_2-$, and X^2 is C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is a linear or branched C_{1-4} alkyl, such as $-CH_2-$, and X^2 is cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 and halogen.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is a linear or branched C_{1-4} alkyl, such as $-CH_2-$, and X^2 is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is linear or branched C_{1-4} alkyl, such as $-CH_2-$, and X^2 is morpholinyl, N-methyl-morpholinyl, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is $-O-$ and X^2 is C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl,

4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is $-O-$ and X^2 is C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is $-O-$ and X^2 is cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperidinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 and halogen.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is $-O-$ and X^2 is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperidinyl, N-methyl piperidinyl, methyl-piperidinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is $-O-$ and X^2 is cyclopropyl, pyrrolidinyl, N-methyl-pyrrolidinyl,

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is $-O-CH_2-$ and X^2 is C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is $-O-CH_2-$ and X^2 is C_{3-6} cycloalkyl, C_6 aryl, 6 membered

heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is $-O-CH_2-$ and X^2 is cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 and halogen.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is $-O-CH_2-$ and X^2 is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is $-O-CH_2-$ and X^2 is pyrrolidinyl, N-methyl-pyrrolidinyl.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is $-O-CH_2-CH_2-$ and X^2 is C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is $-O-CH_2-CH_2-$ and X^2 is C_{3-6} cycloalkyl, C_6 aryl, 6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , and halogen, e.g. F.

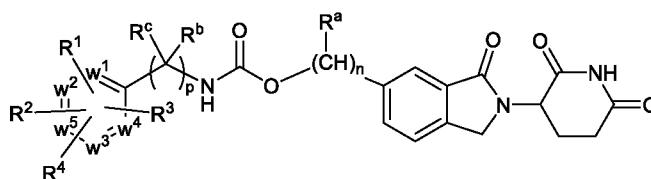
In some embodiments of a compound of formula V, one of R^1 , R^2 , R^3 , and R^4 is a group of formula $-L^3-X^2$, wherein L^3 is $-O-CH_2-CH_2-$, and X^2 is cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is

unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂ and halogen.

In some embodiments of a compound of formula V, one of R¹, R², R³, and R⁴ is a group of formula -L³-X², wherein L³ is -O-CH₂-CH₂- and X² is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula V, one of R¹, R², R³, and R⁴ is a group of formula -L³-X², wherein L³ is -O-CH₂-CH₂- and X² is morpholinyl.

In some embodiments, a compound of formula I is a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula Va:



Va

wherein

one or two of w¹, w², w³, w⁴, w⁵ are independently of each other selected from C, N, S, and O, and the remaining of w¹, w², w³, w⁴, w⁵ are C;

R¹, R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula -L³-X², wherein L³ is a covalent bond, linear or branched C₁₋₆ alkyl, -O-, -C₁₋₄ alkoxy and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or

substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy;

R^a is H, linear or branched C₁₋₄ alkyl, R^b, R^c are independently of each other H, linear or branched C₁₋₄ alkyl; n is 1, or 2; and p is 0 or 1.

- 5 In some embodiments of a compound of formula Va, n is 1. In some embodiments n is 1 and R^a is H. In some embodiments of a compound of formula Va, n is 1 and R^a is methyl. In some embodiments of a compound of formula Va, n is 1, p is 0 and R^a is H. In some embodiments of a compound of formula Va, n is 1, p is 0 and R^a is methyl

- In some embodiments of a compound of formula Va, p is 0. In some embodiments of a
10 compound of formula Va, p is 1. In some embodiments of a compound of formula Va, p is 1, and R^b and R^c are H. In some embodiments of a compound of formula Va, p is 1, R^b is methyl and R^c is H.

- In some embodiments of a compound of formula Va, w¹, w², w³, w⁴, w⁵ are C. In some
embodiments of a compound of formula Va, either w¹ or w² or w³ or w⁴ or w⁵ is N and the
15 remaining 4 of w¹, w², w³, w⁴, w⁵ are C. In some embodiments of a compound of formula Va, w¹, w² or w¹, w³ or w¹, w⁴ or w², w³ are N and the remaining 3 of w¹, w², w³, w⁴, w⁵ are C.

- In some embodiments of a compound of formula Va, L³ is a covalent bond. In some
embodiments of a compound of formula Va, L³ is linear or branched C₁₋₄ alkyl, such as -CH₂-.
In some embodiments of a compound of formula Va, L³ is -O-. In some embodiments of a
20 compound of formula Va, L³ is linear or branched C₁₋₄ alkoxy, such as -O-CH₂-, -O-(CH₂)₂-.

- In some embodiments of a compound of formula Va, R¹, R², R³, and R⁴ are independently of
each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl,
-C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -
OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C<sub>1-
25 6</sub>alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, R¹, R², R³, and R⁴ are independently of
each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂,
OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

- In some embodiments of a compound of formula Va, R¹ is H and R², R³, R⁴ are independently
30 of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆

heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

- 5 In some embodiments of a compound of formula Va, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

- In some embodiments of a compound of formula Va, n is 1, R^a is H and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.
- 10

- In some embodiments of a compound of formula Va, n is 1, R^a is H and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.
- 15

- In some embodiments of a compound of formula Va, n is 1, R^a is CH₃ and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.
- 20

- In some embodiments of a compound of formula Va, n is 1, R^a is CH₃ and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.
- 25

- In some embodiments of a compound of formula Va, n is 1, R^a is H, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.
- 30

In some embodiments of a compound of formula Va, n is 1, R^a is H, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

5 In some embodiments of a compound of formula Va, n is 1, R^a is CH₃, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

10 In some embodiments of a compound of formula Va, n is 1, R^a is CH₃, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

15 In some embodiments of a compound of formula Va, p is 0 and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

20 In some embodiments of a compound of formula Va, p is 0 and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

25 In some embodiments of a compound of formula Va, p is 0, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

30 In some embodiments of a compound of formula Va, p is 0, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, p is 1, R^b, R^c are H, and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, p is 1, R^b, R^c are H, and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, p is 1, R^b is CH₃, R^c is H, and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, p is 1, R^b is CH₃, R^c is H, and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, p is 1, R^b, R^c are H, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, p is 1, R^b, R^c are H, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, p is 1, R^b is CH₃, R^c is H, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋

alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, p is 1, R^b is CH₃, R^c is H, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, R¹ is C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -O-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, 5-10 membered heteroaryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -O-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, R¹ is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, R¹ is -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, R¹ is -O-C₃₋₆ cycloalkyl, -O-C₆₋₁₀ aryl, -O-(5-10 membered heteroaryl), -O-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, R¹ is -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, R¹ is C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, R¹ is a group of formula -L³-X², wherein L³ is a covalent bond, linear or branched C₁₋₄ alkyl, -O-, -C₁₋₄ alkoxy and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperidinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other

selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va, R^1 is a group of formula $-L^3-X^2$,
 5 wherein L^3 is a covalent bond, $-CH_2-$, $-O-$, $-OCH_2-$, $-O(CH_2)_2-$ and X^2 is cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, e.g. $-OMe$, NMe_2 , halogen, e.g. F; and R^2 , R^3 , R^4 are independently of each other
 10 selected from H, halogen, e.g. Cl, F, linear or branched $-C_{1-4}$ alkyl, e.g., Me, Et, t-But, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN , and C_{1-4} alkoxy, e.g. $-OMe$.

In some embodiments of a compound of formula Va, R^1 is a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, $-CH_2-$, $-O-$, $-OCH_2-$, $-O(CH_2)_2-$ and X^2 is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl,
 15 fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; and R^2 , R^3 , R^4 are
 20 independently of each other selected from H, halogen, e.g. Cl, F, linear or branched $-C_{1-4}$ alkyl, e.g., Me, Et, t-But, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN , and C_{1-4} alkoxy, e.g. $-OMe$.

In some embodiments of a compound of formula Va, R^1 is C_{3-6} cycloalkyl, $-C_{1-4}$ alkyl- C_{3-6} cycloalkyl, $-O-C_{3-6}$ cycloalkyl, $-C_{1-4}$ alkoxy- C_{3-6} cycloalkyl, C_{6-10} aryl, $-C_{1-4}$ alkyl- C_{6-10} aryl, $-O-C_{6-10}$ aryl, $-C_{1-4}$ alkoxy- C_{6-10} aryl, 5-10 membered heteroaryl, $-C_{1-4}$ alkyl-(5-10 membered
 25 heteroaryl), $-O-(5-10$ membered heteroaryl), $-C_{1-4}$ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, $-C_{1-4}$ alkyl-(4-8 membered heterocycloalkyl), $-O-(4-8$ membered heterocycloalkyl), $-C_{1-4}$ alkoxy-(4-8 membered heterocycloalkyl), wherein R^1 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$
 30 alkylhydroxy; and R^2 , R^3 , R^4 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-$

(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n is 1, R^a is H; and p is 0.

In some embodiments of a compound of formula Va, R¹ is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n is 1, R^a is H; and p is 0.

In some embodiments of a compound of formula Va, R¹ is -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n is 1, R^a is H; and p is 0.

In some embodiments of a compound of formula Va, R¹ is -O-C₃₋₆ cycloalkyl, -O-C₆₋₁₀ aryl, -O-(5-10 membered heteroaryl), -O-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n is 1, R^a is H; and p is 0.

In some embodiments of a compound of formula Va, R¹ is -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃,

CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n is 1, R^a is H; and p is 0.

In some embodiments of a compound of formula Va, R¹ is C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n is 1, R^a is H; and p is 0.

In some embodiments of a compound of formula Va, R¹ is a group of formula -L³-X², wherein L³ is a covalent bond, linear or branched C₁₋₄ alkyl, -O-, -C₁₋₄ alkoxy and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n is 1, R^a is H; and p is 0.

In some embodiments of a compound of formula Va, R¹ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; and R², R³, R⁴ are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe; and n is 1, R^a is H; and p is 0.

In some embodiments of a compound of formula Va, R¹ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl,

fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; and R², R³, R⁴ are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe; and n is 1, R^a is H; and p is 0.

In some embodiments of a compound of formula Va, R¹ is C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -O-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, 5-10 membered heteroaryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -O-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n is 1, R^a is CH₃; and p is 0.

In some embodiments of a compound of formula Va, R¹ is C₆₋₁₀ aryl, wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n is 1, R^a is CH₃; and p is 0.

In some embodiments of a compound of formula Va, R¹ is C₆₋₁₀ aryl, wherein R¹ is unsubstituted or substituted with linear or branched -C₁₋₄ alkyl, e.g. methyl, -C₁₋₄ alkoxy, e.g. -OMe, and halogen, such as F, Cl, e.g. Cl; and n is 1, R^a is CH₃; and p is 0.

In some embodiments of a compound of formula Va, R¹ is C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -O-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, 5-10 membered heteroaryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -O-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n, p are 1, R^a, R^b, R^c are H.

In some embodiments of a compound of formula Va, R¹ is C₆₋₁₀ aryl, wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n, p are 1, R^a, R^b, R^c are H.

In some embodiments of a compound of formula Va, R¹ is C₆₋₁₀ aryl, wherein R¹ is unsubstituted or substituted with -C₁₋₄ alkoxy, e.g. -OMe; and n, p are 1, R^a, R^b, R^c are H.

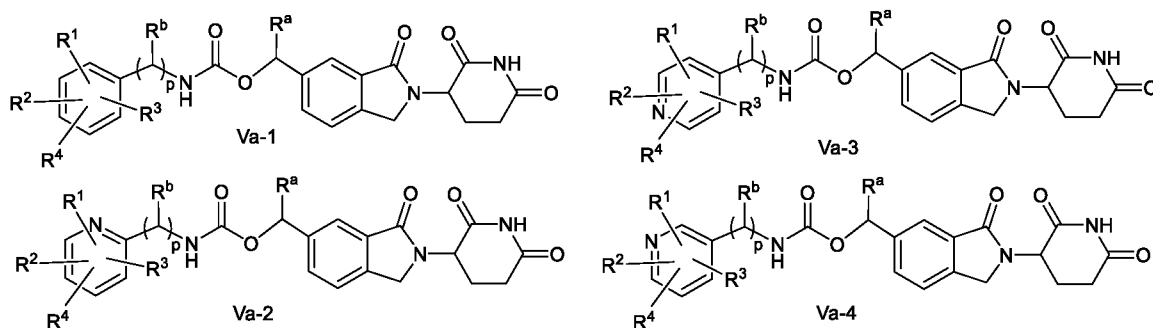
In some embodiments of a compound of formula Va, R¹ is C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -O-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, 5-10 membered heteroaryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -O-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-

(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n, p are 1, R^a, R^c are H, R^b is CH₃.

In some embodiments of a compound of formula Va, R¹ is C₆₋₁₀ aryl, wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n, p are 1, R^a, R^c are H, R^b is CH₃.

In some embodiments of a compound of formula Va, R¹ is C₆₋₁₀ aryl; and n, p are 1, R^a, R^c are H, R^b is CH₃.

More specific embodiments of the compound of formula Va are provided by formula Va-1, wherein w¹ to w⁵ are C, and by formula Va-2, Va-3, Va-4, wherein one of w¹ to w⁵ is N, more specifically, wherein w¹ is N, w² to w⁵ are C; or w² is N, w¹ and w³ to w⁵ are C; or w³ is N, w¹, w² and w⁴, w⁵ are C



wherein

R¹, R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula -L³-X², wherein L³ is a covalent bond, linear or branched C₁₋₆ alkyl, -O-, or -C₁₋₄ alkoxy and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or

substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy;

R^a, R^b are independently of each other H or methyl; and p is 0 or 1.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0. In some
5 embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 1. In some
embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 1 and R^b is H. In some
embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 1 and R^b is methyl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0 and R^a is H.
In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0 and R^a is
10 methyl. In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 1, R^b
is H and R^a is H. In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p
is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, L³ is a covalent
bond. In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, L³ is linear
15 or branched C₁₋₄ alkyl, such as -CH₂-. In some embodiments of a compound of formula Va-1,
Va-2, Va-3, Va-4, L³ is -O-. In some embodiments L³ is linear or branched C₁₋₄ alkoxy, such
as -O-CH₂-, -O-(CH₂)₂-.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹, R², R³, and R⁴
are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or
20 branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -
C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆
alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl
or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹, R², R³, and R⁴
25 are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy,
CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is H and R², R³,
R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or
branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -
30 C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋

$\text{-C}_{1-6}\text{alkylC(O)OH}$, $\text{-C}_{1-6}\text{alkylC(O)O-C}_{1-6}\text{alkyl}$, NH_2 , -C_{1-4} alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R^1 is H and R^2 , R^3 , R^4 are independently of each other selected from H, linear or branched -C_{1-6} alkyl, -C_{1-4} alkoxy, CF_3 , CHF_2 , CMeF_2 , OCF_3 , OCHF_2 , -CN , and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R^a is H and R^1 , R^2 , R^3 , and R^4 are independently of each other selected from H, linear or branched -C_{1-6} alkyl, linear or branched C_{1-6} heteroalkyl, -C_{1-4} alkoxy, CF_3 , CHF_2 , CMeF_2 , $\text{-O-(CH}_2\text{)}_2\text{-OMe}$, OCF_3 , OCHF_2 , -C_{1-6} alkylamino, -CN , $\text{-OC(O)-C}_{1-6}\text{alkyl}$, $\text{-N(H)C(O)-C}_{1-6}\text{alkyl}$, $\text{-C(O)O-C}_{1-6}\text{alkyl}$, -COOH , $\text{-C}_{1-6}\text{alkylC(O)OH}$, $\text{-C}_{1-6}\text{alkylC(O)O-C}_{1-6}\text{alkyl}$, NH_2 , -C_{1-4} alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R^a is H and R^1 , R^2 , R^3 , and R^4 are independently of each other selected from H, linear or branched -C_{1-6} alkyl, -C_{1-4} alkoxy, CF_3 , CHF_2 , CMeF_2 , OCF_3 , OCHF_2 , -CN , and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R^a is CH_3 and R^1 , R^2 , R^3 , and R^4 are independently of each other selected from H, linear or branched -C_{1-6} alkyl, linear or branched C_{1-6} heteroalkyl, -C_{1-4} alkoxy, CF_3 , CHF_2 , CMeF_2 , $\text{-O-(CH}_2\text{)}_2\text{-OMe}$, OCF_3 , OCHF_2 , -C_{1-6} alkylamino, -CN , $\text{-OC(O)-C}_{1-6}\text{alkyl}$, $\text{-N(H)C(O)-C}_{1-6}\text{alkyl}$, $\text{-C(O)O-C}_{1-6}\text{alkyl}$, -COOH , $\text{-C}_{1-6}\text{alkylC(O)OH}$, $\text{-C}_{1-6}\text{alkylC(O)O-C}_{1-6}\text{alkyl}$, NH_2 , -C_{1-4} alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R^a is CH_3 and R^1 , R^2 , R^3 , and R^4 are independently of each other selected from H, linear or branched -C_{1-6} alkyl, -C_{1-4} alkoxy, CF_3 , CHF_2 , CMeF_2 , OCF_3 , OCHF_2 , -CN , and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R^a is CH_3 , and R^1 , R^2 , R^3 , R^4 are independently of each other selected from H, halogen, such as Cl, F, linear or branched -C_{1-4} alkyl, such as methyl, fluorinated C_{1-4} alkoxy, such as -OCF_3 .

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R^a is H, R^1 is H and R^2 , R^3 , R^4 are independently of each other selected from H, linear or branched -C_{1-6} alkyl, linear

or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

- 5 In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R^a is H, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

- In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R^a is CH₃, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl,
 10 linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

- In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R^a is CH₃, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl,
 15 -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

- In some embodiments of a compound of formula Va-1, R^a is CH₃, R¹ is H and R², R³, R⁴ are independently of each other selected from H, halogen, such as Cl, F, linear or branched -C₁₋₄
 20 alkyl, such as methyl, fluorinated C₁₋₄ alkoxy, such as -OCF₃.

- In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0 and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -
 25 COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

- In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0 and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or
 30 Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0, R^a is H and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0, R^a is H and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0, R^a is CH₃ and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0, R^a is CH₃ and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0, R^a is CH₃, and R¹, R², R³, R⁴ are independently of each other selected from H, halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, such as methyl, fluorinated C₁₋₄ alkoxy, such as -OCF₃.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0, R^a is H, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

10 In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0, R^a is H, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

15 In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0, R^a is CH₃, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

20 In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 0, R^a is CH₃, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

25 In some embodiments of a compound of formula Va-1, R^a is CH₃, p is 0, R¹ is H and R², R³, R⁴ are independently of each other selected from H, halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, such as methyl, fluorinated C₁₋₄ alkoxy, such as -OCF₃.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 1, R^b and R^c are H, and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -

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C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 1, R^b and R^c are H, and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or
5 branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, p is 1, R^b and R^c are H, and R¹, R², R³, and R⁴ are independently of each other selected from H and C₁₋₄ alkoxy, e.g. -OMe.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 1, R^b is CH₃,
10 R^c is H, and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

15 In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 1, R^b is CH₃, R^c is H, and R¹, R², R³, and R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 1, R^b and R^c
20 are H, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

25 In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 1, R^b and R^c are H, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, p is 1, R^b and R^c are H, R¹ is H and R²,
30 R³, and R⁴ are independently of each other selected from H and C₁₋₄ alkoxy, e.g. -OMe.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 1, R^b is CH₃, R^c is H, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, p is 1, R^b is CH₃, R^c is H, R¹ is H and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, p is 1, R^b is CH₃, R^c is H, and R¹, R², R³, R⁴ are H.

In some embodiments of a compound of formula, Va-1, Va-2, Va-3, Va-4, R¹ is C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -O-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, 5-10 membered heteroaryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -O-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl,

-C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is a group of formula -L³-X², wherein L³ is a covalent bond, linear or branched C₁₋₄ alkyl, -O-, -C₁₋₄ alkoxy and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; and R², R³, R⁴ are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; and R², R³, R⁴ are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -O-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, 5-10 membered heteroaryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -O-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n is 1, R^a is H; and p is 0.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n is 1, R^a is H; and p is 0.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is a group of formula -L³-X², wherein L³ is a covalent bond, linear or branched C₁₋₄ alkyl, -O-, -C₁₋₄ alkoxy and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperidinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -

N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n is 1, R^a is H; and p is 0.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; and R², R³, R⁴ are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe; and n is 1, R^a is H; and p is 0.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; and R², R³, R⁴ are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe; and n is 1, R^a is H; and p is 0.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -O-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, 5-10 membered heteroaryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -O-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or

branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n is 1, R^a is CH₃; and p is 0.

- 5 In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of
- 10 linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; and R², R³, R⁴ are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe; and n is 1, R^a is CH₃; and p is 0.

- In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is a group of
- 15 formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-
- 20 piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; and R², R³, R⁴ are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe; and n is 1, R^a is CH₃; and p is 0.

- 25 In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -O-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, 5-10 membered heteroaryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -O-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -
- 30 O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein R¹ is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋

alkylhydroxy; and R^2 , R^3 , R^4 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}alkyl$, $-N(H)C(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n, p are 1, R^a , R^b , R^c are H.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R^1 is a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, $-CH_2-$, $-O-$, $-OCH_2-$, $-O(CH_2)_2-$ and X^2 is cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, e.g. $-OMe$, NMe_2 , halogen, e.g. F; and R^2 , R^3 , R^4 are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched $-C_{1-4}$ alkyl, e.g., Me, Et, t-But, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN, and C_{1-4} alkoxy, e.g. $-OMe$; and n, p are 1, R^a , R^b , R^c are H.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R^1 is a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, $-CH_2-$, $-O-$, $-OCH_2-$, $-O(CH_2)_2-$ and X^2 is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; and R^2 , R^3 , R^4 are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched $-C_{1-4}$ alkyl, e.g., Me, Et, t-But, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN, and C_{1-4} alkoxy, e.g. $-OMe$; and n, p are 1, R^a , R^b , R^c are H.

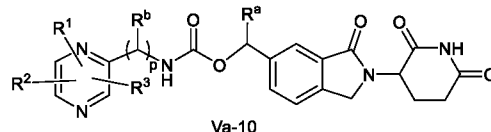
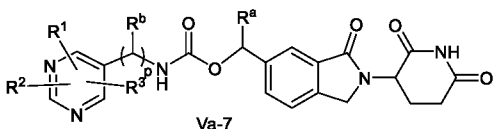
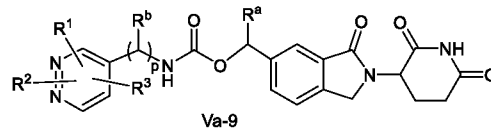
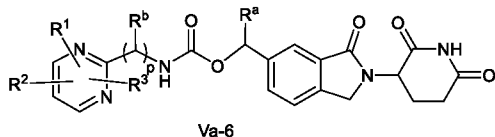
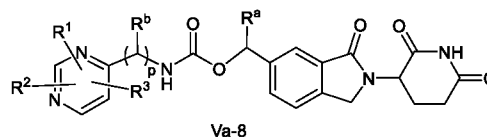
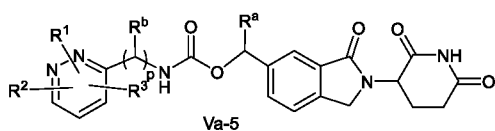
In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R^1 is C_{3-6} cycloalkyl, $-C_{1-4}$ alkyl- C_{3-6} cycloalkyl, $-O-C_{3-6}$ cycloalkyl, $-C_{1-4}$ alkoxy- C_{3-6} cycloalkyl, C_{6-10} aryl, $-C_{1-4}$ alkyl- C_{6-10} aryl, $-O-C_{6-10}$ aryl, $-C_{1-4}$ alkoxy- C_{6-10} aryl, 5-10 membered heteroaryl, $-C_{1-4}$ alkyl-(5-10 membered heteroaryl), $-O-(5-10$ membered heteroaryl), $-C_{1-4}$ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, $-C_{1-4}$ alkyl-(4-8 membered heterocycloalkyl), $-O-(4-8$ membered heterocycloalkyl), $-C_{1-4}$ alkoxy-(4-8 membered heterocycloalkyl), wherein R^1 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, -

C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and R², R³, R⁴ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; and n, p are 1, R^a, R^c are H, R^b is CH₃.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; and R², R³, R⁴ are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe; and n, p are 1, R^a, R^c are H, R^b is CH₃.

In some embodiments of a compound of formula Va-1, Va-2, Va-3, Va-4, R¹ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; and R², R³, R⁴ are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe; and n, p are 1, R^a, R^c are H, R^b is CH₃.

More specific embodiments of the compound of formula V are also provided by formula Va-5, Va-6, Va-7, Va-8, Va-9, Va-10, wherein two of w¹ to w⁵ are N, e.g., wherein w¹, w² are N, w³ to w⁵ are C; or w¹, w⁵ are N, w² to w⁴ are C; or w², w⁴ are N, w¹, w³, w⁵ are C; or w¹, w³ are N, w², w⁴, w⁵ are C; or w², w³ are N, w¹, w⁴, w⁵ are C; or w¹, w⁴ are N, w², w³, w⁵ are C



wherein

R^1 , R^2 , R^3 , R^4 are independently of each other selected from H, linear or branched C_{1-6} alkyl, linear or branched C_{1-6} heteroalkyl, C_{1-4} alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, linear or branched C_{1-6} alkyl, $-O-$, or $-C_{1-4}$ alkoxy and X^2 is C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; R^a , R^b are independently of each other H or methyl; and p is 0 or 1.

In some embodiments of a compound of formula Va-5, Va-6, Va-7, Va-8, Va-9, Va-10, p is 0. In some embodiments of a compound of formula Va-5, Va-6, Va-7, Va-8, Va-9, Va-10, p is 1.

In some embodiments of a compound of formula Va-5, Va-6, Va-7, Va-8, Va-9, Va-10, R^a is H. In some embodiments of a compound of formula Va-5, Va-6, Va-7, Va-8, Va-9, Va-10, R^a is methyl. In some embodiments of a compound of formula Va-5, Va-6, Va-7, Va-8, Va-9, Va-10, p is 0 and R^a is H. In some embodiments of a compound of formula Va-5, Va-6, Va-7, Va-8, Va-9, Va-10, p is 0 and R^a is methyl.

In some embodiments of a compound of formula Va-5, Va-6, Va-7, Va-8, Va-9, Va-10, p is 1 and R^b is H. In some embodiments of a compound of formula Va-5, Va-6, Va-7, Va-8, Va-9, Va-10, p is 1 and R^b is methyl. In some embodiments of a compound of formula Va-5, Va-

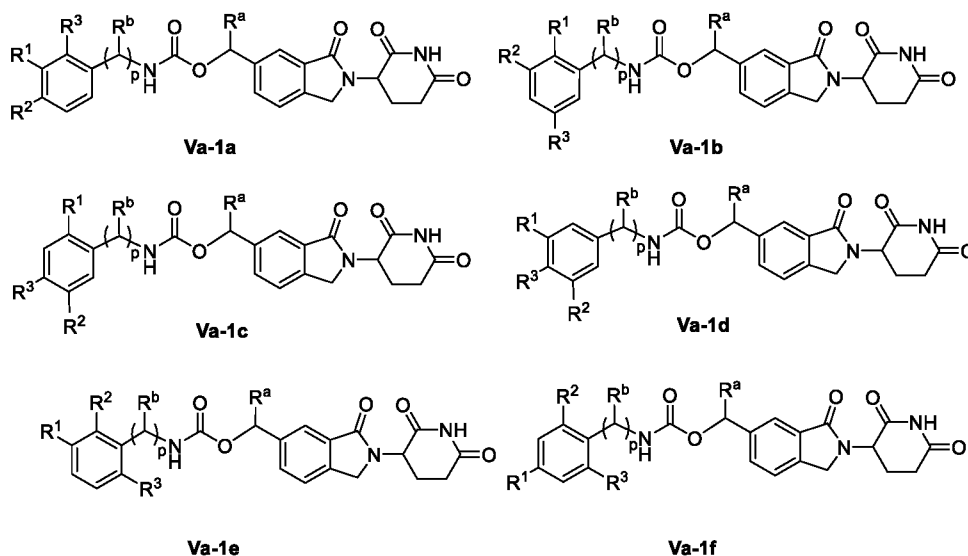
6, Va-7, Va-8, Va-9, Va-10, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Va-5, Va-6, Va-7, Va-8, Va-9, Va-10, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Va-5, Va-6, Va-7, Va-8, Va-9, Va-10, R¹ is 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, halogen, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂.

In some embodiments of a compound of formula Va-5, Va-6, Va-7, Va-8, Va-9, Va-10, R¹ is selected from pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl and R², R³ each are independently selected from H, linear or branched C₁₋₄ alkyl, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, and halogen, such as F, Cl or Br, e.g. F or Cl.

10 In some embodiments of a compound of formula Va-5, Va-6, Va-7, Va-8, Va-9, Va-10, R¹ is piperidinyl.

In some embodiments the compound of formula V and Va-1 is defined by formula, Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f



15 wherein

R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula -L³-X², wherein L³ is a covalent bond, linear or branched C₁₋₆ alkyl, -O-, or -C₁₋₄ alkoxy and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of

linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; p is 0 or 1 and R^a, R^b are independently of each other H or methyl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0. In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 1.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R^a is H. In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R^a is methyl. In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0 and R^a is H. In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0 and R^a is methyl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 1 and R^b is H. In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 1 and R^b is methyl. In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, L³ is a covalent bond. In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, L³ is linear or branched C₁₋₄ alkyl, such as -CH₂-. In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, L³ is -O-. In some embodiments L³ is linear or branched C₁₋₄ alkoxy, such as -O-CH₂-, -O-(CH₂)₂-

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl,

-C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R^a is H and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R^a is H and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R^a is CH₃ and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R^a is CH₃ and R¹, R², R³ are independently of each other selected from H, linear or branched

-C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R^a is CH₃, and R¹, R², R³ are independently of each other selected from H, halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, such as methyl, fluorinated C₁₋₄ alkoxy, such as -OCF₃.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R^a is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆ alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R^a is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R^a is CH₃, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆ alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R^a is CH₃, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R^a is CH₃, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, such as methyl, fluorinated C₁₋₄ alkoxy, such as -OCF₃.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0 and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0 and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0, R^a is H and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0, R^a is H and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0, R^a is CH₃ and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0, R^a is CH₃ and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0, R^a is CH₃, and R¹, R², R³ are independently of each other selected from H, halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, such as methyl, fluorinated C₁₋₄ alkoxy, such as -OCF₃.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0, R^a is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0, R^a is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0, R^a is CH₃, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0, R^a is CH₃, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

- 5 In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R^a is CH₃, p is 0, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, such as methyl, fluorinated C₁₋₄ alkoxy, such as -OCF₃.

- 10 In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 1, R^b and R^c are H, and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

- 15 In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 1, R^b and R^c are H, and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

- 20 In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 1, R^b and R^c are H, and R¹, R², R³ are independently of each other selected from H and C₁₋₄ alkoxy, e.g. -OMe.

- 25 In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 1, R^b is CH₃, R^c is H, and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

- 30 In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 1, R^b is CH₃, R^c is H, and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 1, R^b and R^c are H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 1, R^b and R^c are H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 1, R^b and R^c are H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H and C₁₋₄ alkoxy, e.g. -OMe.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 1, R^b is CH₃, R^c is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 1, R^b is CH₃, R^c is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 1, R^b is CH₃, R^c is H, and R¹, R², R³ are H.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, one of R¹, R², R³ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of

linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, one of R¹, R², R³ is C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -O-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, 5-10 membered heteroaryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -O-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein the C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, and 4-8 membered heterocycloalkyl are unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy, and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl..

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, one of R¹, R², R³ is C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein the C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, and 4-8 membered heterocycloalkyl are unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, one of R¹, R², R³ is a group of formula -L³-X², wherein L³ is a covalent bond, linear or branched C₁₋₄ alkyl, -O-, -C₁₋₄ alkoxy and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl,

pyrrolidinyl, piperdiny, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; and the other two of R^1 , R^2 , R^3 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, one of R^1 , R^2 , R^3 is a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, $-CH_2-$, $-O-$, $-OCH_2-$, $-O(CH_2)_2-$ and X^2 is cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdiny, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, e.g. $-OMe$, NMe_2 , halogen, e.g. F; and the other two of R^1 , R^2 , R^3 are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched $-C_{1-4}$ alkyl, e.g., Me, Et, t-But, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN, and C_{1-4} alkoxy, e.g. $-OMe$.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, one of R^1 , R^2 , R^3 is a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, $-CH_2-$, $-O-$, $-OCH_2-$, $-O(CH_2)_2-$ and X^2 is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdiny, N-methyl piperdiny, methyl-piperdiny, difluoro-piperidiny, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; and the other two of R^1 , R^2 , R^3 are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched $-C_{1-4}$ alkyl, e.g., Me, Et, t-But, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN, and C_{1-4} alkoxy, e.g. $-OMe$.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, R^a is H, one of R^1 , R^2 , R^3 is a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, $-CH_2-$, $-O-$, $-OCH_2-$, $-O(CH_2)_2-$ and X^2 is C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of

linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, R^a is H, one of R¹, R², R³ is C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -O-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, 5-10 membered heteroaryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -O-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein the C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, and 4-8 membered heterocycloalkyl are unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, R^a is H, one of R¹, R², R³ is C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), wherein the C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, and 4-8 membered heterocycloalkyl are unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, R^a is H, one of R¹, R², R³ is a group of formula -L³-X², wherein L³ is a covalent bond, linear or branched C₁₋₄ alkyl, -O-, -C₁₋₄ alkoxy and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, R^a is H, one of R¹, R², R³ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; and the other two of R¹, R², R³ are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, R^a is H, one of R¹, R², R³ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; and the other two of R¹, R², R³ are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e or Va-1f, p is 0, one of R¹, R², R³ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, p is 0, one of R¹, R², R³ is a group selected from C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -O-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, 5-10 membered heteroaryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -O-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), which group is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, p is 0, one of R¹, R², R³ is a group selected from C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), which group is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl,

-C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

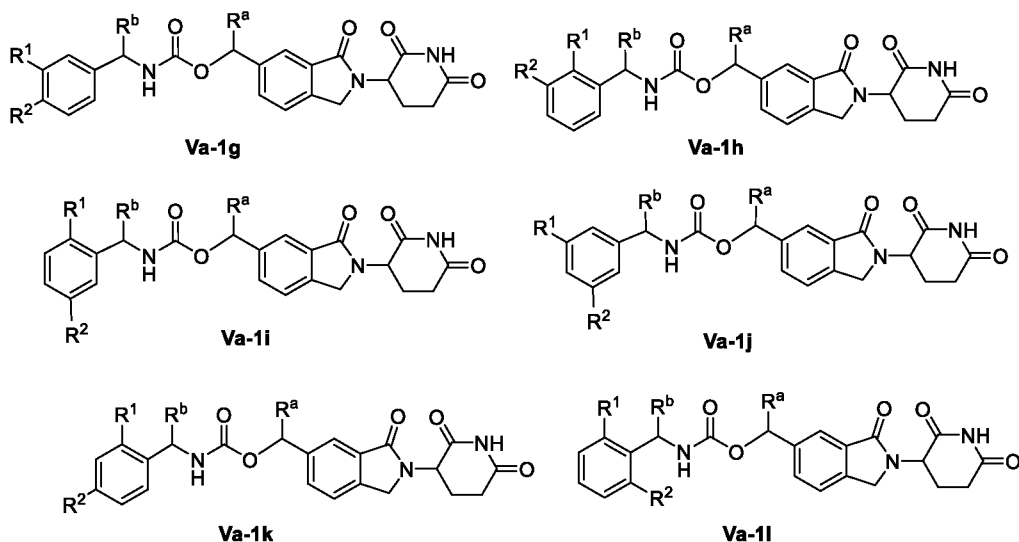
In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, p is 0, one of R¹, R², R³ is a group of formula -L³-X², wherein L³ is a covalent bond, linear or branched C₁₋₄ alkyl, -O-, -C₁₋₄ alkoxy and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, p is 0, one of R¹, R², R³ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; and the other two of R¹, R², R³ are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe..

In some embodiments of a compound of formula Va-1a, Va-1b, Va-1c, Va-1d, Va-1e, Va-1f, p is 0, one of R¹, R², R³ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; and the other two of R¹, R², R³ are independently of each other

selected from H, halogen, e.g. Cl, F, linear or branched $-C_{1-4}$ alkyl, e.g., Me, Et, t-But, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN, and C_{1-4} alkoxy, e.g. $-OMe$.

In some embodiments, the compound of formula Va and Va-1a is a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l,



wherein

R^1 , R^2 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, linear or branched C_{1-6} alkyl, $-O-$, or $-C_{1-4}$ alkoxy and X^2 is C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; and R^a , R^b are independently of each other H or methyl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^a is H. In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^a is methyl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^b is H. In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^b is methyl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, L³ is a covalent bond. In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, L³ is linear or branched C₁₋₄ alkyl, such as -CH₂-. In some
 5 O-. In some embodiments L³ is linear or branched C₁₋₄ alkoxy, such as -O-CH₂-, -O-(CH₂)₂-

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl
 10 or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and
 15 20 halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^a is CH₃ and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and
 25 30 halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^a is CH₃ and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

- 5 In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^a is CH₃, and R¹, R² are independently of each other selected from H, halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, such as methyl, fluorinated C₁₋₄ alkoxy, such as -OCF₃.

- 10 In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^b is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

- 15 In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^b is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

- 20 In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^b is CH₃ and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

- 25 In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^b is CH₃ and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

- 30 In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^b is H, R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -

C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^b is H, R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^b is H, R^a is CH₃ and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^b is H, R^a is CH₃ and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^b is H, R^a is CH₃, and R¹, R² are independently of each other selected from H, halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, such as methyl, fluorinated C₁₋₄ alkoxy, such as -OCF₃.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^b is CH₃, R^a is H, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^b is CH₃, R^a is H, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^b is CH₃, R^a is H, and R¹, R² are independently of each other selected from H and C₁₋₄ alkoxy, e.g. -OMe.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, one of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; the other of R¹, R² is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, one of R¹, R² is selected from a group consisting of C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -O-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, 5-10 membered heteroaryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -O-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), which group is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, one of R¹, R² is selected from a group consisting of C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), which group is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-

(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, one of of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; the other of R¹, R² is a group of formula -L³-X², wherein L³ is a covalent bond, linear or branched C₁₋₄ alkyl, -O-, -C₁₋₄ alkoxy and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, one of of R¹, R² is selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe, the other of R¹, R² is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, one of of R¹, R² is selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe; the other of R¹, R² is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^a is H, one of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; the other of R¹, R² is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^a is H, one of R¹, R² is selected from a group consisting of C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -O-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, 5-10 membered heteroaryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -O-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), which group is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

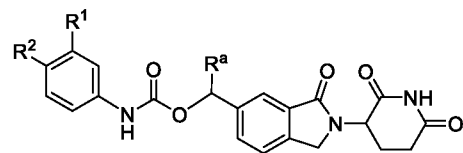
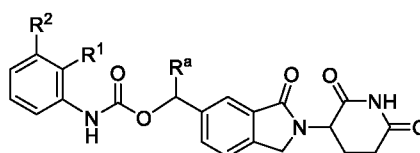
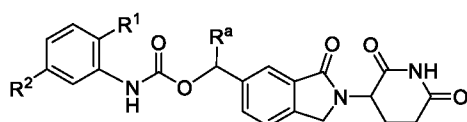
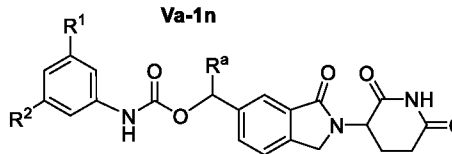
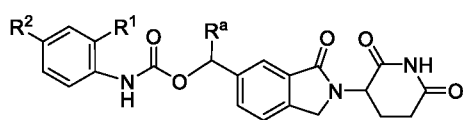
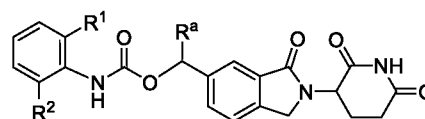
In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^a is H, one of R¹, R² is selected from a group consisting of C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), which group is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^a is H, one of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; the other of R¹, R² is a group of formula -L³-X², wherein L³ is a covalent bond, linear or branched C₁₋₄ alkyl, -O-, -C₁₋₄ alkoxy and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdiny, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^a is H, one of R¹, R² is selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe, the other of R¹, R² is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdiny, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F.

In some embodiments of a compound of formula Va-1g, Va-1h, Va-1i, Va-1j, Va-1k or Va-1l, R^a is H, one of R¹, R² is selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe; the other of R¹, R² is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdiny, N-methyl piperdiny, methyl-piperdiny, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments, the compound of formula Va and Va-1a is a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r,

**Va-1m****Va-1n****Va-1o****Va-1p****Va-1q****Va-1r**

wherein

R^1 , R^2 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, linear or branched C_{1-6} alkyl, $-O-$, or $-C_{1-4}$ alkoxy and X^2 is C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; and R^a is H or methyl.

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, R^a is H. In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, R^a is methyl.

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, L^3 is a covalent bond. In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, L^3 is linear or branched C_{1-4} alkyl, such as $-CH_2-$. In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, L^3 is $-O-$. In some embodiments L^3 is linear or branched C_{1-4} alkoxy, such as $-O-CH_2-$, $-O-(CH_2)_2-$

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, R^1 , R^2 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 ,

OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, R^a is CH₃ and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, R^a is CH₃ and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, -CN, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, R^a is CH₃, and R¹, R² are independently of each other selected from H, halogen, such as Cl, F, linear or branched -C₁₋₄ alkyl, such as methyl, fluorinated C₁₋₄ alkoxy, such as -OCF₃.

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, one of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; the other of R¹, R² is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy.

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, one of R¹, R² is selected from a group consisting of C₃₋₆ cycloalkyl, -C₁₋₄ alkyl-C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, -C₁₋₄ alkoxy-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, -C₁₋₄ alkyl-C₆₋₁₀ aryl, -O-C₆₋₁₀ aryl, -C₁₋₄ alkoxy-C₆₋₁₀ aryl, 5-10 membered heteroaryl, -C₁₋₄ alkyl-(5-10 membered heteroaryl), -O-(5-10 membered heteroaryl), -C₁₋₄ alkoxy-(5-10 membered heteroaryl), 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), which group is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, one of R¹, R² is selected from a group consisting of C₃₋₆ cycloalkyl, -O-C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl-(4-8 membered heterocycloalkyl), -O-(4-8 membered heterocycloalkyl), -C₁₋₄ alkoxy-(4-8 membered heterocycloalkyl), which group is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, one of R^1 , R^2 is selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; the other of R^1 , R^2 is a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, linear or branched C_{1-4} alkyl, $-O-$, $-C_{1-4}$ alkoxy and X^2 is cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, one of R^1 , R^2 is selected from H, halogen, e.g. Cl, F, linear or branched $-C_{1-4}$ alkyl, e.g., Me, Et, t-But, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN, and C_{1-4} alkoxy, e.g. $-OMe$, the other of R^1 , R^2 is a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, $-CH_2-$, $-O-$, $-OCH_2-$, $-O(CH_2)_2-$ and X^2 is cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, e.g. $-OMe$, NMe_2 , halogen, e.g. F.

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, one of R^1 , R^2 is selected from H, halogen, e.g. Cl, F, linear or branched $-C_{1-4}$ alkyl, e.g., Me, Et, t-But, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN, and C_{1-4} alkoxy, e.g. $-OMe$; the other of R^1 , R^2 is a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, $-CH_2-$, $-O-$, $-OCH_2-$, $-O(CH_2)_2-$ and X^2 is cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, difluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, N-methyl-pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, N-methyl-morpholinyl, oxetanyl, methyl-oxetanyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl.

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, R^a is H and

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, R^a is H and

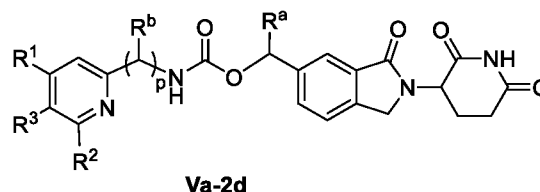
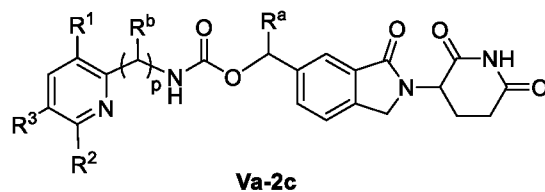
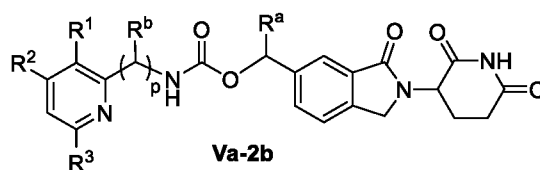
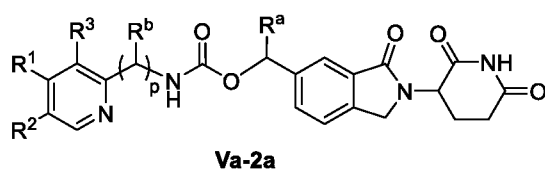
In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, R^a is H and

- 5 In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, R^a is H and

In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, R^a is H and

- 10 In some embodiments of a compound of formula Va-1m, Va-1n, Va-1o, Va-1p, Va-1q or Va-1r, R^a is H and

In some embodiments the compound of formula V and Va-2 is defined by formula Va-2a, Va-2b, Va-2c, Va-2d:



wherein

- 15 R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula -L³-X², wherein L³ is a covalent bond,
- 20 linear or branched C₁₋₆ alkyl, -O-, -C₁₋₄ alkoxy and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂,

halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; p is 0 or 1 and R^a, R^b are independently of each other H or methyl.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, p is 0. In some
5 embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, p is 1.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, R^a is H. In
some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, R^a is methyl. In
some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, p is 0 and R^a is
H. In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, p is 0 and
10 R^a is methyl.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, p is 1 and R^b
is H. In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, p is 1
and R^b is methyl. In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-
2d, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula, p is 1, R^b is
15 methyl and R^a is H.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, L³ is a covalent
bond.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, R¹, R², R³ are
independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched
20 C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆
alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆
alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl
or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, R¹, R², R³ are
25 independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such
as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, one of R¹, R²,
R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear
or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -
30 O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl,

-C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, R^a is H and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, R^a is H and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, R^a is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, R^a is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, p is 0 and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, p is 0 and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

5 In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, p is 0, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

10 In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, p is 0, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

15 In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, p is 0, R^a is H and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

20 In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d p is 0, R^a is H and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

25 In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, p is 0, R^a is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

30 In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, p is 0, R^a is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected

from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, one of R¹, R², R³ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, which group is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.

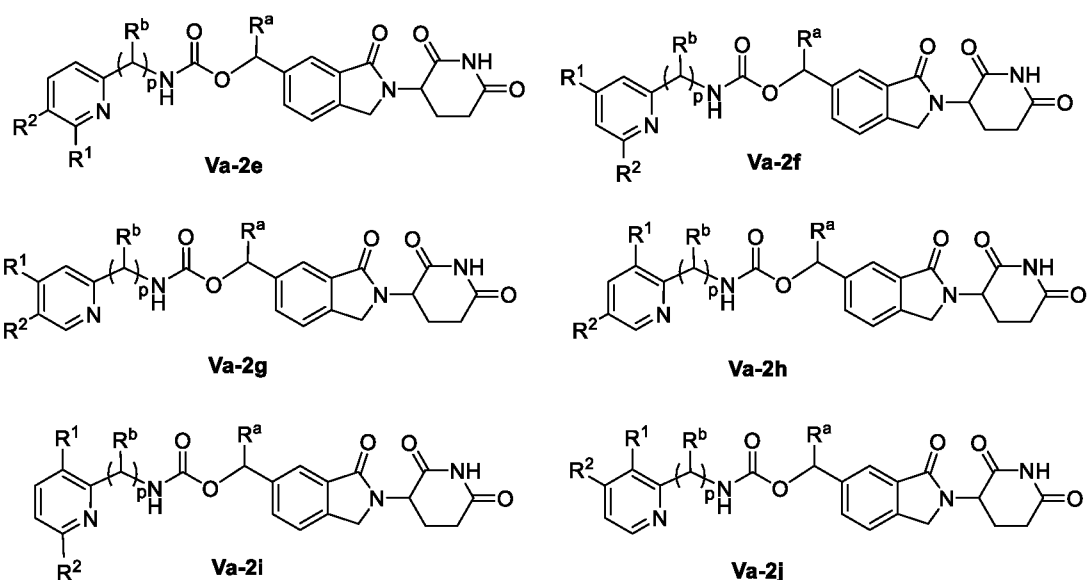
In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, one of R¹, R², R³ is selected from a group consisting of C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, which group is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, one of R¹, R², R³ is selected from a group consisting of cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, which group is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, one of R^1 , R^2 , R^3 is selected from a group consisting of cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, which group is is
 5 unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, e.g. methyl, - C_{1-4} alkoxy, e.g. -OMe, NMe_2 , halogen, e.g. F; and the other two of R^1 , R^2 , R^3 are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched - C_{1-4} alkyl, e.g., Me, Et, t-But, CF_3 , CHF_2 , $CMeF_2$, - OCF_3 , $OCHF_2$, CN, C_{1-4} alkoxy, e.g. -OMe; p is 0 and R^a is H.

10 In some embodiments of a compound of formula Va-2a, Va-2b, Va-2c, Va-2d, one of R^1 , R^2 , R^3 is selected from a group consisting of cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-
 15 azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; and the other two of R^1 , R^2 , R^3 are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched - C_{1-4} alkyl, e.g., Me, Et, t-But, CF_3 , CHF_2 , $CMeF_2$, - OCF_3 , $OCHF_2$, CN, and C_{1-4} alkoxy, e.g. -OMe; p is 0 and R^a is H.

In some embodiments the compound of formula Va and Va-2 is defined by formula Va-2e,
 20 Va-2f, Va-2g, Va-2h, Va-2i, Va-2j:



wherein

R^1 , R^2 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}alkyl$, $-N(H)C(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, linear or branched C_{1-6} alkyl, $-O-$, $-C_{1-4}$ alkoxy and X^2 is C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; p is 0 or 1 and R^a , R^b are independently of each other H or methyl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0. In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 1.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, R^a is H. In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, R^a is methyl. In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0 and R^a is H. In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0 and R^a is methyl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 1 and R^b is H. In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 1 and R^b is methyl. In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, L^3 is a covalent bond.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, R^1 , R^2 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}alkyl$, $-N(H)C(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, linear or branched C_{1-6} alkyl, $-O-$, $-C_{1-4}$ alkoxy and X^2 is C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; p is 0 or 1 and R^a , R^b are independently of each other H or methyl.

$\text{-C}_{1-6}\text{alkylC(O)OH}$, $\text{-C}_{1-6}\text{alkylC(O)O-C}_{1-6}\text{alkyl}$, NH_2 , -C_{1-4} alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, R^1 , R^2 are independently of each other selected from H, linear or branched -C_{1-6} alkyl, -C_{1-4} alkoxy, such as -OMe , OCF_3 , and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, R^1 , R^2 are independently of each other selected from H, linear or branched -C_{1-6} alkyl, linear or branched C_{1-6} heteroalkyl, -C_{1-4} alkoxy, CF_3 , CHF_2 , CMeF_2 , $\text{-O-(CH}_2\text{)}_2\text{-OMe}$, OCF_3 , OCHF_2 , -C_{1-6} alkylamino, -CN , $\text{-OC(O)-C}_{1-6}\text{alkyl}$, $\text{-N(H)C(O)-C}_{1-6}\text{alkyl}$, $\text{-C(O)O-C}_{1-6}\text{alkyl}$, -COOH , $\text{-C}_{1-6}\text{alkylC(O)OH}$, $\text{-C}_{1-6}\text{alkylC(O)O-C}_{1-6}\text{alkyl}$, NH_2 , -C_{1-4} alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, R^1 , R^2 are independently of each other selected from H, linear or branched -C_{1-6} alkyl, -C_{1-4} alkoxy, such as -OMe , OCF_3 , and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, R^a is H and R^1 , R^2 are independently of each other selected from H, linear or branched -C_{1-6} alkyl, linear or branched C_{1-6} heteroalkyl, -C_{1-4} alkoxy, CF_3 , CHF_2 , CMeF_2 , $\text{-O-(CH}_2\text{)}_2\text{-OMe}$, OCF_3 , OCHF_2 , -C_{1-6} alkylamino, -CN , $\text{-OC(O)-C}_{1-6}\text{alkyl}$, $\text{-N(H)C(O)-C}_{1-6}\text{alkyl}$, $\text{-C(O)O-C}_{1-6}\text{alkyl}$, -COOH , $\text{-C}_{1-6}\text{alkylC(O)OH}$, $\text{-C}_{1-6}\text{alkylC(O)O-C}_{1-6}\text{alkyl}$, NH_2 , -C_{1-4} alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, R^a is H and R^1 , R^2 are independently of each other selected from H, linear or branched -C_{1-6} alkyl, -C_{1-4} alkoxy, such as -OMe , OCF_3 , and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, R^a is H, and R^1 , R^2 are independently of each other selected from H, linear or branched -C_{1-6} alkyl, linear or branched C_{1-6} heteroalkyl, -C_{1-4} alkoxy, CF_3 , CHF_2 , CMeF_2 , $\text{-O-(CH}_2\text{)}_2\text{-OMe}$, OCF_3 , OCHF_2 , -C_{1-6} alkylamino, -CN , $\text{-OC(O)-C}_{1-6}\text{alkyl}$, $\text{-N(H)C(O)-C}_{1-6}\text{alkyl}$, $\text{-C(O)O-C}_{1-6}\text{alkyl}$, -COOH , $\text{-C}_{1-6}\text{alkylC(O)OH}$, $\text{-C}_{1-6}\text{alkylC(O)O-C}_{1-6}\text{alkyl}$, NH_2 , -C_{1-4} alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, R^a is H, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0 and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0 and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0, R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0, R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0, R^a is H, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0, R^a is H, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

10 In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, one of R¹, R² is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.

20 In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, one of R¹, R² is a group selected from C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, which group is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy and the other of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.

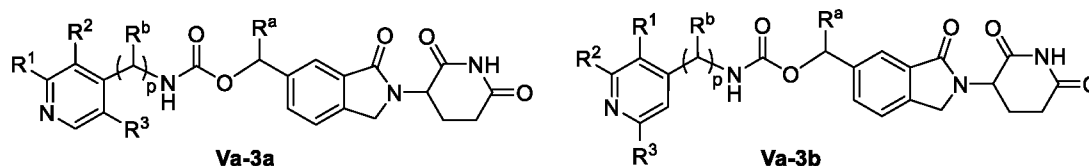
30 In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, one of R¹, R² is a group selected from cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperidinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, wherein X² is

unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂,
 5 -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, one of R¹, R² is a group selected from cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-
 10 azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, which group is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, e.g. methyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; and the other of R¹, R² is selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, C₁₋₄ alkoxy, e.g. -OMe,; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, one of R¹, R² is a group selected from ; and the other of R¹, R² are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe, cyclopropyl, methyl-
 20 cyclopropyl, fluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; p is 0 and R^a is H.

In some embodiments the compound of formula Va and Va-3 is defined by formula Va-3a or
 25 Va-3b:



wherein

R^1 , R^2 , R^3 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}alkyl$, $-N(H)C(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, linear or branched C_{1-6} alkyl, $-O-$, $-C_{1-4}$ alkoxy and X^2 is C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; p is 0 or 1 and R^a , R^b are independently of each other H or methyl.

In some embodiments of a compound of formula Va-3a, Va-3b, p is 0. In some embodiments of a compound of formula Va-3a, Va-3b, p is 1.

In some embodiments of a compound of formula Va-3a, Va-3b, R^a is H. In some embodiments of a compound of formula Va-3a, Va-3b, R^a is methyl. In some embodiments of a compound of formula Va-3a, Va-3b, p is 0 and R^a is H. In some embodiments of a compound of formula Va-3a, Va-3b, p is 0 and R^a is methyl.

In some embodiments of a compound of formula Va-3a, Va-3b, p is 1 and R^b is H. In some embodiments of a compound of formula Va-3a, Va-3b, p is 1 and R^b is methyl. In some embodiments of a compound of formula Va-3a, Va-3b, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Va-3a, Va-3b, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Va-3a, Va-3b, L^3 is a covalent bond.

In some embodiments of a compound of formula Va-3a, Va-3b, R^1 , R^2 , R^3 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}alkyl$, $-N(H)C(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3a, Va-3b, R^1 , R^2 , R^3 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, $-C_{1-4}$ alkoxy, such as $-OMe$, OCF_3 , and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3a, Va-3b, one of R^1 , R^2 , R^3 is H and the other two of R^1 , R^2 , R^3 are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3a, Va-3b, one of R^1 , R^2 , R^3 is H and the other two of R^1 , R^2 , R^3 are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3a, Va-3b, R^a is H and R^1 , R^2 , R^3 are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3a, Va-3b, R^a is H and R^1 , R^2 , R^3 are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3a, Va-3b, R^a is H, one of R^1 , R^2 , R^3 is H and the other two of R^1 , R^2 , R^3 are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3a, Va-3b, R^a is H, one of R^1 , R^2 , R^3 is H and the other two of R^1 , R^2 , R^3 are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3a, Va-3b, p is 0 and R^1 , R^2 , R^3 are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆

alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3a, Va-3b, p is 0 and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3a, Va-3b, p is 0, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3a, Va-3b, p is 0, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3a, Va-3b, p is 0, R^a is H and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3a, Va-3b, p is 0, R^a is H and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3a, Va-3b, p is 0, R^a is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3a, Va-3b, p is 0, R^a is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

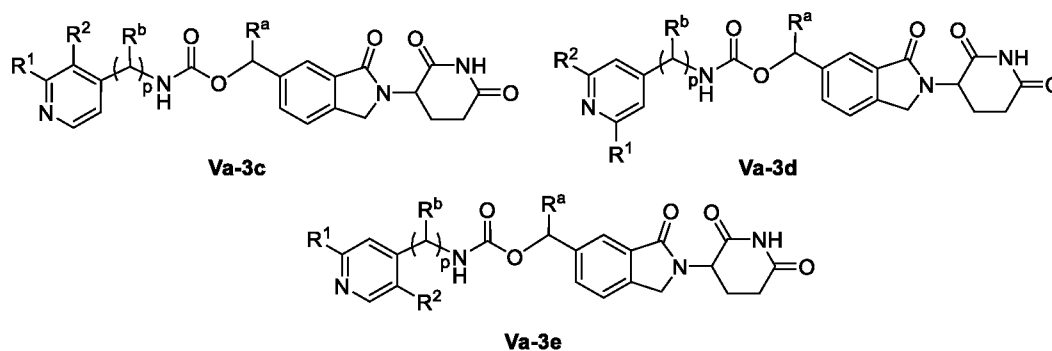
- 5 In some embodiments of a compound of formula Va-3a, Va-3b, one of R¹, R², R³ is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.
- 10
- 15 In some embodiments of a compound of formula Va-3a, Va-3b, one of R¹, R², R³ is a group selected from C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, which group is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.
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- In some embodiments of a compound of formula Va-3a, Va-3b, one of R¹, R², R³ is a group selected from cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, which group is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.
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In some embodiments of a compound of formula Va-3a, Va-3b, one of R^1 , R^2 , R^3 is a group selected from cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, which group is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, e.g. methyl, $-C_{1-4}$ alkoxy, e.g. $-OMe$, NMe_2 , halogen, e.g. F; and the other two of R^1 , R^2 , R^3 are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched $-C_{1-4}$ alkyl, e.g., Me, Et, t-But, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN, C_{1-4} alkoxy, e.g. $-OMe$; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-3a, Va-3b, one of R^1 , R^2 , R^3 is a group selected from cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, cyclobutyl, C_6 aryl, methyl- C_6 aryl, fluoro- C_6 aryl, methoxy- C_6 aryl, pyridinyl, pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; and the other two of R^1 , R^2 , R^3 are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched $-C_{1-4}$ alkyl, e.g., Me, Et, t-But, CF_3 , CHF_2 , $CMeF_2$, $-OCF_3$, $OCHF_2$, CN, and C_{1-4} alkoxy, e.g. $-OMe$; p is 0 and R^a is H.

In some embodiments the compound of formula Va and Va-3 is defined by formula Va-3c, Va-3d, Va-3e:



wherein

R^1 , R^2 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}$ alkyl, $-N(H)C(O)-C_{1-6}$ alkyl, $-C(O)O-C_{1-6}$ alkyl, $-COOH$, $-C_{1-6}$ alkyl $C(O)OH$, $-C_{1-6}$ alkyl $C(O)O-C_{1-6}$ alkyl, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl

or Br, e.g. F or Cl, or a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, linear or branched C_{1-6} alkyl, $-O-$, $-C_{1-4}$ alkoxy and X^2 is C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; p is 0 or 1 and R^a , R^b are independently of each other H or methyl. In some embodiments of a compound of formula Va-3c, Va-3d, Va-3e, p is 0. In some embodiments of a compound of formula Va-3c, Va-3d, Va-3e, p is 1.

In some embodiments of a compound of formula Va-3c, Va-3d, Va-3e R^a is H. In some embodiments of a compound of formula Va-3c, Va-3d, Va-3e R^a is methyl. In some embodiments of a compound of formula Va-3c, Va-3d, Va-3e, p is 0 and R^a is H. In some embodiments of a compound of formula Va-3c, Va-3d, Va-3e, p is 0 and R^a is methyl.

In some embodiments of a compound of formula Va-3c, Va-3d, Va-3e, p is 1 and R^b is H. In some embodiments of a compound of formula Va-3c, Va-3d, Va-3e, p is 1 and R^b is methyl.

In some embodiments of a compound of formula Va-3c, Va-3d, Va-3e, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Va-3c, Va-3d, Va-3e, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, L^3 is a covalent bond.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, R^1 , R^2 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}alkyl$, $-N(H)C(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, R^1 , R^2 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, $-C_{1-4}$ alkoxy, such as $-OMe$, OCF_3 , and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, R^1 , R^2 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$,

-C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j,
 5 R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j,
 R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆
 alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe,
 10 OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j,
 R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆
 15 alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j,
 R^a is H, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆
 alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe,
 OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl,
 20 -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j,
 R^a is H, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆
 alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j,
 p is 0 and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆
 alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe,
 OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl,
 -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and
 30 halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0 and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0, R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0, R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0, R^a is H, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-2e, Va-2f, Va-2g, Va-2h, Va-2i, Va-2j, p is 0, R^a is H, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-3c, Va-3d, Va-3e, one of R^1 , R^2 is a group selected from a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, $-CH_2-$, $-O-$, $-OCH_2-$, $-O(CH_2)_2-$ and X^2 is C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-$ OMe, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; and the other of R^1 , R^2 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-$ OMe, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}$ alkyl, $-N(H)C(O)-C_{1-6}$ alkyl, $-C(O)O-C_{1-6}$ alkyl, $-COOH$, $-C_{1-6}$ alkyl $C(O)OH$, $-C_{1-6}$ alkyl $C(O)O-$ C_{1-6} alkyl, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-3c, Va-3d, Va-3e, one of R^1 , R^2 is a group selected from C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, which group is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-$ OMe, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; and the other of R^1 , R^2 is selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-$ OMe, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.

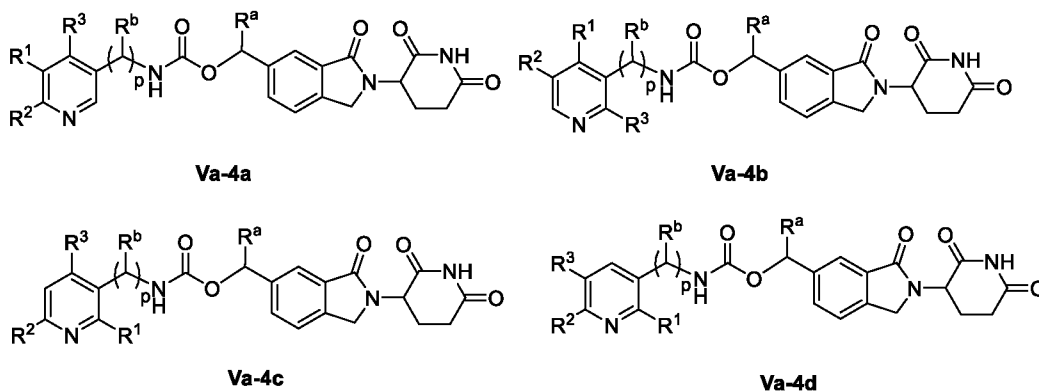
In some embodiments of a compound of formula Va-3c, Va-3d, Va-3e, one of R^1 , R^2 is a group selected from cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, which group is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-$ OMe, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; and the other of R^1 , R^2 is selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-$ OMe, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-C_{1-4}$ alkylhydroxy, halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-3c, Va-3d, Va-3e, one of R^1 , R^2 is a group selected from cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, which group is unsubstituted or substituted with one or more of

linear or branched C₁₋₄ alkyl, e.g. methyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; and the other of R¹, R² is selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, C₁₋₄ alkoxy, e.g. -OMe; p is 0 and R^a is H.

- 5 In some embodiments of a compound of formula Va-3c, Va-3d, Va-3e, one of R¹, R² is a group selected from cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; and the other of R¹, R² is selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe; p is 0 and R^a is H.
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In some embodiments the compound of formula Va and Va-4 is defined by formula Va-4a, Va-4b, Va-4 c or Va-4d:



wherein

- R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula -L³-X², wherein L³ is a covalent bond, linear or branched C₁₋₆ alkyl, -O-, -C₁₋₄ alkoxy and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂,
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halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; p is 0 or 1 and R^a, R^b are independently of each other H or methyl.

In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 0. In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 1.

- 5 In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, R^a is H. In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, R^a is methyl. In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 0 and R^a is H. In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 0 and R^a is methyl.
- 10 In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 1 and R^b is H. In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 1 and R^b is methyl. In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 1, R^b is methyl and R^a is H.
- 15 In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, L³ is a covalent bond.

- In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -
- 20 C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

- In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy,
- 25 such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-

C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, R^a is H and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, R^a is H and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, R^a is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, R^a is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 0 and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 0 and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 0, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

10 In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 0, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

15 In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 0, R^a is H and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

20 In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 0, R^a is H and R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

25 In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 0, R^a is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

30 In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, p is 0, R^a is H, one of R¹, R², R³ is H and the other two of R¹, R², R³ are independently of each other selected

from H, linear or branched $-C_{1-6}$ alkyl, $-C_{1-4}$ alkoxy, such as $-OMe$, OCF_3 , and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, one of R^1 , R^2 is a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, $-CH_2-$, $-O-$, $-OCH_2-$, $-O(CH_2)_2-$ and X^2 is C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; and the other two of R^1 , R^2 , R^3 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}alkyl$, $-N(H)C(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.

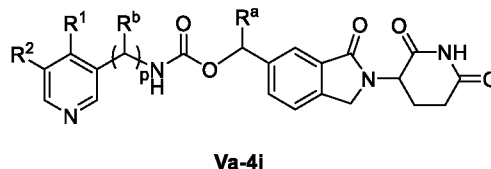
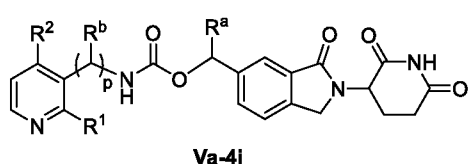
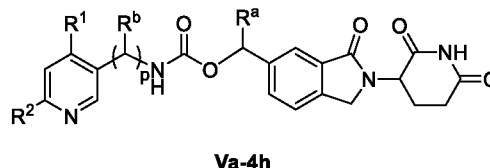
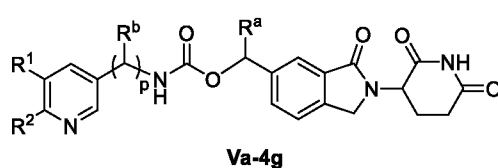
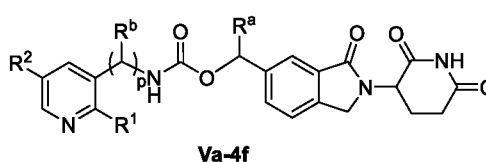
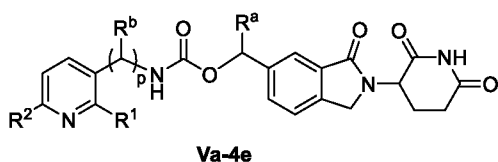
In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, one of R^1 , R^2 is a group selected from C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, which group is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; and the other two of R^1 , R^2 , R^3 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, one of R^1 , R^2 is a group selected from cyclopropyl, cyclobutyl, C_6 aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, which group is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; and the other two of R^1 , R^2 , R^3 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-C_{1-4}$ alkylhydroxy, halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, one of R¹, R² is a group selected from cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, which group is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, e.g. methyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; and the other two of R¹, R², R³ are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, C₁₋₄ alkoxy, e.g. -OMe; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-4a, Va-4b, Va-4c or Va-4d, one of R¹, R² is a group selected from cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; and the other two of R¹, R², R³ are independently of each other selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe; p is 0 and R^a is H.

In some embodiments the compound of formula Va and Va-4 is defined by formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j:



wherein

R^1 , R^2 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}alkyl$, $-N(H)C(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, linear or branched C_{1-6} alkyl, $-O-$, $-C_{1-4}$ alkoxy and X^2 is C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; p is 0 or 1 and R^a , R^b are independently of each other H or methyl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 0. In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 1.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, R^a is H. In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, R^a is methyl. In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 0 and R^a is H. In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 0 and R^a is methyl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 1 and R^b is H. In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 1 and R^b is methyl. In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, L^3 is a covalent bond.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, R^1 , R^2 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}alkyl$, $-N(H)C(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, linear or branched C_{1-6} alkyl, $-O-$, $-C_{1-4}$ alkoxy and X^2 is C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy; p is 0 or 1 and R^a , R^b are independently of each other H or methyl.

alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, R^a is H, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, R^a is H, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 0 and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 0 and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 0, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 0, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 0, R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 0, R^a is H and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 0, R^a is H, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, p is 0, R^a is H, and R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, such as -OMe, OCF₃, and halogen, such as F, Cl or Br, e.g. F or Cl.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, one of R¹, R² is a group of formula -L³-X², wherein L³ is a covalent bond, -CH₂-, -O-, -OCH₂-, -O(CH₂)₂- and X² is C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, one of R¹, R² is a group selected from C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, which group is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.

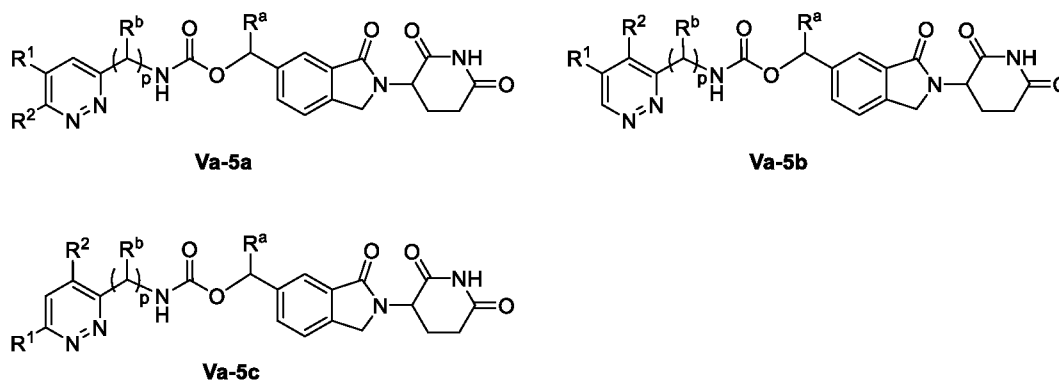
In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, one of R¹, R² is a group selected from cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperidinyl, morpholinyl, oxetanyl, piperazinyl, azetidinyl, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, which group is

unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; and the other of R¹, R² is selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂,
 5 -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, halogen, such as F, Cl or Br, e.g. F or Cl; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, one of R¹, R² is a group selected from cyclopropyl, cyclobutyl, C₆ aryl, pyridinyl, pyrrolidinyl, piperdinyl, morpholinyl, oxetanyl, piperazinyl, azetidiny, 2-oxa-5-
 10 azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl, which group is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, e.g. methyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; and the other of R¹, R² is selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, C₁₋₄ alkoxy, e.g. -OMe; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-4e, Va-4f, Va-4g, Va-4h, Va-4i or Va-4j, one of R¹, R² is a group selected from cyclopropyl, methyl-cyclopropyl, fluoro-cyclopropyl, cyclobutyl, C₆ aryl, methyl-C₆ aryl, fluoro-C₆ aryl, methoxy-C₆ aryl, pyridinyl, pyrrolidinyl, methyl-pyrrolidinyl, piperdinyl, N-methyl piperdinyl, methyl-piperdinyl, difluoro-piperidinyl, morpholinyl, piperazinyl, N-methyl-piperazinyl, azetidiny, methyl-azetidiny, N-dimethyl-
 20 azetidiny, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-azabicyclo[3.2.1]octan-3-yl; and the other of R¹, R² is selected from H, halogen, e.g. Cl, F, linear or branched -C₁₋₄ alkyl, e.g., Me, Et, t-But, CF₃, CHF₂, CMeF₂, -OCF₃, OCHF₂, CN, and C₁₋₄ alkoxy, e.g. -OMe; p is 0 and R^a is H.

In some embodiments the compound of formula Va and Va-5 is defined by formula Va-5a,
 25 Va-5b, Va-5c:



wherein

R^1 and R^2 each are independently selected from H, linear or branched C_{1-4} alkyl, C_{1-4} alkoxy, 4-8 membered heterocycloalkyl, $-C_{1-4}$ alkyl 4-8 membered heterocycloalkyl, $-C_{1-4}$ alkoxy 4-8 membered heterocycloalkyl, $-O-(4-8$ membered heterocycloalkyl), CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, $-OC(O)-C_{1-6}$ alkyl, $-N(H)C(O)-C_{1-6}$ alkyl, $-C(O)O-C_{1-6}$ alkyl, $-COOH$, $-C_{1-6}$ alkyl $C(O)OH$, $-C_{1-6}$ alkyl $C(O)O-C_{1-6}$ alkyl, NH_2 , $-C_{1-4}$ alkoxy, $-C_{1-4}$ alkylhydroxy, C_6 aryloxy and halogen, such as F, Cl or Br, e.g. F or Cl, and C_6 aryl, such as phenyl, wherein the 4-8 membered heterocycloalkyl may be unsubstituted or substituted with C_{1-4} alkyl, such as methyl, ethyl, C_{1-4} alkoxy, such as methoxy, ethoxy, halogen, such as F, Cl or Br, e.g. F or Cl; R^a , R^b are independently of each other H or methyl and p is 0 or 1.

In some embodiments of a compound of formula Va-5a, Va-5b, Va-5c, p is 0. In some embodiments of a compound of formula Va-5a, Va-5b, Va-5c, p is 1.

In some embodiments of a compound of formula Va-5a, Va-5b, Va-5c, R^a is H. In some embodiments of a compound of formula Va-5a, Va-5b, Va-5c, R^a is methyl. In some embodiments of a compound of formula Va-5a, Va-5b, Va-5c, p is 0 and R^a is H. In some embodiments of a compound of formula Va-5a, Va-5b, Va-5c, p is 0 and R^a is methyl.

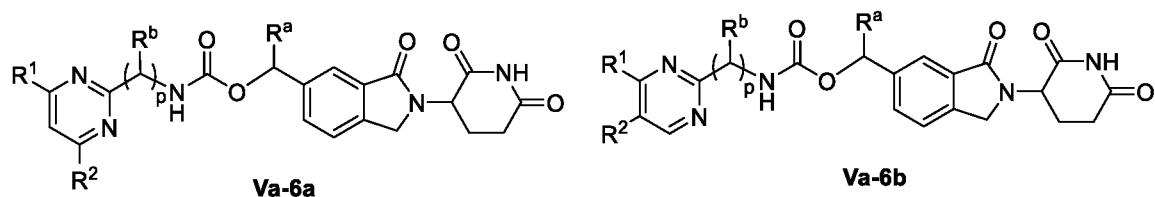
In some embodiments of a compound of formula Va-5a, Va-5b, Va-5c, p is 1 and R^b is H. In some embodiments of a compound of formula Va-5a, Va-5b, Va-5c, p is 1 and R^b is methyl. In some embodiments of a compound of formula Va-5a, Va-5b, Va-5c, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Va-5a, Va-5b, Va-5c, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Va-5a, Va-5b, Va-5c, R^1 , R^2 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched

C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-5a, Va-5b, Va-5c, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, halogen, such as F, Cl or Br, e.g. F or Cl, or piperidinyl, which is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, e.g. methyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; p is 0 and R^a is H.

In some embodiments the compound of formula Va and Va-6 is defined by formula Va-6a, Va-6b:



wherein

R¹ and R² each are independently selected from H, linear or branched C₁₋₄ alkyl, C₁₋₄ alkoxy, 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl 4-8 membered heterocycloalkyl, -C₁₋₄ alkoxy 4-8 membered heterocycloalkyl, -O-(4-8 membered heterocycloalkyl), CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkoxy, -C₁₋₄ alkylhydroxy, C₆ aryloxy and halogen, such as F, Cl or Br, e.g. F or Cl, and C₆ aryl, such as phenyl, wherein the 4-8 membered heterocycloalkyl may be unsubstituted or substituted with C₁₋₄ alkyl, such as methyl, ethyl, C₁₋₄ alkoxy, such as methoxy, ethoxy, halogen, such as F, Cl or Br, e.g. F, Cl; R^a, R^b are independently of each other H or methyl and p is 0 or 1.

In some embodiments of a compound of formula Va-6a, Va-6b, p is 0. In some embodiments of a compound of formula Va-6a, Va-6b, p is 1.

In some embodiments of a compound of formula Va-6a, Va-6b, R^a is H. In some embodiments of a compound of formula Va-6a, Va-6b, R^a is methyl. In some embodiments

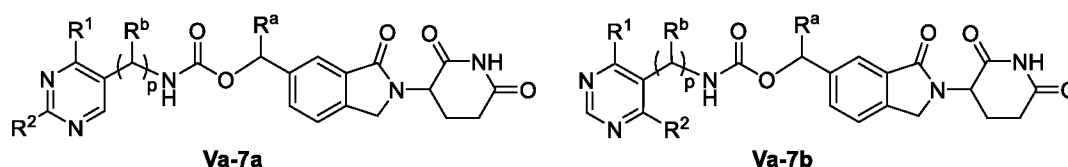
of a compound of formula Va-6a, Va-6b, p is 0 and R^a is H. In some embodiments of a compound of formula Va-6a, Va-6b, p is 0 and R^a is methyl.

In some embodiments of a compound of formula Va-6a, Va-6b, p is 1 and R^b is H. In some embodiments of a compound of formula Va-6a, Va-6b, p is 1 and R^b is methyl. In some
5 embodiments of a compound of formula Va-6a, Va-6b, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Va-6a, Va-6b, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Va-6a, Va-6b, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄
10 alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-6a, Va-6b, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂,
15 OCF₃, OCHF₂, halogen, such as F, Cl or Br, e.g. F or Cl, or piperidinyl, which is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, e.g. methyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; p is 0 and R^a is H.

In some embodiments the compound of formula Va and Va-7 is defined by formula Va-7a,
20 Va-7b:



wherein

R¹ and R² each are independently selected from H, linear or branched C₁₋₄ alkyl, C₁₋₄ alkoxy, 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl 4-8 membered heterocycloalkyl, -C₁₋₄ alkoxy 4-8
25 membered heterocycloalkyl, -O-(4-8 membered heterocycloalkyl), CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkoxy, -C₁₋₄ alkylhydroxy, C₆ aryloxy and halogen, such as F, Cl or Br, e.g. F or Cl, and C₆ aryl, such as

phenyl, wherein the 4-8 membered heterocycloalkyl may be unsubstituted or substituted with C₁₋₄ alkyl, such as methyl, ethyl, C₁₋₄ alkoxy, such as methoxy, ethoxy, halogen, such as F, Cl or Br, e.g. F, Cl; R^a, R^b are independently of each other H or methyl and p is 0 or 1.

In some embodiments of a compound of formula Va-7a, Va-7b, p is 0. In some embodiments of a compound of formula Va-7a, Va-7b, p is 1.

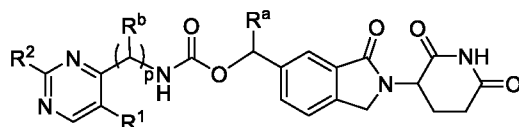
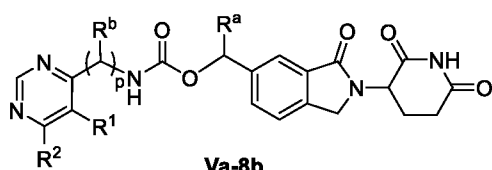
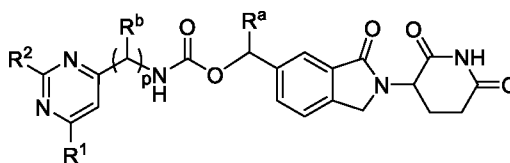
In some embodiments of a compound of formula Va-7a, Va-7b, and R^a is H. In some embodiments of a compound of formula Va-7a, Va-7b, R^a is methyl. In some embodiments of a compound of formula Va-7a, Va-7b, p is 0 and R^a is H. In some embodiments of a compound of formula Va-7a, Va-7b, p is 0 and R^a is methyl.

In some embodiments of a compound of formula Va-7a, Va-7b, p is 1 and R^b is H. In some embodiments of a compound of formula Va-7a, Va-7b, p is 1 and R^b is methyl. In some embodiments of a compound of formula Va-7a, Va-7b, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Va-7a, Va-7b, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Va-7a, Va-7b, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-7a, Va-7b, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, halogen, such as F, Cl or Br, e.g. F or Cl, or piperidiny, which is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, e.g. methyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; p is 0 and R^a is H.

-CIn some embodiments the compound of formula Va and Va-8 is defined by formula Va-8a, Va-8b, Va-8c:

**Va-8a****Va-8b****Va-8c**

wherein

R^1 and R^2 each are independently selected from H, linear or branched C_{1-4} alkyl, C_{1-4} alkoxy, 4-8 membered heterocycloalkyl, $-C_{1-4}$ alkyl 4-8 membered heterocycloalkyl, $-C_{1-4}$ alkoxy 4-8 membered heterocycloalkyl, $-O-(4-8$ membered heterocycloalkyl), CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, $-OC(O)-C_{1-6}$ alkyl, $-N(H)C(O)-C_{1-6}$ alkyl, $-C(O)O-C_{1-6}$ alkyl, $-COOH$, $-C_{1-6}$ alkyl $C(O)OH$, $-C_{1-6}$ alkyl $C(O)O-C_{1-6}$ alkyl, NH_2 , $-C_{1-4}$ alkoxy, $-C_{1-4}$ alkylhydroxy, C_6 aryloxy and halogen, such as F, Cl or Br, e.g. F or Cl, and C_6 aryl, such as phenyl, wherein the 4-8 membered heterocycloalkyl may be unsubstituted or substituted with C_{1-4} alkyl, such as methyl, ethyl, C_{1-4} alkoxy, such as methoxy, ethoxy, halogen, such as F, Cl or Br, e.g. F, Cl; R^a , R^b are independently of each other H or methyl and p is 0 or 1.

In some embodiments of a compound of formula Va-8a, Va-8b, Va-8c, p is 0. In some embodiments of a compound of formula Va-8a, Va-8b, Va-8c, p is 1.

In some embodiments of a compound of formula Va-8a, Va-8b, Va-8c, R^a is H. In some embodiments of a compound of formula Va-8a, Va-8b, Va-8c, R^a is methyl. In some embodiments of a compound of formula Va-8a, Va-8b, Va-8c, p is 0 and R^a is H. In some embodiments of a compound of formula Va-8a, Va-8b, Va-8c, p is 0 and R^a is methyl.

In some embodiments of a compound of formula Va-8a, Va-8b, Va-8c, p is 1 and R^b is H. In some embodiments of a compound of formula Va-8a, Va-8b, Va-8c, p is 1 and R^b is methyl.

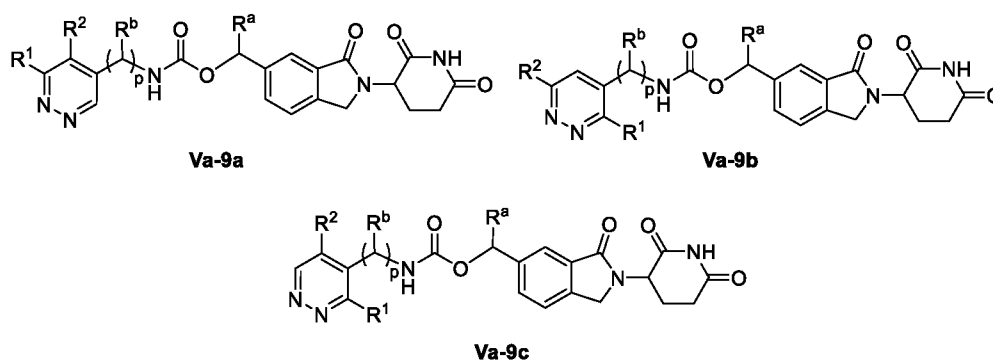
In some embodiments of a compound of formula Va-8a, Va-8b, Va-8c, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Va-8a, Va-8b, Va-8c, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Va-8a, Va-8b, Va-8c, R^1 , R^2 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched

C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-8a, Va-8b, Va-8c, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, halogen, such as F, Cl or Br, e.g. F or Cl, or piperidinyl, which is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, e.g. methyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; p is 0 and R^a is H.

In some embodiments the compound of formula Va and Va-9 is defined by formula Va-9a, Va-9b, Va-9c:



wherein

R¹ and R² each are independently selected from H, linear or branched C₁₋₄ alkyl, C₁₋₄ alkoxy, 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl 4-8 membered heterocycloalkyl, -C₁₋₄ alkoxy 4-8 membered heterocycloalkyl, -O-(4-8 membered heterocycloalkyl), CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkoxy, -C₁₋₄ alkylhydroxy, C₆ aryloxy and halogen, such as F, Cl or Br, e.g. F or Cl, and C₆ aryl, such as phenyl, wherein the 4-8 membered heterocycloalkyl may be unsubstituted or substituted with C₁₋₄ alkyl, such as methyl, ethyl, C₁₋₄ alkoxy, such as methoxy, ethoxy, halogen, such as F, Cl or Br, e.g. F, Cl; R^a, R^b are independently of each other H or methyl and p is 0 or 1.

In some embodiments of a compound of formula Va-9a, Va-9b, Va-9c, p is 0. In some embodiments of a compound of formula Va-9a, Va-9b, Va-9c, p is 1.

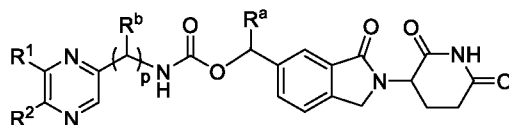
In some embodiments of a compound of formula Va-9a, Va-9b, Va-9c, R^a is H. In some embodiments of a compound of formula Va-9a, Va-9b, Va-9c, R^a is methyl. In some embodiments of a compound of formula Va-9a, Va-9b, Va-9c, p is 0 and R^a is H. In some embodiments of a compound of formula Va-9a, Va-9b, Va-9c, p is 0 and R^a is methyl.

- 5 In some embodiments of a compound of formula Va-9a, Va-9b, Va-9c, p is 1 and R^b is H. In some embodiments of a compound of formula Va-9a, Va-9b, Va-9c, p is 1 and R^b is methyl. In some embodiments of a compound of formula Va-9a, Va-9b, Va-9c, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Va-9a, Va-9b, Va-9c, p is 1, R^b is methyl and R^a is H.
- 10 In some embodiments of a compound of formula Va-9a, Va-9b, Va-9c, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; p is 0 and R^a is H.
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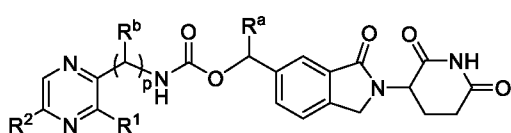
In some embodiments of a compound of formula Va-9a, Va-9b, Va-9c, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, halogen, such as F, Cl or Br, e.g. F or Cl, or piperidinyl, which is unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, e.g. methyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; p is 0 and R^a is H.

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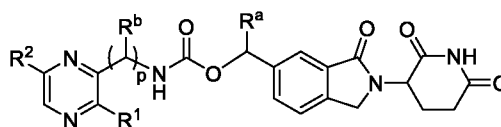
In some embodiments the compound of formula Va and Va-10 is defined by formula Va-10a, Va-10b, Va-10c



Va-10a



Va-10b



Va-10c

wherein

R¹ and R² each are independently selected from H, linear or branched C₁₋₄ alkyl, C₁₋₄ alkoxy, 4-8 membered heterocycloalkyl, -C₁₋₄ alkyl 4-8 membered heterocycloalkyl, -C₁₋₄ alkoxy 4-8 membered heterocycloalkyl, -O-(4-8 membered heterocycloalkyl), CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, -OC(O)-C₁₋₆alkyl, -N(H)C(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, -C₁₋₄ alkoxy, -C₁₋₄ alkylhydroxy, C₆ aryloxy and halogen, such as F, Cl or Br, e.g. F or Cl, and C₆ aryl, such as phenyl, wherein the 4-8 membered heterocycloalkyl may be unsubstituted or substituted with C₁₋₄ alkyl, such as methyl, ethyl, C₁₋₄ alkoxy, such as methoxy, ethoxy, halogen, such as F, Cl or Br, e.g. F, Cl; R^a, R^b are independently of each other H or methyl and p is 0 or 1.

In some embodiments of a compound of formula Va-10a, Va-10b, Va-10c, p is 0. In some embodiments of a compound of formula Va-10a, Va-10b, Va-10c, p is 1.

In some embodiments of a compound of formula Va-10a, Va-10b, Va-10c, R^a is H. In some embodiments of a compound of formula Va-10a, Va-10b, Va-10c, R^a is methyl. In some embodiments of a compound of formula Va-10a, Va-10b, Va-10c, p is 0 and R^a is H. In some embodiments of a compound of formula Va-10a, Va-10b, Va-10c, p is 0 and R^a is methyl.

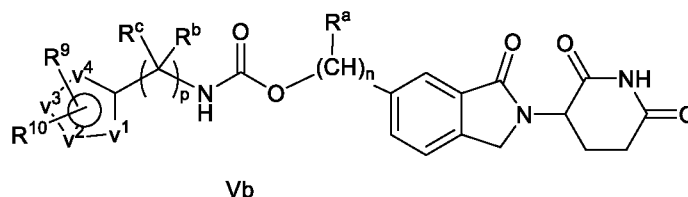
In some embodiments of a compound of formula Va-10a, Va-10b, Va-10c, p is 1 and R^b is H. In some embodiments of a compound of formula Va-10a, Va-10b, Va-10c, p is 1 and R^b is methyl. In some embodiments of a compound of formula Va-10a, Va-10b, Va-10c, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Va-10a, Va-10b, Va-10c, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Va-10a, Va-10b, Va-10c, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, -C₁₋₆ alkylamino, -CN, -C₁₋₄ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and -C₁₋₄ alkylhydroxy; p is 0 and R^a is H.

In some embodiments of a compound of formula Va-10a, Va-10b, Va-10c, R¹, R² are independently of each other selected from H, linear or branched -C₁₋₆ alkyl, -C₁₋₄ alkoxy, CF₃, CHF₂, CMeF₂, OCF₃, OCHF₂, halogen, such as F, Cl or Br, e.g. F or Cl, or piperidiny, which is

unsubstituted or substituted with one or more of linear or branched C₁₋₄ alkyl, e.g. methyl, -C₁₋₄ alkoxy, e.g. -OMe, NMe₂, halogen, e.g. F; p is 0 and R^a is H.

In some embodiments a compound of formula I is a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula Vb:



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wherein one or two of v¹, v², v³, and v⁴ are selected from O, N, NMe, NH, or S while two or three of v¹, v², v³, and v⁴ are C;

R⁹, R¹⁰ each are independently selected from H, linear or branched -C₁₋₄ alkyl, -CF₃, -CHF₂, halogen, preferably F, Cl, Br, more preferably F or Cl;

- 10 R^a is H, linear or branched C₁₋₄ alkyl; R^b, R^c are independently of each other H, linear or branched C₁₋₄ alkyl; n is 1, or 2; and p is 0 or 1.

In some embodiments of a compound of formula Vb, one or two of v¹, v², v³, and v⁴ are selected from N, NMe, NH, or S and the remaining of v¹, v², v³, and v⁴ are C. In some embodiments of compounds of formula Vb, one of v¹, v², v³, v⁴ is N, one of v¹, v², v³, v⁴ is S and the remaining of v¹, v², v³, and v⁴ are C.

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In some embodiments of a compound of formula Vb, n is 1. In some embodiments of a compound of formula Vb, n is 1 and R^a is H. In some embodiments of a compound of formula Vb, n is 1 and R^a is methyl. In some embodiments n is 1, p is 0 and R^a is H. In some embodiments of a compound of formula Vb, n is 1, p is 0 and R^a is methyl.

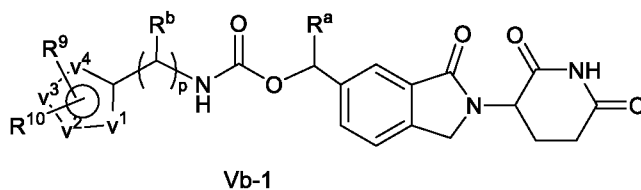
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In some embodiments of a compound of formula Vb, p is 0. In some embodiments of a compound of formula Vb, p is 1. In some embodiments of a compound of formula Vb, p is 1, and R^b and R^c are H. In some embodiments of a compound of formula Vb, p is 1, R^b is methyl and R^c is H.

In some embodiments of compounds of formula Vb, R⁹, R¹⁰ each are independently selected from H, methyl, ethyl and CF₃.

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In some embodiments the compound of formula Vb is defined by formula Vb-1



wherein one or two of v^1 , v^2 , v^3 , and v^4 are selected from C, O, N, NMe, NH, or S while two or three of v^1 , v^2 , v^3 , and v^4 are C;

- 5 R⁹, R¹⁰ each are independently selected from H, linear or branched -C₁₋₄ alkyl, -CF₃, -CHF₂, halogen, preferably F, Cl, Br, more preferably F or Cl;

R^a, R^b are independently of each other H, linear or branched C₁₋₄ alkyl; and p is 0 or 1.

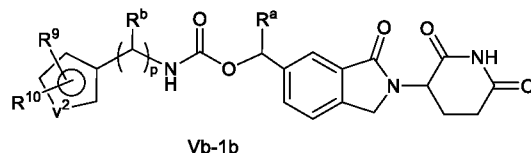
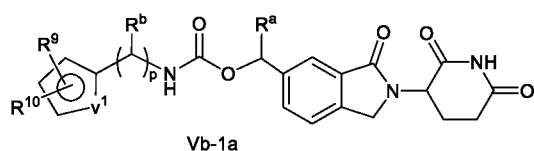
In some embodiments of a compound of formula Vb-1, one or two of v^1 , v^2 , v^3 , and v^4 are selected from N, NMe, NH, or S and the remaining of v^1 , v^2 , v^3 , and v^4 are C. In some embodiments of compounds of formula Vb-1, one of v^1 , v^2 , v^3 , v^4 is N, one of v^1 , v^2 , v^3 , v^4 is S and the remaining of v^1 , v^2 , v^3 , and v^4 are C.

In some embodiments of a compound of formula Vb-1, R^a is H. In some embodiments of a compound of formula Vb-1, R^a is methyl. In some embodiments of a compound of formula Vb-1, p is 0 and R^a is H. In some embodiments of a compound of formula Vb-1, p is 0 and R^a is methyl. In some embodiments of a compound of formula Vb-1, p is 1. In some embodiments of a compound of formula Vb-1, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Vb-1a and Vb-1b, p is 1, R^b is methyl and R^a is H.

In some embodiments of compounds of formula Vb-1 or pharmaceutically acceptable salts or stereoisomers thereof, R⁹, R¹⁰ each are independently selected from H, methyl, ethyl and CF₃.

- 20 In some embodiments of compounds of formula Vb-1, one or two of v^1 , v^2 , v^3 , v^4 are independently of each other selected from N and S (with the proviso that no –S-S- linkages are formed), while two or three of v^1 , v^2 , v^3 , and v^4 are C.

In some embodiments the compound of formula Vb-1 is defined by formula Vb-1a or Vb-1b



wherein v^1 (in a compound of formula Vb-1a) and v^2 (in a compound of formula Vb-1b) are selected from O, N, NMe, NH, and S;

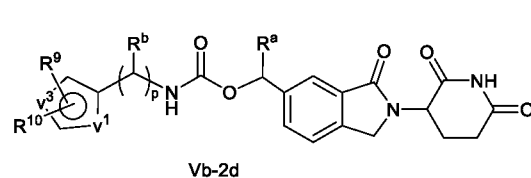
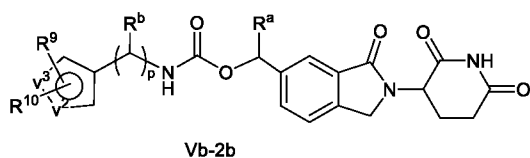
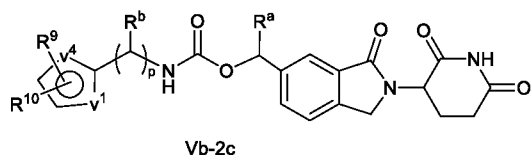
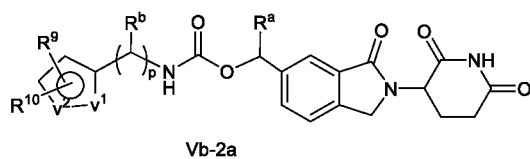
R^9 , R^{10} each are independently selected from H, linear or branched $-C_{1-4}$ alkyl, $-CF_3$, $-CHF_2$, halogen, preferably F, Cl, Br, more preferably F or Cl;

R^a , R^b are independently of each other H, linear or branched C_{1-4} alkyl; and p is 0 or 1.

In some embodiments of a compound of formula Vb-1a and Vb-1b, R^a is H. In some embodiments of a compound of formula Vb-1a and Vb-1b, R^a is methyl. In some embodiments of a compound of formula Vb-1a and Vb-1b, p is 0 and R^a is H. In some embodiments of a compound of formula Vb-1a and Vb-1b, p is 0 and R^a is methyl. In some embodiments of a compound of formula Vb-1a and Vb-1b, p is 1. In some embodiments of a compound of formula Vb-1a and Vb-1b, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Vb-1a and Vb-1b, p is 1, R^b is methyl and R^a is H.

In some embodiments of compounds of formula Vb-1a, Vb-1b or pharmaceutically acceptable salts or stereoisomers thereof, R^9 , R^{10} each are independently selected from H, methyl, ethyl and CF_3 .

In some embodiments the compound of formula Vb is defined by formula Vb-2a, Vb-2b, Vb-2c, or Vb-2d



wherein v^1 , v^2 , v^3 , v^4 are independently of each other selected from O, N, NMe, NH, and S, more specifically v^1 , v^2 (in a compound of formula Vb-2a), v^2 , v^3 (in a

compound of formula Vb-2b), v^1 , v^4 (in a compound of formula Vb-2c), and v^1 , v^3 (in a compound of formula Vb-2d) are independently of each other selected from O, N, NMe, NH, and S;

R^9 , R^{10} each are independently selected from H, linear or branched $-C_{1-4}$ alkyl, $-CF_3$, $-CHF_2$,
5 halogen, such as F, Cl;

R^a , R^b are independently of each other H, linear or branched C_{1-4} alkyl; and p is 0 or 1.

In some embodiments of a compound of formula Vb-2a, Vb-2b, Vb-2c, or Vb-2d, R^a is H. In some embodiments of a compound of formula Vb-2a, Vb-2b, Vb-2c, or Vb-2d, R^a is methyl.

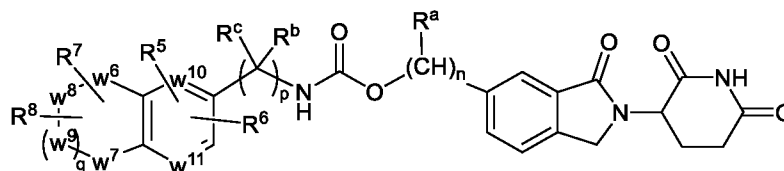
In some embodiments of a compound of formula Vb-2a, Vb-2b, Vb-2c, or Vb-2d, p is 0 and
10 R^a is H. In some embodiments of a compound of formula Vb-2a, Vb-2b, Vb-2c, or Vb-2d, p is 0 and R^a is methyl. In some embodiments of a compound of formula Vb-2a, Vb-2b, Vb-2c, or Vb-2d, p is 1. In some embodiments of a compound of formula Vb-2a, Vb-2b, Vb-2c, or Vb-2d, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Vb-2a, Vb-2b, Vb-2c, or Vb-2d, p is 1, R^b is methyl and R^a is H.

15 In some embodiments of compounds of formula Vb-2a, Vb-2b, Vb-2c, or Vb-2d, R^9 , R^{10} each are independently selected from H, methyl, ethyl and CF_3 .

In some embodiments of compounds of formula Vb-2a, Vb-2b, Vb-2c, or Vb-2d, v^1 , v^2 , v^3 , v^4 are independently of each other selected from N and S, more specifically v^1 , v^2 (in a compound of formula Vb-2a), v^2 , v^3 (in a compound of formula Vb-2b), v^1 , v^4 (in a
20 compound of formula Vb-2c), and v^1 , v^3 (in a compound of formula Vb-2d) are independently of each other selected from N and S.

In some embodiments of compounds of formula Vb-2a, v^1 is S and v^2 is N. In some embodiments of compounds of formula Vb-2a, v^1 is N and v^2 is S. In some embodiments of compounds of formula Vb-2b, v^2 is S and v^3 is N. In some embodiments of compounds of
25 formula Vb-2c, v^1 is S and v^4 is N. In some embodiments of compounds of formula Vb-2d, v^1 is N and v^3 is S. In some embodiments of compounds of formula Vb-2d, v^1 is S and v^3 is N.

In some embodiments a compound of formula I is a fused 6(saturated)-6(aromatic) ring system or a fused 5(saturated)-6(aromatic) ring system, more specifically a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula VIa:



VIa

wherein one or two of w^6 , w^7 , w^8 , w^9 are selected from C and O and the remaining of w^6 , w^7 , w^8 , w^9 are C; w^{10} , w^{11} are independently of each other selected from C and N;

- 5 R^5 , R^6 , R^7 , R^8 are independently of each other selected from H, linear or branched C_{1-4} alkyl, such as methyl, halogen, such as F or Cl, e.g. F;

R^a is H, linear or branched C_{1-4} alkyl; R^b , R^c are independently of each other H, linear or branched C_{1-4} alkyl; q is 0, 1; n is 1 or 2; and p is 0 or 1.

- In some embodiments of a compound of formula VIa, R^a is H. In some embodiments of a compound of formula VIa, R^a is methyl. In some embodiments of a compound of formula VIa, n is 1. In some embodiments of a compound of formula VIa, n is 1 and R^a is H. In some embodiments of a compound of formula VIa, n is 1 and R^a is methyl.

- In some embodiments of a compound of formula VIa, p is 0. In some embodiments of a compound of formula VIa, p is 0 and R^a is H. In some embodiments of a compound of formula VIa, p is 0 and R^a is methyl. In some embodiments of a compound of formula VIa, p is 1. In some embodiments of a compound of formula VIa, p is 1, and R^b and R^c are H. In some embodiments of a compound of formula VIa, p is 1, R^b is methyl and R^c is H.

In some embodiments of a compound of formula VIa, one of w^{10} and w^{11} is C. In some embodiments of a compound of formula VIa, one of w^{10} and w^{11} is C and the other is N.

- 20 In some embodiments of a compound of formula VIa, q is 0 and w^8 is C. In some embodiments of a compound of formula VIa, q is 0, w^8 is C and w^6 , w^7 are selected from C and O. In some embodiments of a compound of formula VIa, q is 0, w^8 is C and w^6 , w^7 are O. In some embodiments of a compound of formula VIa, q is 0, w^8 is C and one of w^6 , w^7 is C and the other of w^6 , w^7 is O.

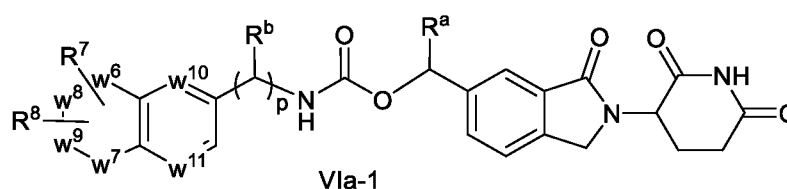
- 25 In some embodiments of a compound of formula VIa, q is 1, and w^6 , w^7 , w^8 , w^9 are C. In some embodiments of a compound of formula VIa, q is 1, and w^6 is O and w^7 , w^8 , w^9 are C. In some embodiments of a compound of formula VIa, q is 1, and w^7 is O and w^6 , w^8 , w^9 are C. In some

embodiments of a compound of formula VIa, q is 1, and w^8 is O and w^6, w^7, w^9 are C. In some embodiments of a compound of formula VIa, q is 1, and w^9 is O and w^6, w^7, w^8 are C.

In some embodiments of a compound of formula VIa, R^5, R^6 are H.

In some embodiments of a compound of formula VIa, R^7, R^8 are independently of each other selected from H, linear or branched C_{1-4} alkyl, such as methyl, halogen, such as F or Cl, e.g. F. R^7, R^8 may be attached to the same ring atom or to different ring atoms.

Some embodiments of a compound of formula VIa are provided by formula VIa-1



wherein one or two of w^6, w^7, w^8, w^9 are selected from C and O and the remaining of w^6, w^7, w^8, w^9 are C; w^{10}, w^{11} are independently of each other selected from C and N;

R^7, R^8 are independently of each other selected from H, linear or branched C_{1-4} alkyl, such as methyl, halogen, such as F or Cl, e.g. F; R^a, R^b are independently of each other H, linear or branched C_{1-4} alkyl; and p is 0 or 1.

In some embodiments of a compound of formula VIa-1, p is 0. In some embodiments of a compound of formula VIa-1, p is 1.

In some embodiments of a compound of formula VIa-1, R^a is H. In some embodiments of a compound of formula VIa-1, R^a is methyl. In some embodiments of a compound of formula VIa-1, p is 0 and R^a is H. In some embodiments of a compound of formula VIa-1, p is 0 and R^a is methyl. In some embodiments of a compound of formula VIa-1, p is 1 and R^b is H. In some embodiments of a compound of formula VIa-1, p is 1 and R^b is methyl.

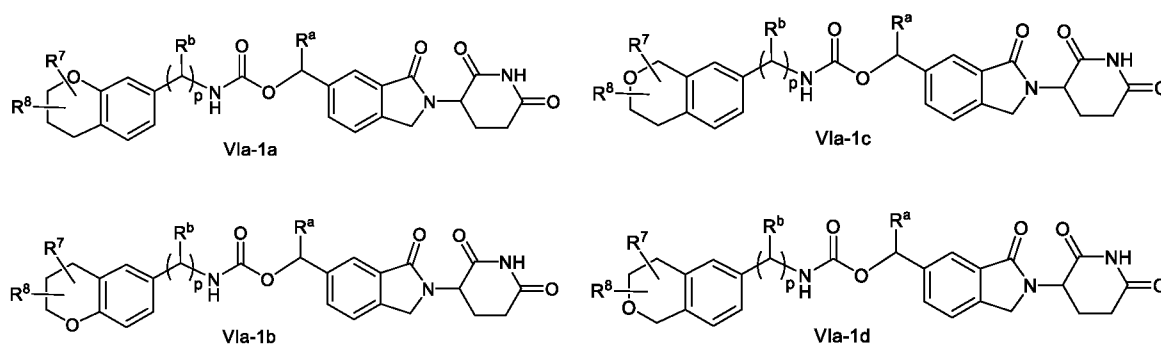
In some embodiments of a compound of formula VIa-1, one of w^{10} and w^{11} are C. In some embodiments of a compound of formula VIa-1, one of w^{10} and w^{11} is C and the other is N.

In some embodiments of a compound of formula VIa-1, w^6, w^7, w^8, w^9 are C. In some embodiments of a compound of formula VIa-1, w^6 is O and w^7, w^8, w^9 are C. In some embodiments of a compound of formula VIa-1, w^7 is O and w^6, w^8, w^9 are C. In some

embodiments of a compound of formula Vla-1, w^8 is O and w^6 , w^7 , w^9 are C. In some embodiments of a compound of formula Vla-1, w^9 is O and w^6 , w^7 , w^8 are C.

In some embodiments of a compound of formula Vla-1, R^7 , R^8 are independently of each other selected from H, linear or branched C_{1-4} alkyl, such as methyl, halogen, such as F or Cl, e.g. F. R^7 , R^8 may be attached to the same ring atom or to different ring atoms.

Some embodiments of a compound of formula Vla-1 are provided by formula Vla-1a, Vla-1b, Vla-1c, Vla-1d



wherein

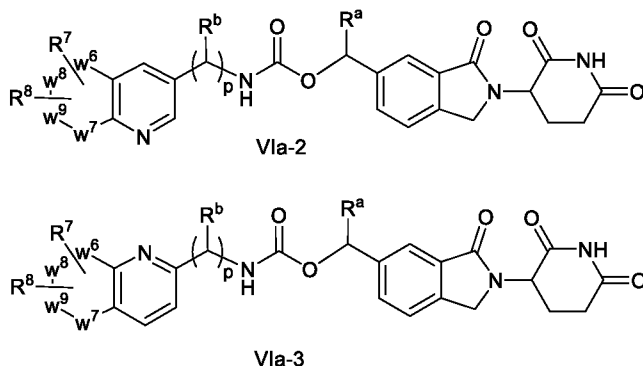
- 10 R^7 , R^8 are independently of each other selected from H, linear or branched C_{1-4} alkyl, such as methyl, halogen, such as F or Cl, e.g. F; R^a , R^b are independently of each other H, linear or branched C_{1-4} alkyl, and p is 0 or 1.

In some embodiments of a compound of formula Vla-1a, Vla-1b, Vla-1c, Vla-1d, p is 0. In some embodiments of a compound of formula Vla-1a, Vla-1b, Vla-1c, Vla-1d, p is 1.

- 15 In some embodiments of a compound of formula Vla-1a, Vla-1b, Vla-1c, Vla-1d, R^a is H. In some embodiments of a compound of formula Vla-1a, Vla-1b, Vla-1c, Vla-1d, R^a is methyl. In some embodiments of a compound of formula Vla-1a, Vla-1b, Vla-1c, Vla-1d, p is 0 and R^a is H. In some embodiments of a compound of formula Vla-1a, Vla-1b, Vla-1c, Vla-1d, p is 0 and R^a is methyl.
- 20 In some embodiments of a compound of formula Vla-1a, Vla-1b, Vla-1c, Vla-1d, p is 1 and R^b is H. In some embodiments of a compound of formula Vla-1a, Vla-1b, Vla-1c, Vla-1d, p is 1 and R^b is methyl. In some embodiments of a compound of formula Vla-1a, Vla-1b, Vla-1c, Vla-1d, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Vla-1a, Vla-1b, Vla-1c, Vla-1d, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Vla-1a, Vla-1b, Vla-1c, Vla-1d, R^7 , R^8 are independently of each other selected from H, linear or branched C_{1-4} alkyl, such as methyl, halogen, such as F or Cl, e.g. F. R^7 , R^8 may be attached to the same ring atom or to different ring atoms.

- 5 Some embodiments of a compound of formula Vla and Vla-1 are provided by formula Vla-2, Vla-3



wherein one or two of w^6 , w^7 , w^8 , w^9 are selected from C and O and the remaining of w^6 , w^7 , w^8 , w^9 are C;

- 10 R^7 , R^8 are independently of each other selected from H, linear or branched C_{1-4} alkyl, such as methyl, halogen, such as F or Cl, e.g. F; R^a , R^b are independently of each other H, linear or branched C_{1-4} alkyl; and p is 0 or 1.

In some embodiments of a compound of formula Vla-2 or Vla-3, p is 0. In some embodiments of a compound of formula Vla-2 or Vla-3, p is 1.

- 15 In some embodiments of a compound of formula Vla-2 or Vla-3, R^a is H. In some embodiments of a compound of formula Vla-2 or Vla-3, R^a is methyl. In some embodiments of a compound of formula Vla-2 or Vla-3, p is 0 and R^a is H. In some embodiments of a compound of formula Vla-2 or Vla-3, p is 0 and R^a is methyl.

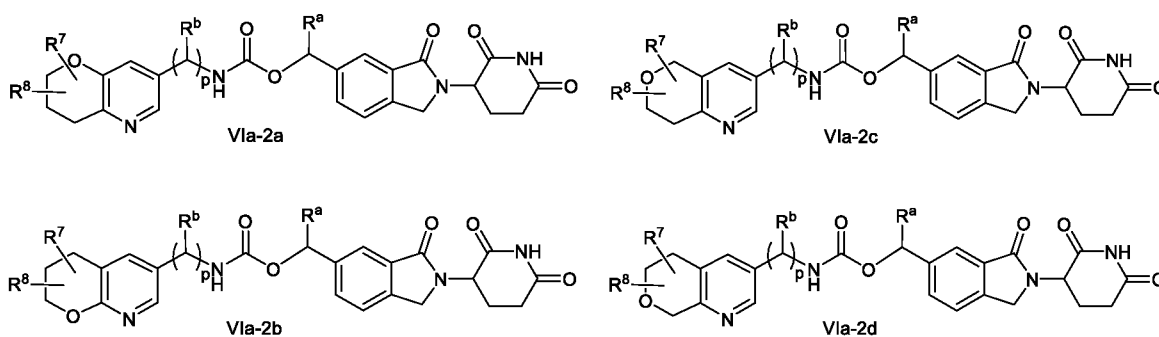
- In some embodiments of a compound of formula Vla-2 or Vla-3, p is 1 and R^b is H. In some
20 embodiments of a compound of formula Vla-2 or Vla-3, p is 1 and R^b is methyl. In some
embodiments of a compound of formula Vla-2 or Vla-3, p is 1, R^b is H and R^a is H. In some
embodiments of a compound of formula Vla-2 or Vla-3, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Vla-2 or Vla-3, w^6 , w^7 , w^8 , w^9 are C. In some
embodiments of a compound of formula Vla-2 or Vla-3, w^6 is O and w^7 , w^8 , w^9 are C. In some

embodiments of a compound of formula Vla-2 or Vla-3, w^7 is O and w^6 , w^8 , w^9 are C. In some embodiments of a compound of formula Vla-2 or Vla-3, w^8 is O and w^6 , w^7 , w^9 are C. In some embodiments of a compound of formula Vla-2 or Vla-3, w^9 is O and w^6 , w^7 , w^8 are C.

In some embodiments of a compound of formula Vla-2 or Vla-3, R^7 , R^8 are independently of each other selected from H, linear or branched C_{1-4} alkyl, such as methyl, halogen, such as F or Cl, e.g. F. R^7 , R^8 may be attached to the same ring atom or to different ring atoms.

Some embodiments of a compound of formula Vla-2 are provided by formula Vla-2a, Vla-2b, Vla-2c, Vla-2d



10 wherein

R^7 , R^8 are independently of each other selected from H, linear or branched C_{1-4} alkyl, such as methyl, halogen, such as F or Cl, e.g. F; R^a , R^b are independently of each other H, linear or branched C_{1-4} alkyl, and p is 0 or 1.

In some embodiments of a compound of formula Vla-2a, Vla-2b, Vla-2c, Vla-2d, p is 0. In some embodiments of a compound of formula Vla-2a, Vla-2b, Vla-2c, Vla-2d, p is 1.

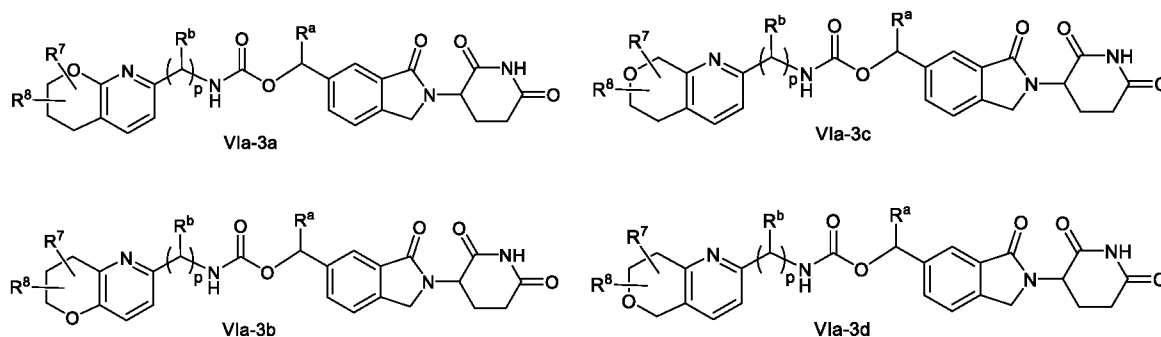
In some embodiments of a compound of formula Vla-2a, Vla-2b, Vla-2c, Vla-2d, R^a is H. In some embodiments of a compound of formula Vla-2a, Vla-2b, Vla-2c, Vla-2d, R^a is methyl. In some embodiments of a compound of formula Vla-2a, Vla-2b, Vla-2c, Vla-2d, p is 0 and R^a is H. In some embodiments of a compound of formula Vla-2a, Vla-2b, Vla-2c, Vla-2d, p is 0 and R^a is methyl.

In some embodiments of a compound of formula Vla-2a, Vla-2b, Vla-2c, Vla-2d, p is 1 and R^b is H. In some embodiments of a compound of formula Vla-2a, Vla-2b, Vla-2c, Vla-2d, p is 1 and R^b is methyl. In some embodiments of a compound of formula Vla-2a, Vla-2b, Vla-2c,

Vla-2d, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Vla-2a, Vla-2b, Vla-2c, Vla-2d, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Vla-2a, Vla-2b, Vla-2c, Vla-2d, R⁷, R⁸ are independently of each other selected from H, linear or branched C₁₋₄ alkyl, such as methyl, halogen, such as F or Cl, e.g. F. R⁷, R⁸ may be attached to the same ring atom or to different ring atoms.

Some embodiments of a compound of formula Vla-1 are provided by formula Vla-1a, Vla-1b, Vla-1c, Vla-1d



wherein

R⁷ R⁸ are independently of each other selected from H, linear or branched C₁₋₄ alkyl, such as methyl, halogen, such as F or Cl, e.g. F; R^a, R^b are independently of each other H, linear or branched C₁₋₄ alkyl, and p is 0 or 1.

In some embodiments of a compound of formula Vla-3a, Vla-3b, Vla-3c, Vla-3d, p is 0. In some embodiments of a compound of formula Vla-3a, Vla-3b, Vla-3c, Vla-3d, p is 1.

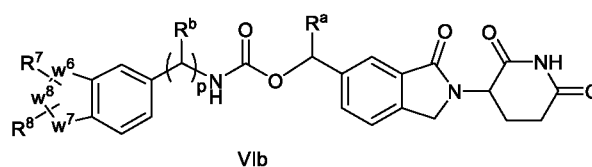
In some embodiments of a compound of formula Vla-3a, Vla-3b, Vla-3c, Vla-3d, R^a is H. In some embodiments of a compound of formula Vla-3a, Vla-3b, Vla-3c, Vla-3d, R^a is methyl. In some embodiments of a compound of formula Vla-3a, Vla-3b, Vla-3c, Vla-3d, p is 0 and R^a is H. In some embodiments of a compound of formula Vla-3a, Vla-3b, Vla-3c, Vla-3d, p is 0 and R^a is methyl.

In some embodiments of a compound of formula Vla-3a, Vla-3b, Vla-3c, Vla-3d, p is 1 and R^b is H. In some embodiments of a compound of formula Vla-3a, Vla-3b, Vla-3c, Vla-3d, p is 1 and R^b is methyl. In some embodiments of a compound of formula Vla-3a, Vla-3b, Vla-3c,

Vla-3d, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Vla-3a, Vla-3b, Vla-3c, Vla-3d, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Vla-3a, Vla-3b, Vla-3c, Vla-3d, R⁷, R⁸ are independently of each other selected from H, linear or branched C₁₋₄ alkyl, such as methyl, halogen, such as F or Cl, e.g. F. R⁷, R⁸ may be attached to the same ring atom or to different ring atoms.

In some embodiments the compound of formula Via, q is 0 and thus formula Vla is provided by formula VIb



wherein

w⁶, w⁷, w⁸ are independently of each other selected from C and O;

R⁷ R⁸ are independently of each other selected from H, linear or branched C₁₋₄ alkyl, such as methyl, halogen, such as F or Cl, e.g. F; R^a, R^b are independently of each other H, linear or branched C₁₋₄ alkyl and p is 0 or 1.

In some embodiments of a compound of formula VIb, w⁶, w⁷, w⁸ are independently of each other selected from C and O; with the proviso that neighbouring groups cannot be both O.

In some embodiments of a compound of formula VIb, p is 0. In some embodiments of a compound of formula VIb, p is 1.

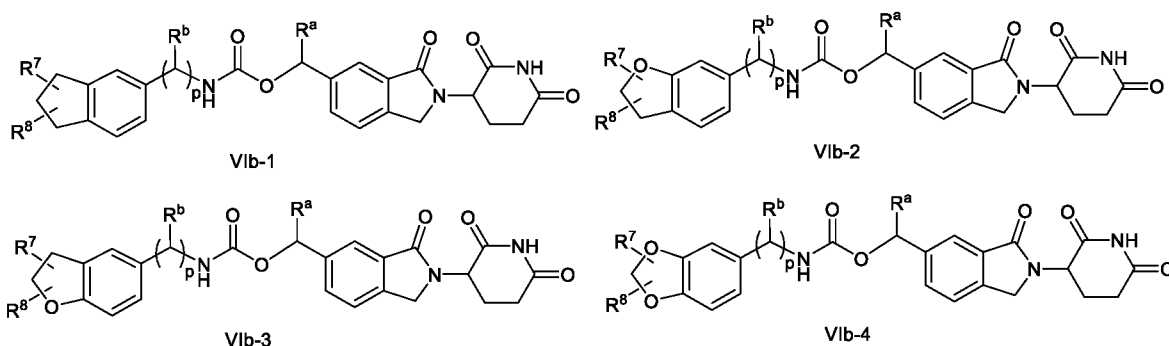
In some embodiments of a compound of formula VIb, R^a is H. In some embodiments of a compound of formula VIb, R^a is methyl. In some embodiments of a compound of formula VIb, p is 0 and R^a is H. In some embodiments of a compound of formula VIb, p is 0 and R^a is methyl.

In some embodiments of a compound of formula VIb, p is 1 and R^b is H. In some embodiments of a compound of formula VIb, p is 1 and R^b is methyl. In some embodiments of a compound of formula VIb, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula VIb, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula VIb, w^8 is C. In some embodiments of a compound of formula VIb, w^8 is C and w^6 , w^7 are selected from C and O. In some embodiments of a compound of formula VIb, w^8 is C and w^6 , w^7 are O. In some embodiments of a compound of formula VIb, w^8 is C and one of w^6 , w^7 is C and the other of w^6 , w^7 is O.

- 5 In some embodiments of a compound of formula VIb, R^7 , R^8 are independently of each other selected from H, linear or branched C_{1-4} alkyl, such as methyl, halogen, such as F or Cl, e.g. F. R^7 , R^8 may be attached to the same ring atom or to different ring atoms.

In some embodiments the compound of formula VIb is provided by formula VIb-1, VIb-2, VIb-3, VIb-4



10

wherein

R^7 , R^8 are independently of each other selected from H, linear or branched C_{1-4} alkyl, such as methyl, halogen, such as F or Cl, e.g. F; R^a , R^b are independently of each other H, linear or branched C_{1-4} alkyl, and p is 0 or 1.

- 15 In some embodiments of a compound of formula VIb-1, VIb-2, VIb-3, or VIb-4, p is 0. In some embodiments of a compound of formula VIb-1, VIb-2, VIb-3, or VIb-4, p is 1.

In some embodiments of a compound of formula VIb-1, VIb-2, VIb-3, or VIb-4, R^a is H. In some embodiments of a compound of formula VIb-1, VIb-2, VIb-3, or VIb-4, R^a is methyl. In some embodiments of a compound of formula VIb-1, VIb-2, VIb-3, or VIb-4, p is 0 and R^a is H. In some embodiments of a compound of formula VIb-1, VIb-2, VIb-3, or VIb-4, p is 0 and R^a is methyl.

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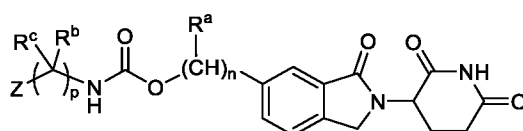
In some embodiments of a compound of formula VIb-1, VIb-2, VIb-3, or VIb-4, p is 1 and R^b is H. In some embodiments of a compound of formula VIb-1, VIb-2, VIb-3, or VIb-4, p is 1 and R^b is methyl. In some embodiments of a compound of formula VIb-1, VIb-2, VIb-3, or

Vlb-4, p is 1, R^b is H and R^a is H. In some embodiments of a compound of formula Vlb-1, Vlb-2, Vlb-3, or Vlb-4, p is 1, R^b is methyl and R^a is H.

In some embodiments of a compound of formula Vlb-1, Vlb-2, Vlb-3, or Vlb-4, R⁷, R⁸ are independently of each other selected from H, linear or branched C₁₋₄ alkyl, such as methyl, halogen, such as F or Cl, e.g. F. In some embodiments of a compound of formula Vlb-1, Vlb-2, Vlb-3, or Vlb-4, R⁷, R⁸ are H. In some embodiments of a compound of formula Vlb-1, Vlb-2, Vlb-3, or Vlb-4, R⁷, R⁸ are methyl. In some embodiments of a compound of formula Vlb-1, Vlb-2, Vlb-3, or Vlb-4, one of R⁷, R⁸ is H, the other is methyl.

R⁷, R⁸ may be attached to the same ring atom or to different ring atoms.

- 10 In some embodiments a compound of formula I is a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula VIIa:



VIIa

wherein

- 15 Z is H, linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, 4-8 membered heterocycloalkyl, wherein Z is unsubstituted or substituted with linear or branched C₁₋₄ alkyl, C₆ aryl, C₆ aryloxy, 6 membered heteroaryl or CF₃; or Z together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with linear or branched C₁₋₄ alkyl, C₆ aryl, C₆ aryloxy, 6 membered heteroaryl or CF₃;
- 20 R^a is H, linear or branched C₁₋₄ alkyl, such as methyl; R^b, R^c are independently of each other H, linear or branched C₁₋₄ alkyl, such as methyl; n is 1, or 2; and p is 0 or 1.

In some embodiments of a compound of formula VIIa, R^a is H. In some embodiments of a compound of formula VIIa, R^a is methyl. In some embodiments of a compound of formula VIIa, n is 1. In some embodiments of a compound of formula VIIa, n is 1 and R^a is H. In some
25 embodiments of a compound of formula VIIa, n is 1 and R^a is methyl.

In some embodiments of a compound of formula VIIa, p is 0. In some embodiments of a compound of formula VIIa, p is 1. In some embodiments of a compound of formula VIIa, p is

1, and R^b and R^c are H. In some embodiments of a compound of formula VIIa, p is 1, R^b is methyl and R^c is H.

In some embodiments of a compound of formula VIIa, n is 1 and p is 1. In some embodiments of a compound of formula VIIa, n is 1, p is 1, R^a is H and R^b , R^c are H. In some embodiments of a compound of formula VIIa, n is 1, p is 1, R^a is methyl and R^b , R^c are H.

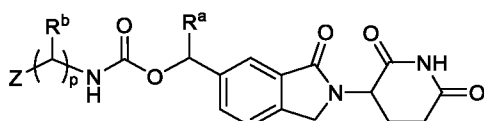
In some embodiments of a compound of formula VIIa, n is 1 and p is 0. In some embodiments of a compound of formula VIIa, n is 1, p is 0 and R^a is H. In some embodiments of a compound of formula VIIa, n is 1, p is 0 and R^a is methyl.

In some embodiments of a compound of formula VIIa-1, Z is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, 4-6 membered heterocycloalkyl, wherein Z is unsubstituted or substituted with linear or branched C_{1-4} alkyl, C_6 aryl, C_6 aryloxy, 6 membered heteroaryl; or Z together with the N atom of the carbamate forms a 4-6 membered heterocycloalkyl, which is unsubstituted or substituted with C_{1-4} alkyl, C_6 aryl, C_6 aryloxy, 6 membered heteroaryl.

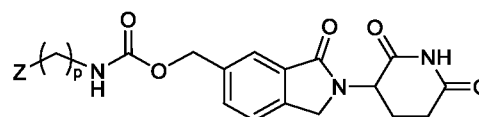
In some embodiments of a compound of formula VIIa-1, Z is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, 5-6 membered heterocycloalkyl, wherein Z is unsubstituted or substituted with linear or branched C_{1-4} alkyl, C_6 aryl, C_6 aryloxy, 6 membered heteroaryl; or Z together with the N atom of the carbamate forms a pyrrolidiny, piperdiny, morpholiny, piperaziny, which is unsubstituted or substituted with C_{1-4} alkyl, C_6 aryl, C_6 aryloxy, 6 membered heteroaryl.

In some embodiments of a compound of formula VIIa-1, Z is linear or branched C_{1-4} alkyl, cyclopropyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidiny, 1,3-dioxanyl, wherein Z is unsubstituted or substituted with C_{1-4} alkyl, phenyl, pyridiny; or Z together with the N atom of the carbamate forms a pyrrolidiny, piperdiny, piperaziny, which is unsubstituted or substituted with C_6 aryl, C_6 aryloxy.

In some embodiments a compound of formula I is a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula VIIa-1, e.g. VIIa-1a:



VIIa-1



VIIa-1a

wherein Z is H, linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, 4-8 membered heterocycloalkyl, wherein Z is unsubstituted or substituted with linear or branched C₁₋₄ alkyl, C₆ aryl, C₆ aryloxy, 6 membered heteroaryl or CF₃; or Z together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with linear or branched C₁₋₄ alkyl, C₆ aryl, C₆ aryloxy, 6 membered heteroaryl or CF₃;

R^a, R^b are independently of each other H, linear or branched C₁₋₄ alkyl, such as methyl; and p is 0 or 1.

In some embodiments of a compound of formula VIIa-1, R^a is H. In some embodiments of a compound of formula VIIa, R^a is methyl.

In some embodiments of a compound of formula VIIa-1, p is 0. In some embodiments of a compound of formula VIIa-1, p is 0 and R^a is H. In some embodiments of a compound of formula VIIa-1, p is 0 and R^a is methyl.

In some embodiments of a compound of formula VIIa-1, p is 1. In some embodiments of a compound of formula VIIa-1, p is 1 and R^b is H. In some embodiments of a compound of formula VIIa-1, p is 1 and R^b is methyl. In some embodiments of a compound of formula VIIa-1, p is 1 and R^a and R^b are H. In some embodiments of a compound of formula VIIa-1, p is 1, R^a is methyl and R^b is H. In some embodiments of a compound of formula VIIa-1, p is 1, R^a and R^b are methyl.

In some embodiments of a compound of formula VIIa-1a, p is 0. In some embodiments of a compound of formula VIIa-1a, p is 1.

In some embodiments of a compound of formula VIIa-1, Z is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, 4-6 membered heterocycloalkyl, wherein Z is unsubstituted or substituted with linear or branched C₁₋₄ alkyl, C₆ aryl, C₆ aryloxy, 6 membered heteroaryl; or Z together with the N atom of the carbamate forms a 4-6 membered heterocycloalkyl, which is unsubstituted or substituted with C₁₋₄ alkyl, C₆ aryl, C₆ aryloxy, 6 membered heteroaryl.

In some embodiments of a compound of formula VIIa-1, Z is linear or branched -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, 5-6 membered heterocycloalkyl, wherein Z is unsubstituted or substituted with linear or branched C₁₋₄ alkyl, C₆ aryl, C₆ aryloxy, 6 membered heteroaryl; or Z together with the N atom of the carbamate forms a pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, which is unsubstituted or substituted with C₁₋₄ alkyl, C₆ aryl, C₆ aryloxy, 6 membered heteroaryl.

In some embodiments of a compound of formula VIIa-1, Z is linear or branched C₁₋₄ alkyl, cyclopropyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, wherein Z is unsubstituted or substituted with C₁₋₄ alkyl, phenyl, pyridinyl; or Z together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, piperazinyl, which is unsubstituted or substituted with C₆ aryl, C₆ aryloxy.

In some embodiments of a compound of formula VIIa-1, p is 0 and Z is linear or branched - C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, 4-6 membered heterocycloalkyl, wherein Z is unsubstituted or substituted with linear or branched C₁₋₄ alkyl, C₆ aryl, C₆ aryloxy, 6 membered heteroaryl.

In some embodiments of a compound of formula VIIa-1, p is 0 and Z is linear or branched - C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, 5-6 membered heterocycloalkyl, wherein Z is unsubstituted or substituted with linear or branched C₁₋₄ alkyl, C₆ aryl, C₆ aryloxy, 6 membered heteroaryl.

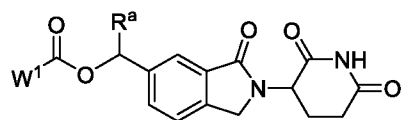
In some embodiments of a compound of formula VIIa-1, p is 0 and Z is linear or branched C₁₋₄ alkyl, cyclopropyl, cyclopentyl, cyclohexyl, bicyclo[1.1.1]pentyl, piperidinyl, 1,3-dioxanyl, wherein Z is unsubstituted or substituted with C₁₋₄ alkyl, phenyl, pyridinyl.

In some embodiments of a compound of formula VIIa-1, p is 1 and Z is linear or branched - C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, 4-6 membered heterocycloalkyl, wherein Z is unsubstituted or substituted with linear or branched C₁₋₄ alkyl, C₆ aryl, C₆ aryloxy, 6 membered heteroaryl; or Z together with the N atom of the carbamate forms a 4-6 membered heterocycloalkyl, which is unsubstituted or substituted with C₁₋₄ alkyl, C₆ aryl, C₆ aryloxy, 6 membered heteroaryl.

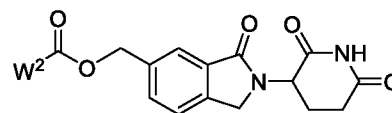
In some embodiments of a compound of formula VIIa-1, p is 1 and Z is linear or branched - C₁₋₆ alkyl, -C₃₋₆ cycloalkyl, wherein Z is unsubstituted or substituted with linear or branched C₁₋₄ alkyl, C₆ aryl; or Z together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, morpholinyl, piperazinyl, which is unsubstituted or substituted with C₁₋₄ alkyl, C₆ aryl, C₆ aryloxy, 6 membered heteroaryl.

In some embodiments of a compound of formula VIIa-1, p is 1 and Z is linear or branched C₁₋₆ alkyl, cyclopropyl; or Z together with the N atom of the carbamate forms a pyrrolidinyl, piperdinyl, piperazinyl, which is unsubstituted or substituted with C₆ aryl, C₆ aryloxy.

In more specific embodiments, the present disclosure is directed towards a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula VIII, e.g. VIIIa

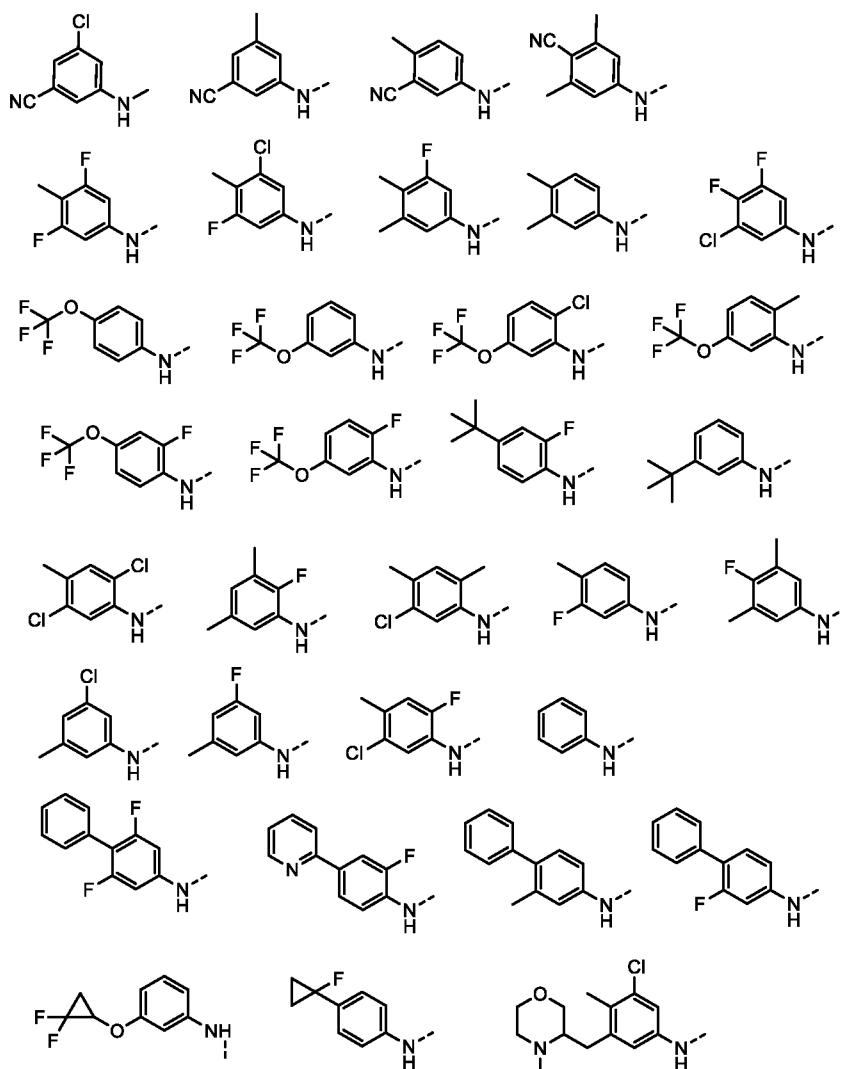


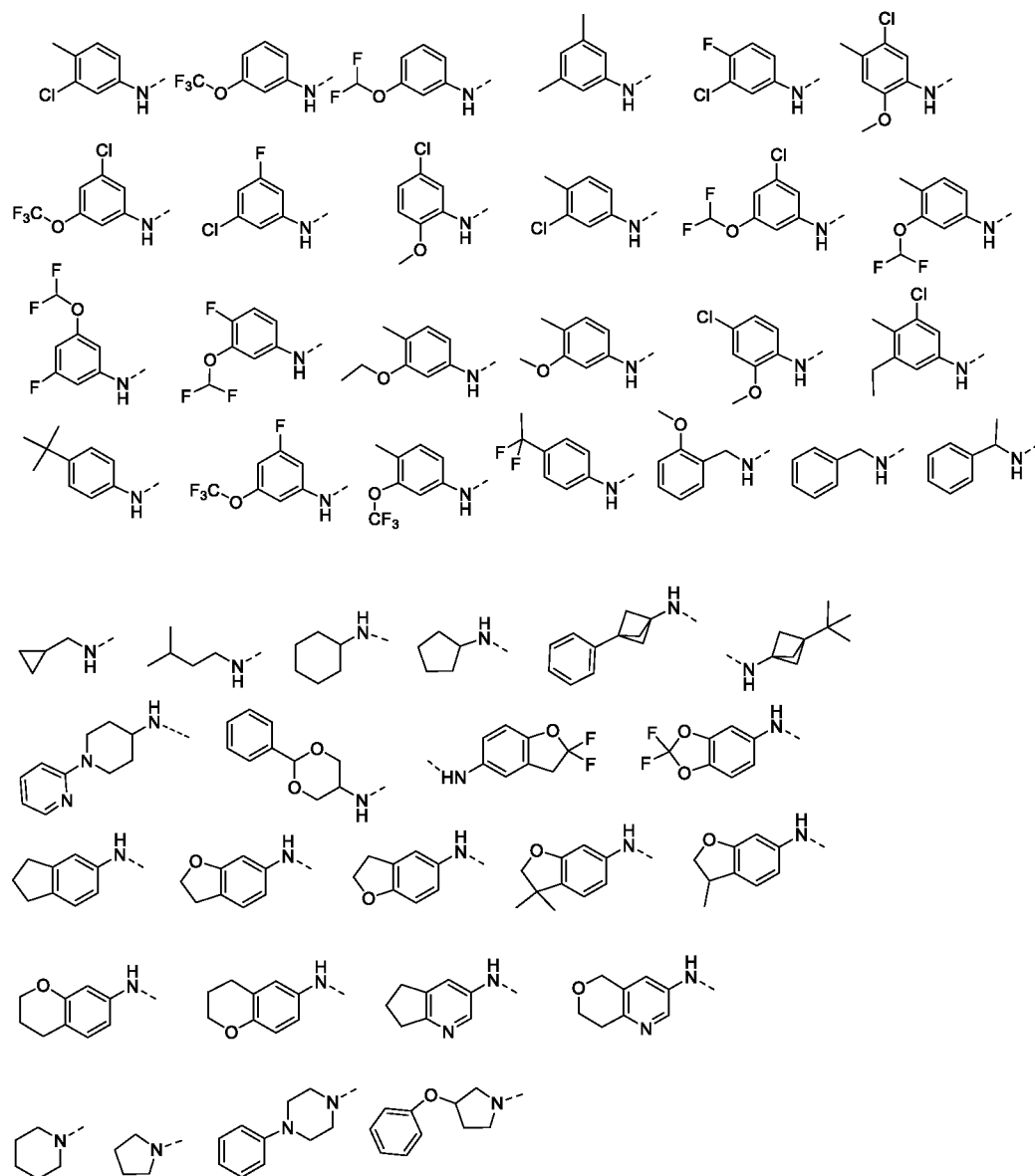
VIII

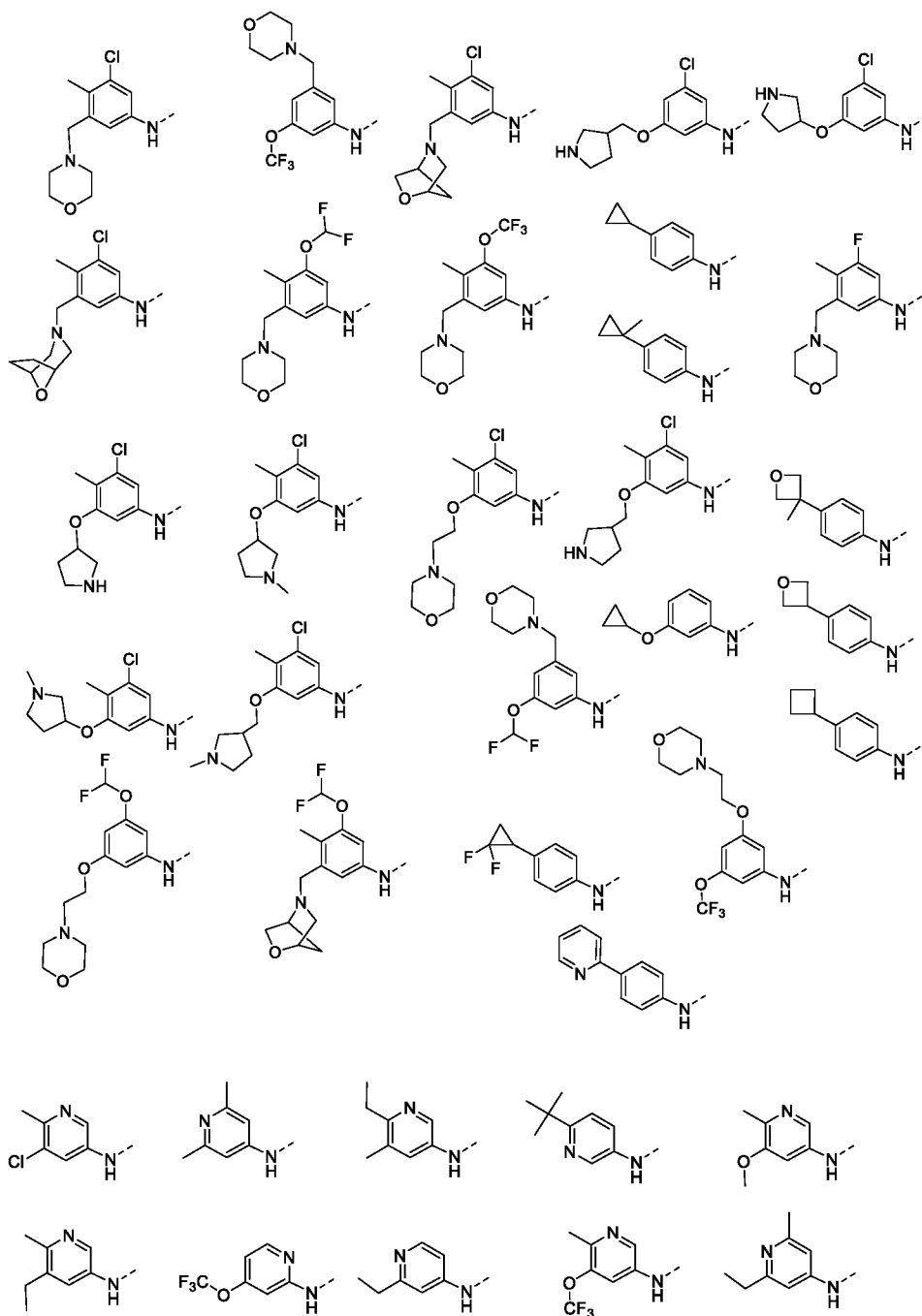


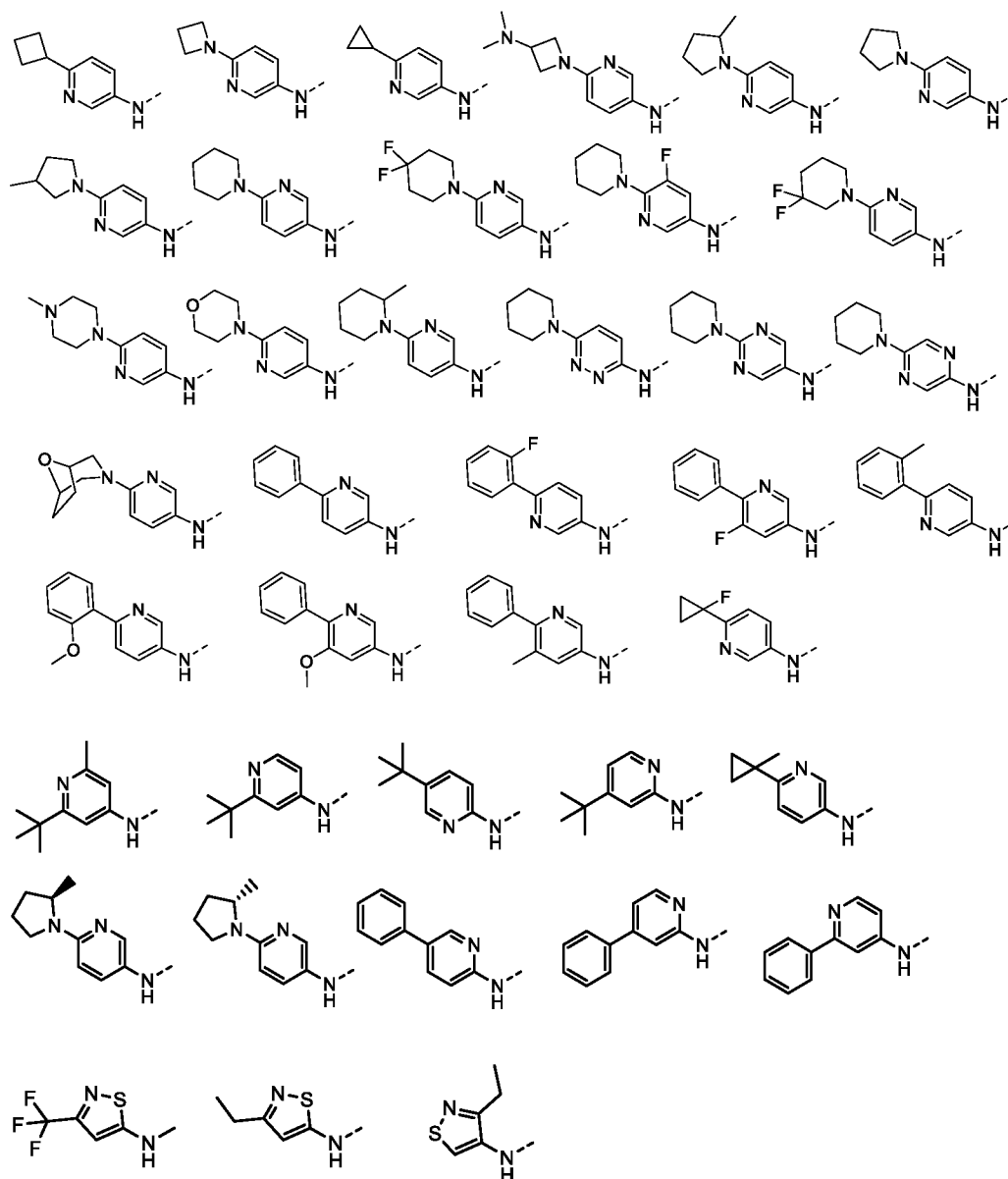
VIIIa

wherein R^a is H or methyl and W^1 and W^2 are selected from









In more specific embodiments of a compound of formula VIII, R^a is H.

- 5 In further specific embodiments, the disclosure is directed to the specific examples disclosed in Table 1.

In some embodiments, the disclosure is directed to the (S) enantiomer of the compounds of any of formula I-VIII. In some embodiments, the disclosure is directed to the (R) enantiomer of the compounds of any of formula I-VIII. In some embodiments, the disclosure is directed to the racemate of the compounds of any of formula I-VIII.

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The compounds of the disclosure may contain one or more asymmetric centers in the molecule. A compound without designation of the stereochemistry is to be understood to include all the optical isomers (e.g., diastereomers, enantiomers, etc.) in pure or substantially

pure form, as well as mixtures thereof (e.g. a racemic mixture, or an enantiomerically enriched mixture). It is well known in the art how to prepare such optically active forms (e.g. by resolution of the racemic form by recrystallization techniques, by synthesis from optically-active starting materials, by chiral synthesis, by chromatographic separation using a chiral stationary phase, and other methods).

The compounds may be isotopically-labeled compounds, for example, compounds including various isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, fluorine, iodine, or chlorine. The disclosed compounds may exist in tautomeric forms and mixtures and separate individual tautomers are contemplated. In addition, some compounds may exhibit polymorphism.

The compounds of the disclosure include the free form as well as the pharmaceutically acceptable salts and stereoisomers thereof. The pharmaceutically acceptable salts include all the typical pharmaceutically acceptable salts. The pharmaceutically acceptable salts of the present compounds can be synthesized from the compounds of this disclosure which contain a basic or acidic moiety by conventional chemical methods, see e.g. Berge et al, "Pharmaceutical Salts," J. Pharm. Sci., 1977:66:1-19. Furthermore, the compounds of the disclosure also include lyophilized and polymorphs of the free form.

For example, conventional pharmaceutically acceptable salts for a basic compound include those derived from inorganic acids such as hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric, nitric and the like, as well as salts prepared from organic acids such as acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, pantoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxy-benzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isethionic, trifluoroacetic and the like. Conventional pharmaceutically acceptable salts for an acidic compound include those derived from inorganic bases include aluminum, ammonium, calcium, copper, ferric, ferrous, lithium, magnesium, manganic salts, manganous, potassium, sodium, zinc and the like. Salts derived from pharmaceutically acceptable organic bases include salts of primary, secondary and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as arginine, betaine, caffeine, choline, N,N-dibenzylethylenediamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethylmorpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lysine,

methylglucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethylamine, trimethylamine tripropylamine, tromethamine and the like.

The compounds of the disclosure may exist in solid, i.e. crystalline (e.g., polymorphs, i.e., different crystalline structures that have the same chemical composition but differ in packing, geometrical arrangement) or noncrystalline form (optionally as solvates) or liquid form. In the solid state, it may exist in, or as a mixture thereof. In crystalline solvates, solvent molecules are incorporated into the crystalline lattice during crystallization. The formation of solvates may include non-aqueous solvents such as, but not limited to, ethanol, isopropanol, DMSO, acetic acid, ethanolamine, or ethyl acetate, or aqueous solvents such as water (also called "hydrates"). Different polymorphs may be produced, for example, by changing or adjusting the reaction conditions or reagents.

In a further aspect, the disclosure also provides methods of preparation of the compounds of formula I-VIII of the disclosure. In some embodiments, they are prepared according to the general procedure A.

In yet another aspect, the disclosure further provides a pharmaceutical composition comprising a therapeutically-effective amount of one or more of the compounds of the disclosure or pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable carriers and/or excipients (also referred to as diluents). The excipients are acceptable in the sense of being compatible with the other ingredients of the formulation and not deleterious to the recipient thereof (i.e., the patient). The term "therapeutically-effective amount", or "therapeutically effective amount" as used herein refers to the amount of a compound (as such or in form of a pharmaceutical composition) of the present disclosure which is effective for producing some desired therapeutic effect.

Pharmaceutical compositions may be in unit dose form containing a predetermined amount of a compound of the disclosure per unit dose. Such a unit may contain a therapeutically effective dose of a compound of the disclosure or salt thereof or a fraction of a therapeutically effective dose such that multiple unit dosage forms might be administered at a given time to achieve the desired therapeutically effective dose. Preferred unit dosage formulations are those containing a daily dose or sub-dose, or an appropriate fraction thereof, of a compound of the disclosure or salt thereof.

The compounds of the disclosure may be administered by any acceptable means in solid or liquid form, including (1) oral administration, for example, drenches (aqueous or non-aqueous solutions or suspensions), tablets, e.g., those targeted for buccal, sublingual, and systemic absorption, boluses, powders, granules, pastes for application to the tongue; (2) 5 parenteral administration, for example, by subcutaneous, intramuscular, intravenous or epidural injection as, for example, a sterile solution or suspension, or sustained-release formulation; (3) topical application, for example, as a cream, ointment, or a controlled-release patch or spray applied to the skin; (4) intravaginally or intrarectally, for example, as a pessary, cream or foam; (5) sublingually; (6) ocularly; (7) transdermally; (8) nasally; (9) 10 pulmonary; or (10) intrathecally.

The phrase "pharmaceutically-acceptable carrier" as used herein means a pharmaceutically-acceptable material, composition or vehicle, such as a liquid or solid filler, diluent, excipient, manufacturing aid (e.g., lubricant, talc magnesium, calcium or zinc stearate, or steric acid), or solvent encapsulating material, involved in carrying or transporting the subject compound 15 from one organ, or portion of the body, to another organ, or portion of the body. Each carrier must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient. Some examples of materials which can serve as pharmaceutically-acceptable carriers include: (1) sugars, such as lactose, glucose and sucrose; (2) starches, such as corn starch and potato starch; (3) cellulose, and its derivatives, 20 such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; (4) powdered tragacanth; (5) malt; (6) gelatin; (7) talc; (8) excipients, such as cocoa butter and suppository waxes; (9) oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; (10) glycols, such as propylene glycol; (11) polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol; (12) esters, such as ethyl oleate and ethyl 25 laurate; (13) agar; (14) buffering agents, such as magnesium hydroxide and aluminum hydroxide; (15) alginic acid; (16) pyrogen-free water; (17) isotonic saline; (18) Ringer's solution; (19) ethyl alcohol; (20) pH buffered solutions; (21) polyesters, polycarbonates and/or polyanhydrides; and (22) other non-toxic compatible substances employed in pharmaceutical compositions.

30 Such compositions may contain further components conventional in pharmaceutical preparations, e.g. wetting agents, emulsifiers and lubricants, such as sodium lauryl sulfate and magnesium stearate, as well as coloring agents, release agents, coating agents, sweetening, flavoring and perfuming agents, preservatives and antioxidants, pH modifiers,

bulking agents, and further active agents. Examples of pharmaceutically-acceptable antioxidants include: (1) water soluble antioxidants, such as ascorbic acid, cysteine hydrochloride, sodium bisulfate, sodium metabisulfite, sodium sulfite and the like; (2) oil-soluble antioxidants, such as ascorbyl palmitate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), lecithin, propyl gallate, alpha-tocopherol, and the like; and (3) metal chelating agents, such as citric acid, ethylenediamine tetraacetic acid (EDTA), sorbitol, tartaric acid, phosphoric acid, and the like.

Such compositions may be prepared by any method known in the art, for example, by bringing into association the active ingredient with one or more carriers and/or excipients.

Different compositions and examples of carriers and/or excipients are well known to the skilled person and are described in detail in, e.g., Remington: The Science and Practice of Pharmacy. Pharmaceutical Press, 2013; Rowe, Sheskey, Quinn: Handbook of Pharmaceutical Excipients. Pharmaceutical Press, 2009. Excipients that may be used in the preparation of the pharmaceutical compositions may include one or more of buffers, stabilizing agents, surfactants, wetting agents, lubricating agents, emulsifiers, suspending agents, preservatives, antioxidants, opaquing agents, glidants, processing aids, colorants, sweeteners, perfuming agents, flavoring agents, diluents and other known additives to provide a composition suitable for an administration of choice.

As indicated above, the compounds of the present disclosure may be in solid or liquid form and administered by various routes in any convenient administrative form, e.g., tablets, powders, capsules, solutions, dispersions, suspensions, syrups, sprays, suppositories, gels, emulsions, patches, etc.

In solid dosage forms of the disclosure for oral administration (capsules, tablets, pills, dragees, powders, granules, trouches and the like), a compound is mixed with one or more pharmaceutically-acceptable carriers, such as sodium citrate or dicalcium phosphate, and/or any of the following: (1) fillers or extenders, such as starches, lactose, sucrose, glucose, mannitol, and/or silicic acid; (2) binders, such as, for example, carboxymethylcellulose, alginates, gelatin, polyvinyl pyrrolidone, sucrose and/or acacia; (3) humectants, such as glycerol; (4) disintegrating agents, such as agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates, and sodium carbonate; (5) solution retarding agents, such as paraffin; (6) absorption accelerators, such as quaternary ammonium compounds and surfactants, such as poloxamer and sodium lauryl sulfate; (7) wetting agents, such as, for

example, cetyl alcohol, glycerol monostearate, and non-ionic surfactants; (8) absorbents, such as kaolin and bentonite clay; (9) lubricants, such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, zinc stearate, sodium stearate, stearic acid, and mixtures thereof; (10) coloring agents; and (11) controlled release agents such as crospovidone or ethyl cellulose. In the case of capsules, tablets and pills, the pharmaceutical compositions may also comprise buffering agents. Solid compositions of a similar type may also be employed as fillers in soft and hard-shelled gelatin capsules using such excipients as lactose or milk sugars, as well as high molecular weight polyethylene glycols and the like. A tablet may be made by compression or molding, optionally with one or more accessory ingredients. Compressed tablets may be prepared using binder (for example, gelatin or hydroxypropylmethyl cellulose), lubricant, inert diluent, preservative, disintegrant (for example, sodium starch glycolate or cross-linked sodium carboxymethyl cellulose), surface-active or dispersing agent. Molded tablets may be made by molding in a suitable machine a mixture of the powdered compound moistened with an inert liquid diluent. The tablets, and other solid dosage forms of the pharmaceutical compositions of the present disclosure, such as dragees, capsules, pills and granules, may optionally be scored or prepared with coatings and shells, such as enteric coatings and other coatings well known in the pharmaceutical-formulating art. They may also be formulated so as to provide slow or controlled release of the active ingredient therein using, for example, hydroxypropylmethyl cellulose in varying proportions to provide the desired release profile, other polymer matrices, liposomes and/or microspheres. They may be formulated for rapid release, e.g., freeze-dried. They may be sterilized by, for example, filtration through a bacteria-retaining filter, or by incorporating sterilizing agents in the form of sterile solid compositions which can be dissolved in sterile water, or some other sterile injectable medium immediately before use. These compositions may also optionally contain opacifying agents and may be of a composition that they release the active ingredient(s) only, or preferentially, in a certain portion of the gastrointestinal tract, optionally, in a delayed manner. Examples of embedding compositions which can be used include polymeric substances and waxes. The active ingredient can also be in micro-encapsulated form, if appropriate, with one or more of the above-described excipients.

Liquid dosage forms for oral administration of the compounds of the disclosure include pharmaceutically acceptable emulsions, microemulsions, solutions, suspensions, syrups and elixirs. In addition to the active ingredient, the liquid dosage forms may contain inert diluents

commonly used in the art, such as, for example, water or other solvents, solubilizing agents and emulsifiers, such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor and sesame oils), glycerol, tetrahydrofuryl
5 alcohol, polyethylene glycols and fatty acid esters of sorbitan, and mixtures thereof. An oral composition can also include adjuvants such as wetting agents, emulsifying and suspending agents, sweetening, flavoring, coloring, perfuming and preservative agents.

In form of suspensions, a compound may contain suspending agents as, for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline
10 cellulose, aluminum metahydroxide, bentonite, agar-agar and tragacanth, and mixtures thereof.

Dosage forms for rectal or vaginal administration of a compound of the disclosure include a suppository, which may be prepared by mixing one or more compounds of the disclosure with one or more suitable nonirritating excipients or carriers comprising, for example, cocoa
15 butter, polyethylene glycol, a suppository wax or a salicylate, and which is solid at room temperature, but liquid at body temperature and, therefore, will melt in the rectum or vaginal cavity and release the active compound. Other suitable forms include pessaries, tampons, creams, gels, pastes, foams or spray formulations containing such carriers as are known in the art to be appropriate.

Dosage forms for the topical or transdermal administration of a compound of the disclosure include powders, sprays, ointments, pastes, creams, lotions, gels, solutions, patches and inhalants. The active compound may be mixed under sterile conditions with a pharmaceutically-acceptable carrier, and with any preservatives, buffers, or propellants which may be required. Such ointments, pastes, creams and gels may contain, in addition to a
25 compound of the disclosure, excipients, such as animal and vegetable fats, oils, waxes, paraffins, starch, tragacanth, cellulose derivatives, polyethylene glycols, silicones, bentonites, silicic acid, talc and zinc oxide, or mixtures thereof.

Dosage forms such as powders and sprays for administration of a compound of the disclosure, may contain excipients such as lactose, talc, silicic acid, aluminum hydroxide, calcium silicates
30 and polyamide powder, or mixtures of these substances. Sprays can additionally contain customary propellants, such as chlorofluorohydrocarbons and volatile unsubstituted hydrocarbons, such as butane and propane.

Dosage forms such as transdermal patches for administration of a compound of the disclosure may include absorption enhancers or retarders to increase or decrease the flux of the compound across the skin. The rate of such flux can be controlled by either providing a rate controlling membrane or dispersing the compound in a polymer matrix or gel. Other dosage forms contemplated include ophthalmic formulations, eye ointments, powders, solutions and the like. It is understood that all contemplated compositions must be stable under the conditions of manufacture and storage, and preserved against the contaminating action of microorganisms, such as bacteria and fungi.

The dosage levels of a compound of the disclosure in the pharmaceutical compositions of the disclosure may be adjusted in order to obtain an amount of a compound of the disclosure which is effective to achieve the desired therapeutic response for a particular patient, composition, and mode of administration, without being deleterious to the patient. The dosage of choice will depend upon a variety of factors including the nature of the particular compound of the present disclosure used, the route of administration, the time of administration, the rate of excretion or metabolism of the particular compound used, the rate and extent of absorption, the duration of the treatment, other drugs, compounds and/or materials used in combination with the particular compound, the age, sex, weight, condition, general health and prior medical history of the patient being treated, and like factors well known in the medical arts. A medical practitioner having ordinary skill in the art can readily determine and prescribe the effective amount of the pharmaceutical composition required.

Typically, a suitable daily dose of a compound of the disclosure will be that amount of the compound, which is the lowest dose effective to produce a therapeutic effect. Such an effective dose will generally depend upon the factors described above. Generally, oral, intravenous, intracerebroventricular and subcutaneous doses of the compounds of this disclosure for a patient, when used for the indicated analgesic effects, will range from about 0.0001 to about 100 mg, more usual 0.1 to 100 mg/kg per kilogram of body weight of recipient (patient, mammal) per day. Acceptable daily dosages may be from about 1 to about 1000 mg/day, and for example, from about 1 to about 100 mg/day.

A compound of the disclosure, or a pharmaceutically acceptable salt, or stereoisomer, thereof, may be administered once daily (QD) or divided into multiple daily doses such as twice daily (BID), three times daily (TID), and four times daily (QID) or may be administered in regular intervals of more than one day, such as every two days (Q2D). Administration may

be continuous (i.e., daily for consecutive days or every day) or intermittent, e.g., in cycles (i.e., including days, weeks, or months of rest without drug). In some embodiments, a compound of the disclosure, or a pharmaceutically acceptable salt, or stereoisomer thereof, is administered every day for at least 21 days. In some embodiments, a compound of the disclosure, or a pharmaceutically acceptable salt or stereoisomer thereof, is administered every two days for at least 21 days.

The term "intermittent" or "intermittently" as used herein is intended to mean stopping and starting at either regular or irregular intervals. For example, intermittent administration of a compound of the disclosure, or a pharmaceutically acceptable salt, or stereoisomer, thereof, is administration for one to six days per week, administration in cycles (e.g., daily administration for two to eight consecutive weeks, then a rest (or holiday) period with no administration for up to one week), or administration on alternate days. The term "cycling" as used herein is intended to mean that a compound of the disclosure, or a pharmaceutically acceptable salt, or stereoisomer, thereof, is administered daily or continuously but with a rest period. In some embodiments, the rest period is the same length as the treatment period. In other embodiments, the rest period has different length from the treatment period. In some embodiments, a compound of the disclosure, or a pharmaceutically acceptable salt, or stereoisomer, thereof, is administered intermittently once per day for 5 days followed by a rest of 3 days (i.e. 5 days on/3 days off). This intermittent administration is repeated for 3 to 4 cycles. In some embodiments, a compound of the disclosure, or a pharmaceutically acceptable salt, or stereoisomer thereof, is administered intermittently once per day for 5 days followed by a rest of 9 days (i.e. 5 days on/9 days off). This intermittent administration is repeated for 2 cycles. It is understood that dosing regimen also depend on factors as indicated above, e.g. on the administration, and can be readily arrived at by one skilled in medicine or the pharmacy art.

The compounds of the disclosure modulate the activity of cereblon. Thus, the compounds and compositions of the disclosure can be useful as a medicament, i.e. as a medicament in therapy, more specifically for the treatment of cancer, as detailed below. Therefore, in a further aspect, the present disclosure provides a method of treatment of a mammal, for example, a human, suffering from cancer, as detailed below. The term "treatment" is intended to encompass prophylaxis, therapy and cure. Such treatment comprises the step of administering a therapeutically effective amount of a compound of Formula I or salt thereof

(or of a pharmaceutical composition containing a compound of Formula I or salt thereof) to said mammal, for example, a human.

Thus, the disclosure is directed towards the use of the compounds of the disclosure or pharmaceutically acceptable salts or stereoisomers thereof or a pharmaceutical composition thereof for the treatment of a disease associated or caused with GSPT1, in particular the treatment of cancer, as detailed below, in a mammal, for example a human.

Myc-driven Cancers

Described herein, in some embodiments, are cancers exhibiting increased expression of one or more of c-Myc, L-Myc, N-Myc, EIF4EBP1, and EIF4EBP2 as well as ones with increase phosphorylation of one or both of EIF4EBP1 and EIF4EBP2.

Myc-driven cancers refer to cancers where there is abnormal activation of Myc oncogene, either due to transcriptional overexpression (e.g., caused by gene amplification, translocation, alterations in upstream signaling pathways) and/or protein stabilization. A myc-driven cancer cell includes a cancer cell that has an increased expression or overexpression (and/or increased activity) of at least one myc transcription factor such as N-myc and/or L-myc and/or C-myc, or a surrogate marker thereof, relative to a control cell such as a normal (e.g., non-cancerous) cell of the same or corresponding cell type. The term "cancerous" when referring to a sample such as a cell or tissue, generally refers to any sample, such as cells or tissues that exhibit, or are predisposed to exhibiting, unregulated growth, including, for example, a neoplastic cell/tissue such as a premalignant cell/tissue or a cancer cell (e.g., carcinoma cell or sarcoma cell).

In some embodiments the Myc-driven cancer or tumor as defined herein refers to a blood borne tumor cancer, such as a hematological cancer, preferably a cancer of hematopoietic and lymphoid tissues and lymphatic system, such as blood cancer, bone marrow cancer, lymph node cancer, acute lymphoblastic leukemia (ALL), chronic lymphocytic lymphoma (CLL), small lymphocytic lymphoma (SLL), acute myelogenous leukemia (AML), chronic myelogenous leukemia (CML), acute monocytic leukemia (AMoL), Hodgkin's lymphoma, non-Hodgkin's lymphomas and multiple myeloma (MM).

In some embodiments, the Myc-driven cancer or tumour is a solid tumor cancer, such as breast cancer, colorectal cancer, lung cancer, e.g. SCLC, NSCLC, neuroendocrine cancer, e.g., neuroendocrine prostate cancer (for example, NEPC (castration-resistant

neuroendocrine prostate cancer)) and lung neuroendocrine tumors (Lu-NETs), liver cancer, stomach cancer, pancreatic cancer, gastric cancer, esophageal cancer, bladder cancer, skin cancer, brain cancer, cervical cancer, ovarian cancer, melanoma and head and neck cancer.

In some embodiments the Myc-driven cancer as used herein refers in particular to breast cancer and SCLC. In some embodiments the myc-driven cancer as used herein refers in particular to NSCLC. In some embodiments, the cancer is solid tumor cancer exhibiting amplification of the N-Myc gene and/or the L-Myc gene. In some embodiments the Myc-driven cancer as used herein refers to neuroendocrine cancer, for example, neuroendocrine prostate cancer (for example, NEPC (castration-resistant neuroendocrine prostate cancer)) and lung neuroendocrine tumors (Lu-NETs), acute myelogenous leukemia (AML), lymphoma, and multiple myeloma (MM).

Solid and liquid cancers

The term "solid cancer" or "solid tumor" refers to disease of tissues or organs, such as to malignant, neoplastic, or cancerous solid tumors, i.e. sarcomas, carcinomas. The tissue structure of solid tumors includes interdependent tissue compartments and usually does not contain cysts or fluid areas. A solid cancer or solid tumor includes cancers of the bladder, bone, brain, breast, cervix, chest, colon, endometrium, esophagus, eye, head, kidney, liver, lymph nodes, lung, upper aerodigestive tract (including nasal cavity and paranasal sinuses, nasopharynx or cavum, oral cavity, oropharynx, larynx, hypopharynx and salivary glands), neck, ovaries, pancreas, prostate, rectum, skin, stomach, testis, throat, and uterus. Specific cancers include, but are not limited to, advanced malignancy, amyloidosis, neuroblastoma, meningioma, hemangiopericytoma, multiple brain metastase, glioblastoma multiforms, glioblastoma, brain stem glioma, poor prognosis malignant brain tumor, malignant glioma, recurrent malignant glioma, anaplastic astrocytoma, anaplastic oligodendroglioma, neuroendocrine tumor, e.g., neuroendocrine prostate cancer (for example, NEPC (castration-resistant neuroendocrine prostate cancer)) and lung neuroendocrine tumors (Lu-NETs), rectal adenocarcinoma, colorectal cancer, including stage 3 and stage 4 colorectal cancer, unresectable colorectal carcinoma, metastatic hepatocellular carcinoma, Kaposi's sarcoma, malignant melanoma, cervical cancer, ovarian cancer, malignant mesothelioma, malignant pleural effusion mesothelioma syndrome, peritoneal carcinoma, papillary serous carcinoma, gynecologic sarcoma, soft tissue sarcoma, scleroderma, cutaneous vasculitis, Langerhans cell histiocytosis, leiomyosarcoma, fibrodysplasia ossificans progressive, hormone refractory

prostate cancer, resected high-risk soft tissue sarcoma, unresectable hepatocellular carcinoma, fallopian tube cancer, androgen independent prostate cancer, androgen dependent stage IV non-metastatic prostate cancer, hormone-insensitive prostate cancer, chemotherapy -insensitive prostate cancer, papillary thyroid carcinoma, follicular thyroid carcinoma, medullary thyroid carcinoma, and leiomyoma. In some embodiments, a solid cancer or solid tumor is a cancer of the breast, lung, stomach, colon, bladder, brain, pancreas, liver, head and neck, prostate, ovaries, upper aerodigestive tract and the like.

The term "blood borne cancer" or "blood borne tumor" (also typically referred to as "hematological cancer") refers to cancer of the body's blood-forming and immune system-the bone marrow and lymphatic tissue. The tissue structure of blood-borne cancers or tumors includes an abnormal mass of cells that is fluid in nature. Such cancers include leukemias (malignant neoplasms of the blood-forming tissues), lymphomas (Non-Hodgkin's Lymphoma), Hodgkin's disease (Hodgkin's Lymphoma) and myeloma. In one embodiment, the myeloma is multiple myeloma (MM). In some embodiments, the leukemia is, for example, acute myelogenous leukemia (AML), acute lymphocytic leukemia (ALL), adult T-cell leukemia, chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), hairy cell leukemia, myelodysplasia, myeloproliferative disorders, chronic myelogenous leukemia (CML), acute monocytic leukemia (AMoL), myelodysplastic syndrome (MDS), human lymphotropic virus- type 1 (HTLV-1) leukemia, mastocytosis, or B-cell acute lymphoblastic leukemia. The leukemia can be relapsed, refractory or resistant to conventional therapy. In some embodiments, the lymphoma is, for example, diffuse large B-cell lymphoma (DLBCL), B-cell immunoblastic lymphoma, small non-cleaved cell lymphoma, human lymphotropic virus-type 1 (HTLV-1) leukemia/lymphoma, adult T-cell lymphoma, peripheral T-cell lymphoma (PTCL), cutaneous T-cell lymphoma (CTCL), mantle cell lymphoma (MCL), Hodgkin's lymphoma (HL), non-Hodgkin's lymphoma (NHL), AIDS-related lymphoma, follicular lymphoma, small lymphocytic lymphoma, T-cell/histiocyte rich large B-cell lymphoma, transformed lymphoma, primary mediastinal (thymic) large B-cell lymphoma, splenic marginal zone lymphoma, Richter's transformation, nodal marginal zone lymphoma, or ALK -positive large B-cell lymphoma. In one embodiment, the hematological cancer is indolent lymphoma including, for example, DLBCL, follicular lymphoma, or marginal zone lymphoma. In some embodiments blood-borne cancers or hematological cancers include acute lymphoblastic leukemia (ALL), chronic lymphocytic lymphoma (CLL), small lymphocytic lymphoma (SLL), acute myelogenous leukemia (AML), chronic myelogenous leukemia

(CML), acute monocytic leukemia (AMoL), Hodgkin's lymphoma, non-Hodgkin's lymphomas and multiple myeloma (MM).

In particular embodiments, the compounds of the disclosure or pharmaceutically acceptable salts or stereoisomers thereof or a pharmaceutical composition thereof are used for the treatment of cancer associated with GSPT1, such as solid cancers including but not limited to cancers of the bladder, bone, brain, breast, cervix, chest, colon, endometrium, esophagus, eye, head, kidney, liver, lymph nodes, lung, upper aerodigestive tract (including nasal cavity and paranasal sinuses, nasopharynx or cavum, oral cavity, oropharynx, larynx, hypopharynx and salivary glands), neck, ovaries, pancreas, prostate, rectum, skin, stomach, testis, throat, uterus, amyloidosis, neuroblastoma, meningioma, hemangiopericytoma, multiple brain metastase, glioblastoma multiforms, glioblastoma, brain stem glioma, poor prognosis malignant brain tumor, malignant glioma, recurrent malignant glioma, anaplastic astrocytoma, anaplastic oligodendroglioma, neuroendocrine tumor, e.g., neuroendocrine prostate cancer such as castration-resistant neuroendocrine prostate cancer (NEPC) and lung neuroendocrine tumors (Lu-NETs), rectal adenocarcinoma, colorectal cancer, including stage 3 and stage 4 colorectal cancer, unresectable colorectal carcinoma, metastatic hepatocellular carcinoma, Kaposi's sarcoma, malignant melanoma, malignant mesothelioma, malignant pleural effusion mesothelioma syndrome, peritoneal carcinoma, papillary serous carcinoma, gynecologic sarcoma, soft tissue sarcoma, scleroderma, cutaneous vasculitis, Langerhans cell histiocytosis, leiomyosarcoma, fibrodysplasia ossificans progressive, hormone refractory prostate cancer, resected high-risk soft tissue sarcoma, unresectable hepatocellular carcinoma, fallopian tube cancer, androgen independent prostate cancer, androgen dependent stage IV non-metastatic prostate cancer, hormone-insensitive prostate cancer, chemotherapy -insensitive prostate cancer, papillary thyroid carcinoma, follicular thyroid carcinoma, medullary thyroid carcinoma, and leiomyoma; and blood bourne (liquid) or hematological cancers, including but not limited to leukemias, lymphomas, and myelomas, such as diffuse large B-cell lymphoma (DLBCL), B-cell immunoblastic lymphoma, small non-cleaved cell lymphoma, human lymphotropic virus-type 1 (HTLV-1) leukemia/lymphoma, adult T-cell lymphoma, peripheral T-cell lymphoma (PTCL), cutaneous T-cell lymphoma (CTCL), mantle cell lymphoma (MCL), Hodgkin's lymphoma (HL), non-Hodgkin's lymphoma (NHL), AIDS-related lymphoma, follicular lymphoma, small lymphocytic lymphoma, T-cell/histiocyte rich large B-cell lymphoma, transformed lymphoma, primary mediastinal (thymic) large B-cell lymphoma, splenic marginal zone lymphoma, Richter's transformation,

nodal marginal zone lymphoma, ALK-positive large B-cell lymphoma, indolent lymphoma (for example, DLBCL, follicular lymphoma, or marginal zone lymphoma), acute myelogenous leukemia (AML), acute lymphocytic leukemia (ALL), adult T-cell leukemia, chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), hairy cell leukemia, myelodysplasia, myeloproliferative disorders, chronic myelogenous leukemia (CML), acute monocytic leukemia (AMoL), myelodysplastic syndrome (MDS), human lymphotropic virus-type 1 (HTLV-1) leukemia, mastocytosis, B-cell acute lymphoblastic leukemia, Non-Hodgkin's Lymphoma, Hodgkin's Lymphoma, and multiple myeloma (MM).

Such a use (or method of treatment) of a subject comprises administering to a subject in need of such treatment a therapeutically effective amount of a compound of the disclosure or pharmaceutically acceptable salts thereof or a pharmaceutical composition thereof by targeting cereblon.

Disclosed herein, in part, is a method of treating a Myc-driven cancer in a subject in need thereof, comprising administering the subject a therapeutically effective amount of a compound described herein or a composition as described herein.

In some embodiments, the Myc-driven cancer is a Myc-driven lung cancer.

In some embodiments, the Myc-driven cancer is characterized by high driven Myc tumor.

In some embodiments, the Myc-driven cancer is a Myc-driven small cell lung cancer.

In some embodiments, the Myc-driven small cell lung cancer is a high L-Myc small cell lung cancer.

In some embodiments, the Myc-driven cancer is a Myc-driven non-small cell lung cancer.

In some embodiments, the Myc-driven non-small cell lung cancer is a high N-Myc non-small cell lung cancer.

In some embodiments, the compound or the composition is administered to the subject via oral administration.

In another aspect, provided herein is a method of degrading GSPT1 in a subject suffering from cancer, comprising administering to the subject a therapeutically effective amount of a compound described herein or a composition described herein.

In some embodiments, the cancer is a Myc-driven cancer.

In some embodiments, the Myc-driven cancer is a Myc-driven lung cancer.

In some embodiments, the Myc-driven cancer is a Myc-driven small cell lung cancer.

5 In some embodiments, the Myc-driven small cell lung cancer is a high L-Myc small cell lung cancer.

In some embodiments, the Myc-driven cancer is a Myc-driven non-small cell lung cancer.

In some embodiments, the Myc-driven non-small cell lung cancer is a high N-Myc non-small cell lung cancer.

10 In some embodiments, the compound or the composition is administered to the subject via oral administration.

In another aspect, the disclosure is directed to a method of reducing the level of GSPT1 in a subject suffering from cancer, comprising administering the subject a therapeutically effective amount of a compound or a composition as described herein.

In some embodiments, the cancer is a Myc-driven cancer.

15 In some embodiments, the Myc-driven cancer is a Myc-driven lung cancer.

In some embodiments, the Myc-driven cancer is a Myc-driven small cell lung cancer.

In some embodiments, the Myc-driven small cell lung cancer is a high L-Myc small cell lung cancer.

In some embodiments, the Myc-driven cancer is a Myc-driven non-small cell lung cancer.

20 In some embodiments, the Myc-driven non-small cell lung cancer is a high N-Myc non-small cell lung cancer.

In some embodiments, the compound or the composition is administered to the subject via oral administration.

25 The present disclosure contemplates administration of a compound of the disclosure alone or in combination with one or more additional therapeutic agents, such as other Tyrosine kinase inhibitors: Erlotinib hydrochloride (e.g. Tarceva(R) by Genentech/Roche), Linifanib (or ABT

869, by Genentech), sunitinib malate (e.g. Sutent(R) by Pfizer), bosutinib (or SKI-606, described in US 6,780,996), dasatinib (e.g. Sprycel(R) by Bristol-Myers Squibb), armala (e.g. pazopanib, e.g. Votrient(R) by GlaxoSmithKline), imatinib and imatinib mesylate (e.g. Gilvec(R) and Gleevec(R) by Novartis); Vascular Endothelial Growth Factor (VEG) receptor inhibitors (Bevacizumab, or Avastin(R) by Genentech/Roche), axitinib, (or AG013736, described in WO 01/002369), Brivanib Alaninate (or BMS-582664), motesanib (or AMG-706, described in PCT WO 02/066470), pasireotide (e.g. SOM230, described in WO 02/010192), sorafenib (e.g. Nexavar(R)); HER2 receptor inhibitors: Trastuzumab (e.g. Herceptin(R) by Genentech/Roche), neratinib (or HKI-272, described WO 05/028443), lapatinib or lapatinib ditosylate (e.g. Tykerb(R) by GlaxoSmithKline); CD20 antibodies: Rituximab (e.g. Riuxan(R) and MabThera(R) by Genentech/Roche), tositumomab (e.g. Bexxar(R) by GlaxoSmithKline), ofatumumab (e.g. Arzerra(R) by GlaxoSmithKline); Bcr/Abl kinase inhibitors: nilotinib hydrochloride (e.g. Tasigna(R) by Novartis); DNA Synthesis inhibitors: Capecitabine (e.g. Xeloda(R) by Roche), gemcitabine hydrochloride (e.g. Gemzar(R) by Eli Lilly and Company), nelarabine (or Arranon(R) and Atriance(R) by GlaxoSmithKline); Antineoplastic agents: oxaliplatin (e.g. Eloxatin(R) by Sanofi-Aventis described in US 4,169,846); Epidermal growth factor receptor (EGFR) inhibitors: Gefitinib (or Iressa(R)), Afatinib (or Tovok(R) by Boehringer Ingelheim), cetuximab (e.g. Erbitux(R) by Bristol-Myers Squibb), panitumumab (e.g. Vectibix(R) by Amgen); HER dimerization inhibitors: Pertuzumab (e.g. Omnitarg(R), by Genentech); Human Granulocyte colony-stimulating factor (G-CSF) modulators: Filgrastim (e.g. Neupogen(R) by Amgen); Immunomodulators: Aflutuzumab (by Roche(R)), pegfilgrastim (e.g. Neulasta(R) by Amgen), lenalidomide (e.g. CC-5013, e.g. Revlimid(R)), thalidomide (e.g. Thalomid(R)); CD40 inhibitors: Dacetuzumab (e.g. SGN-40 or huS2C6, by Seattle Genetics, Inc); Pro-apoptotic receptor agonists (PARAs): Dulanermin (e.g. AMG-951, by Amgen/Genentech); Hedgehog antagonists: Vismodegib (or GDC-0449, described in WO 06/028958); Phospholipase A2 inhibitors: Anagrelide (e.g. Agrylin(R)); BCL-2 inhibitors: Navitoclax (or ABT-263, described in WO 09/155386); Mitogen-activated protein kinase kinase (MEK) inhibitors: XL-518 (Cas No. 1029872-29-4, by ACC Corp.); Aromatase inhibitors: Exemestane (e.g. Aromasin(R) by Pfizer), letrozole (e.g. Femara(R) by Novartis), anastrozole (e.g. Arimidex(R)); Topoisomerase I inhibitors: Irinotecan (e.g. Camptosar(R) by Pfizer), topotecan hydrochloride (e.g. Hycamtin(R) by GlaxoSmithKline); Topoisomerase II inhibitors: etoposide (e.g. VP-16 and Etoposide phosphate, e.g. Toposar(R), VePesid(R) and Etopophos(R)), teniposide (e.g. VM-26, e.g. Vumon(R)); mTOR inhibitors: Temsirolimus

(e.g. Torisel(R) by Pfizer), ridaforolimus (formally known as deferolimus, (or AP23573 and MK8669, described in WO 03/064383), everolimus (e.g. Afinitor(R) by Novartis); Osteoclastic bone resorption inhibitors: zoledronic acid (or Zometa(R) by Novartis); CD33 Antibody Drug Conjugates: Gemtuzumab ozogamicin (e.g. Mylotarg(R) by Pfizer/Wyeth);

5 CD22 Antibody Drug Conjugates: Inotuzumab ozogamicin (also referred to as CMC-544 and WAY-207294, by Hangzhou Sage Chemical Co., Ltd.); CD20 Antibody Drug Conjugates: Ibritumomab tiuxetan (e.g. Zevalin(R)); Somatostatin analogs: octreotide (e.g. octreotide acetate, e.g. Sandostatin(R) and Sandostatin LAR(R)); Synthetic Interleukin-11 (IL-11): oprelvekin (e.g. Neumega(R) by Pfizer/Wyeth); Synthetic erythropoietin: Darbepoetin alfa

10 (e.g. Aranesp(R) by Amgen); Receptor Activator for Nuclear Factor kappa B (RANK) inhibitors: Denosumab (e.g. Prolia(R) by Amgen); Thrombopoietin mimetic peptibodies: Romiplostim (e.g. Nplate(R) by Amgen; Cell growth stimulators: Palifermin (e.g. Kepivance(R) by Amgen); Anti-Insulin-like Growth Factor-1 receptor (IGF-1R) antibodies: Figitumumab (e.g. CP-751,871, by ACC Corp), robatumumab (CAS No. 934235-44-6);

15 Anti-CS1 antibodies: Elotuzumab (HuLuc63, CAS No. 915296-00-3); CD52 antibodies: Alemtuzumab (e.g. Campath(R)); CTLA-4 inhibitors: Tremelimumab (IgG2 monoclonal antibody by Pfizer, formerly known as ticilimumab, CP-675,206), ipilimumab (CTLA-4 antibody, e.g. MDX-010, CAS No. 477202-00-9); Histone deacetylase inhibitors (HDI): Voninostat (e.g. Zolinza(R) by Merck); Alkylating agents: Temozolomide (e.g. Temodar(R)

20 and Temodal(R) by Schering-Plough/Merck), dactinomycin (e.g. actinomycin-D and e.g. Cosmegen(R)), melphalan (e.g. L-PAM, L-sarcolysin, and phenylalanine mustard, e.g. Alkeran(R)), altretamine (e.g. hexamethylmelamine (HMM), e.g. Hexalen(R)), carmustine (e.g. BiCNU(R)), bendamustine (e.g. Treanda(R)), busulfan (e.g. Busulfex(R) and Myleran(R)), carboplatin (e.g. Paraplatin(R)), lomustine (e.g. CCNU, e.g. CeeNU(R)),

25 cisplatin (e.g. CDDP, e.g. Platinol(R) and Platinol(R)-AQ), chlorambucil (e.g. Leukeran(R)), cyclophosphamide (e.g. Cytoxan(R) and Neosar(R)), dacarbazine (e.g. DTIC, DIC and imidazole carboxamide, e.g. DTIC-Dome(R)), altretamine (e.g. hexamethylmelamine (HMM) e.g. Hexalen(R)), ifosfamide (e.g. Ifex(R)), procarbazine (e.g. Matulane(R)), mechlorethamine (e.g. nitrogen mustard, mustine and mechlorethamine hydrochloride, e.g.

30 Mustargen(R)), streptozocin (e.g. Zanosar(R)), thiotepa (e.g. thiophosphoamide, TESPA and TSPA, e.g. Thioplex(R); Biologic response modifiers: bacillus calmette-guerin (e.g. theraCys(R) and TICE(R) BCG), denileukin diftitox (e.g. Ontak(R)); Anti-tumor antibiotics: doxorubicin (e.g. Adriamycin(R) and Rubex(R)), bleomycin (e.g. lenoxane(R)), daunorubicin (e.g. daunorubicin hydrochloride, daunomycin, and rubidomycin hydrochloride, e.g.

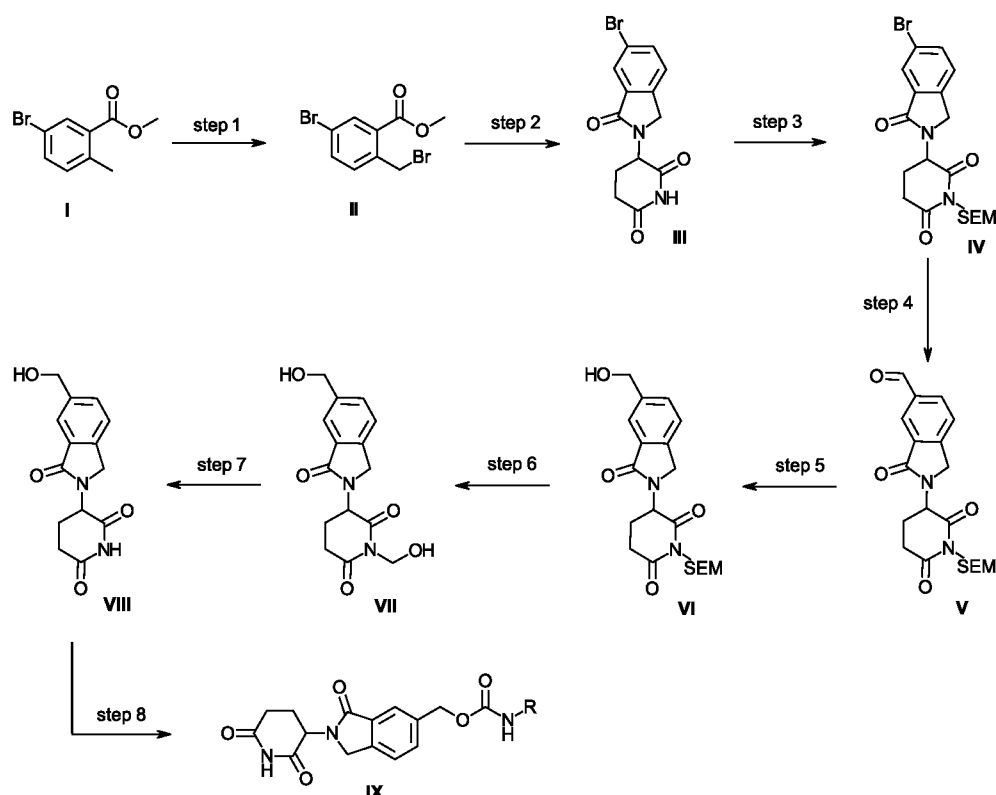
Cerubidine(R)), daunorubicin liposomal (daunorubicin citrate liposome, e.g. DaunoXome(R)), mitoxantrone (e.g. DHAD, e.g. Novantrone(R)), epirubicin (e.g. Ellence™), idarubicin (e.g. Idamycin(R), Idamycin PFS(R)), mitomycin C (e.g. Mutamycin(R)); Anti-microtubule agents: Estramustine (e.g. Emcyl(R)); Cathepsin K
 5 inhibitors: Odanacatib (or MK-0822, by Lanzhou Chon Chemicals, ACC Corp., and ChemieTek, described in WO 03/075836); Epothilone B analogs: Ixabepilone (e.g. Lxempra(R) by Bristol-Myers Squibb); Heat Shock Protein (HSP) inhibitors: Tanespimycin (17-allylamino-17-demethoxygeldanamycin, e.g. KOS-953 and 17-AAG, by SIGMA, described in US 4,261,989); TpoR agonists: Eltrombopag (e.g. Promacta(R) and
 10 Revolade(R) by GlaxoSmithKline); Anti-mitotic agents: Docetaxel (e.g. Taxotere(R) by Sanofi-Aventis); Adrenal steroid inhibitors: aminoglutethimide (e.g. Cytadren(R)); Anti-androgens: Nilutamide (e.g. Nilandron(R) and Anandron(R)), bicalutamide (sold under tradename Casodex(R)), flutamide (e.g. Fulexin™); Androgens: Fluoxymesterone (e.g. halotestin(R)); Proteasome inhibitors: Bortezomib (e.g. Velcade(R)); CDK1 inhibitors:
 15 Alvocidib (e.g. flovopirdol or HMR-1275, described in US 5,621,002); Gonadotropin-releasing hormone (GnRH) receptor agonists: Leuprolide or leuprolide acetate (e.g. Viadure(R) by Bayer AG, Eligard(R) by Sanofi-Aventis and Lupron(R) by Abbott Lab); Taxane anti-neoplastic agents: Cabazitaxel, larotaxel; 5HT1a receptor agonists: Xaliproden (or SR57746, described in US 5,266,573); HPC vaccines: Cervarix(R) sold by GlaxoSmithKline,
 20 Gardasil(R) sold by Merck; Iron Chelating agents: Deferasinox (e.g. Exjade(R) by Novartis); Anti-metabolites: Claribine (2-chlorodeoxyadenosine, e.g. leustatin(R)), 5-fluorouracil (e.g. Adrucil(R)), 6-thioguanine (e.g. Purinethol(R)), pemetrexed (e.g. Alimta(R)), cytarabine (e.g. arabinosylcytosine (Ara-C), e.g. Cytosar-U(R)), cytarabine liposomal (e.g. Liposomal Ara-C, e.g. DepoCyt™), decitabine (e.g. Dacogen(R)), hydroxyurea (e.g. Hydrea(R),
 25 Droxia™ and Mylocel™), fludarabine (e.g. Fludara(R)), floxuridine (e.g. FUDR(R)), cladribine (e.g. 2-chlorodeoxyadenosine (2-CdA) e.g. Leustatin™), methotrexate (e.g. amethopterin, methotrexate sodim (MTX), e.g. Rheumatrex(R) and Trexall™), pentostatin (e.g. Nipent(R)); Bisphosphonates: Pamidronate (e.g. Aredia(R)), zoledronic acid (e.g. Zometa(R)); Demethylating agents: 5-azacitidine (e.g. Vidaza(R)), decitabine (e.g.
 30 Dacogen(R)); Plant Alkaloids: Paclitaxel protein-bound (e.g. Abraxane(R)), vinblastine (e.g. vinblastine sulfate, vincaleukoblastine and VLB, e.g. Alkaban-AQ(R) and Velban(R)), vincristine (e.g. vincristine sulfate, LCR, and VCR, e.g. Oncovin(R) and Vincasar Pfs(R)), vinorelbine (e.g. Navelbine(R)), paclitaxel (e.g. Taxol and Onxal™); Retinoids: Alitretinoin (e.g. Panretin(R)), tretinoin (all-trans retinoic acid, e.g. ATRA, e.g. Vesanoid(R)), Isotretinoin

(13-cis-retinoic acid, e.g. Accutane(R), Amnesteem(R), Claravis(R), Clarus(R), Decutan(R), Isotane(R), Izotech(R), Oratane(R), Isotret(R), and Sotret(R)), bexarotene (e.g. Targretin(R)); Glucocorticosteroids: Hydrocortisone (e.g. cortisone, hydrocortisone sodium succinate, hydrocortisone sodium phosphate, and e.g. Ala-Cort(R), Hydrocortisone Phosphate, Solu-Cortef(R), Hydrocort Acetate(R) and Lanacort(R)), dexamethasone, prednisolone (e.g. Delta-Cortel(R), Orapred(R), Pediapred(R) and Prelone(R)), prednisone (e.g. Deltasone(R), Liquid Red(R), Meticorten(R) and Orasone(R)), methylprednisolone (e.g. 6-Methylprednisolone, Methylprednisolone Acetate, Methylprednisolone Sodium Succinate, e.g. Duralone(R), Medralone(R), Medrol(R), M-Prednisol(R) and Solu-Medrol(R)); Cytokines: interleukin-2 (e.g. aldesleukin and IL-2, e.g. Proleukin(R)), interleukin-11 (e.g. oprelvekin, e.g. Neumega(R)), alpha interferon alfa (e.g. IFN-alpha, e.g. Intron(R) A, and Roferon-A(R)); Luteinizing hormone releasing hormone (LHRH) agonists: Goserelin (e.g. Zoladex(R)); Progesterones: megestrol (e.g. megestrol acetate, e.g. Megace(R)); Miscellaneous cytotoxic agents: Arsenic trioxide (e.g. Trisenox(R)), asparaginase (e.g. L-asparaginase, Erwinia L-asparaginase, e.g. Elspar(R) and Kidrolase(R)); Anti-nausea drugs: NK-1 receptor antagonists: Casopitant (e.g. Rezonic(R) and Zunrisa(R) by GlaxoSmithKline); and Cytoprotective agents: Amifostine (e.g. Ethyol(R)), leucovorin (e.g. calcium leucovorin, citrovorum factor and folinic acid).

Examples

The compounds provided herein can be prepared from readily available starting materials using the following general methods and procedures. It will be appreciated that where typical or preferred process conditions (*i.e.*, reaction temperatures, times, mole ratios of reactants, solvents, pressures, *etc.*) are given, other process conditions can also be used unless otherwise stated. Optimum reaction conditions may vary with the particular reactants or solvent used, but such conditions can be determined by one skilled in the art by routine optimization.

Example 1: General Procedure A



II: To a solution of methyl 5-bromo-2-methylbenzoate I (100 g, 436 mmol, 1.00 eq) in trichloromethane (800 mL) was added *N*-bromosuccinimide (77.6 g, 436 mmol, 1.00 eq) and (*E*)-2,2'-(diazene-1,2-diyl)bis(2-methylpropanenitrile) (10.5 g, 43.3 mmol, 0.10 eq).

5 The solution was degassed by purging with nitrogen, and the reaction was stirred at 80 °C for 12 h under nitrogen atmosphere. The mixture was concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 1/0 to 20/1) to afford methyl 5-bromo-2-(bromomethyl)benzoate II. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 7.98 (d, *J* = 2.0 Hz, 1H), 7.81-7.79 (m, 1H), 7.57-7.55 (m, 1H), 4.97 (s, 2H), 3.87 (m, 3H).

10

III: To a solution of methyl 5-bromo-2-(bromomethyl)benzoate II (72.5 g, 235 mmol 1.00 eq) and 3-aminopiperidine-2,6-dione hydrochloride (46.6 g, 283 mmol, 1.20 eq, hydrochloride) in acetonitrile (600 mL) was added diisopropylethylamine (123 mL, 706 mmol, 3.00 eq) in one portion under nitrogen. The reaction was stirred at 80 °C for 4 h. After cooling to room temperature, the mixture was concentrated under reduced pressure to give a residue. The residue was triturated with hydrochloric acid (1 M)/ethyl acetate (300 mL/200 mL) at 25 °C for 30 min. The mixture was filtered, and the filter cake was washed with ethyl acetate (100 mL) and dried under reduced pressure to afford 3-(6-bromo-1-oxoisindolin-2-yl)piperidine-2,6-dione III. ¹H NMR (400MHz, DMSO-*d*₆) δ = 11.04 (s, 1H), 7.86 (d, *J* =

15

1.6 Hz, 1H), 7.82 (dd, $J = 1.8, 8.1$ Hz, 1H), 7.60 (d, $J = 8.1$ Hz, 1H), 5.12 (dd, $J = 5.1, 13.3$ Hz, 1H), 4.49 - 4.28 (m, 2H), 2.99 - 2.84 (m, 1H), 2.60 (br d, $J = 17.5$ Hz, 1H), 2.39 (dq, $J = 4.4, 13.2$ Hz, 1H), 2.13 - 1.91 (m, 1H).

IV: To a solution of 3-(6-bromo-1-oxoisindolin-2-yl)piperidine-2,6-dione **III** (40.0 g, 123 mmol, 1.00 eq) in dimethylformamide (200 mL) was added 1,8-Diazabicyclo[5.4.0]-7-undecene (48.0 mL, 318 mmol, 2.57 eq) and 2-(chloromethoxy)ethyltrimethylsilane (stabilized with diisopropylethylamine) (40.0 mL, 226 mmol, 1.83 eq) dropwise at 0 °C. The reaction was stirred at 25 °C for 6 h. The mixture was diluted with water (500 mL) and ethyl acetate (800 mL). The organic phase was washed with brine (200 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 4/1 to 1/1) to afford 3-(6-bromo-1-oxoisindolin-2-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)piperidine-2,6-dione **IV**. ^1H NMR (400 MHz, DMSO- d_6) $\delta = 7.90$ (d, $J = 1.6$ Hz, 1H), 7.86 (dd, $J = 2.0, 8.1$ Hz, 1H), 7.63 (d, $J = 8.1$ Hz, 1H), 5.26 (dd, $J = 5.1, 13.4$ Hz, 1H), 5.07 (q, $J = 9.8$ Hz, 2H), 4.50 (d, $J = 17.6$ Hz, 1H), 4.36 - 4.28 (m, 1H), 3.60 - 3.49 (m, 2H), 3.13 - 3.01 (m, 1H), 2.86 - 2.78 (m, 1H), 2.48 - 2.36 (m, 1H), 2.12 - 2.05 (m, 1H), 0.90 - 0.83 (m, 2H), 0.02 - -0.01 (m, 9H).

V: To a solution of 3-(6-bromo-1-oxoisindolin-2-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)piperidine-2,6-dione **IV** (53.0 g, 117 mmol, 1 eq) in dimethylformamide (300 mL) was added diisopropylethylamine (100 mL, 574 mmol, 4.91 eq), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (8.48 g, 11.6 mmol, 0.10 eq) and triethylsilane (150 mL, 939 mmol, 8.00 eq). The reaction was stirred at 80 °C for 12 h under carbon monoxide atmosphere (50 Psi). The mixture was diluted with ethyl acetate (1.00 L) and water (1.00 L). The organic layer was separated and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 1/1) to afford 2-(2,6-dioxo-1-((2-(trimethylsilyl)ethoxy)methyl)piperidin-3-yl)-3-oxoisindoline-5-carbaldehyde **V**. ^1H NMR (400 MHz, DMSO- d_6) $\delta = 10.16$ (s, 1H), 8.29 (s, 1H), 8.19 (d, $J = 7.8$ Hz, 1H), 7.87 (d, $J = 7.8$ Hz, 1H), 5.30 (br dd, $J = 4.9, 13.4$ Hz, 1H), 5.13 - 5.03 (m, 2H), 4.65 (br d, $J = 18.4$ Hz, 1H), 4.50 - 4.40 (m, 1H), 3.62 - 3.51 (m, 2H), 3.17 - 3.06 (m, 1H), 2.83 (br d, $J = 15.8$ Hz, 1H), 2.44 (br dd, $J = 4.1, 13.1$ Hz, 1H), 2.15 - 2.07 (m, 1H), 0.86 (br t, $J = 7.6$ Hz, 2H), 0.00 (s, 9H).

VI: To a solution of 2-(2,6-dioxo-1-((2-(trimethylsilyl)ethoxy)methyl)piperidin-3-yl)-3-oxoisindoline-5-carbaldehyde **V** (38.0 g, 94.4 mmol, 1.00 eq) in dimethylformamide (100 mL) and dichloromethane (500 mL) was added sodium triacetoxyborohydride (64.0 g, 302 mmol, 3.20 eq) and acetic acid (27.9 g, 465 mmol, 4.93 eq). The reaction was stirred at 50 °C for 2 h. The mixture was diluted with water (500 mL) and dichloromethane (500 mL). The organic layer was separated and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5/1 to 0/1) to give 3-(6-(hydroxymethyl)-1-oxoisindolin-2-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)piperidine-2,6-dione **VI**. ¹H NMR (400MHz, DMSO-*d*₆) δ = 7.70 (s, 1H), 7.62 - 7.52 (m, 2H), 5.35 (t, *J* = 5.8 Hz, 1H), 5.29 - 5.20 (m, 1H), 5.06 (q, *J* = 9.8 Hz, 2H), 4.61 (d, *J* = 5.8 Hz, 2H), 4.47 (br d, *J* = 17.1 Hz, 1H), 4.28 (d, *J* = 16.9 Hz, 1H), 3.61 - 3.49 (m, 2H), 3.11 - 3.02 (m, 1H), 2.84 - 2.77 (m, 1H), 2.40 (br d, *J* = 8.7 Hz, 1H), 2.11 - 2.03 (m, 1H), 0.89 - 0.81 (m, 2H), 0.01 - -0.03 (m, 9H).

VII: A solution of 3-(6-(hydroxymethyl)-1-oxoisindolin-2-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)piperidine-2,6-dione **VI** (17.0 g, 42.0 mmol, 1.00 eq) in hydrochloric acid/dioxane (150 mL) (6 M) was stirred at 50 °C for 2 h. The mixture was concentrated under reduced pressure to afford 1-(hydroxymethyl)-3-(6-(hydroxymethyl)-1-oxoisindolin-2-yl)piperidine-2,6-dione **VII**.

VIII: To a solution of 1-(hydroxymethyl)-3-(6-(hydroxymethyl)-1-oxoisindolin-2-yl)piperidine-2,6-dione **VII** (13.0 g, 42.7 mmol, 1 eq) in acetonitrile (50.0 mL) was added ammonium hydroxide 30% (0.500 mL, 0.09 eq). The reaction was stirred at 25 °C for 1 h. The pH was adjusted to pH = 5 by addition of 0.5 M hydrochloric acid, and the mixture was concentrated under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC to afford 3-(6-(hydroxymethyl)-1-oxoisindolin-2-yl)piperidine-2,6-dione **VIII**. ¹H NMR (400MHz, DMSO-*d*₆) δ = 11.24 - 10.78 (m, 1H), 7.69 (s, 1H), 7.60 - 7.53 (m, 2H), 5.35 (t, *J* = 5.8 Hz, 1H), 5.12 (dd, *J* = 5.1, 13.4 Hz, 1H), 4.61 (d, *J* = 5.5 Hz, 2H), 4.49 - 4.40 (m, 1H), 4.35 - 4.26 (m, 1H), 2.98 - 2.86 (m, 1H), 2.66 - 2.57 (m, 1H), 2.40 (dd, *J* = 4.4, 13.1 Hz, 1H), 2.01 (dtd, *J* = 2.2, 5.2, 12.6 Hz, 1H).

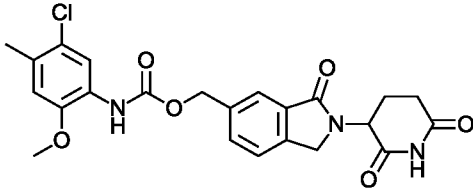
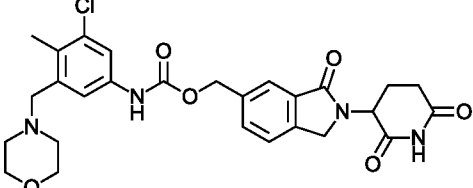
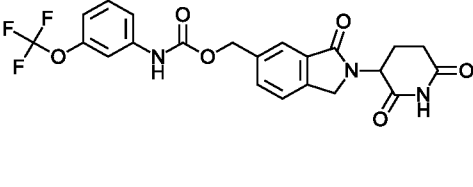
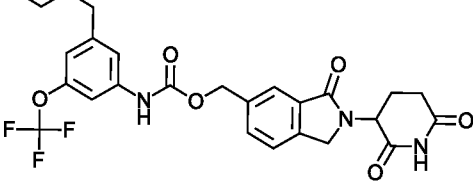
IX: Variant i): To a solution of 3-(6-(hydroxymethyl)-1-oxoisindolin-2-yl)piperidine-2,6-dione **VIII** (1.00 eq) in dimethylformamide or acetonitrile (0.04 – 0.73 M reaction) was added the phenyl carbamate (0.66 – 1.70 eq) and sodium hydride (60% dispersion in mineral oil) (1.70 – 3.00 eq) at 0 °C. The reaction was stirred at a temperature range of 0 to

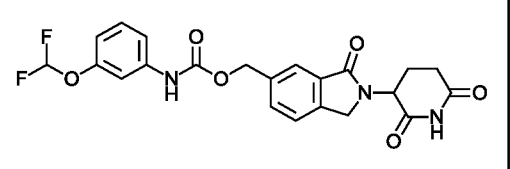
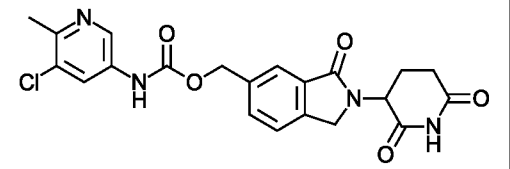
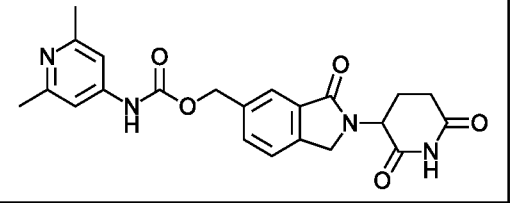
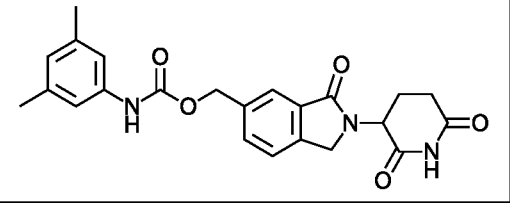
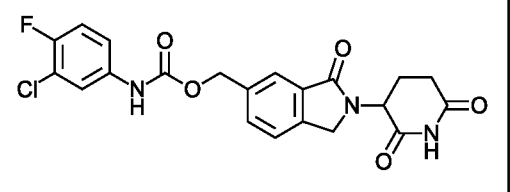
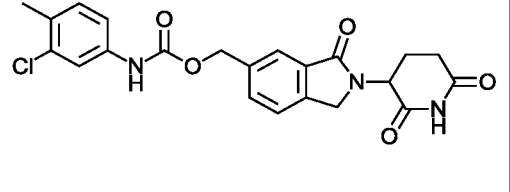
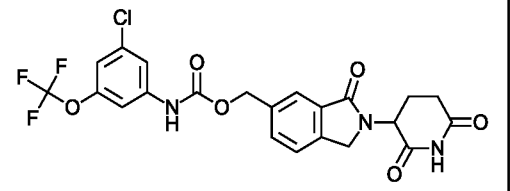
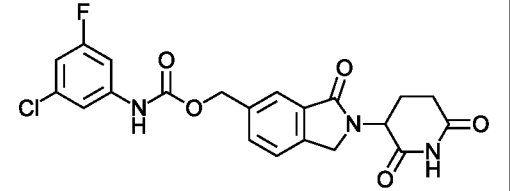
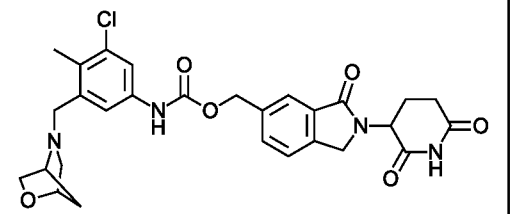
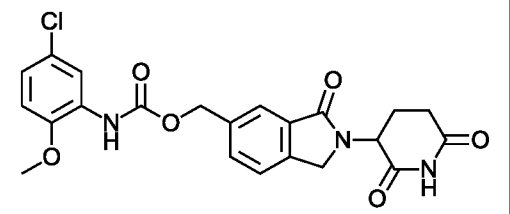
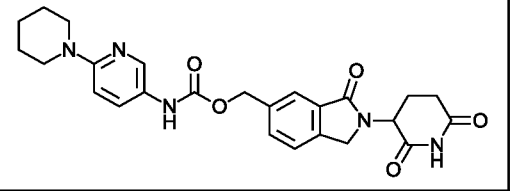
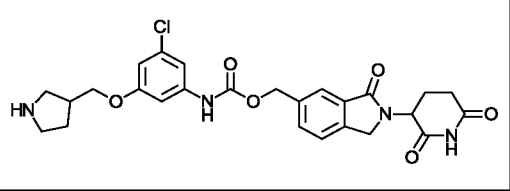
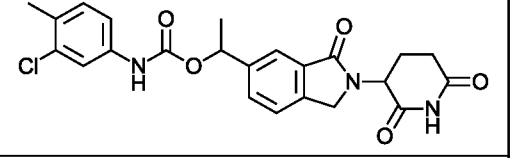
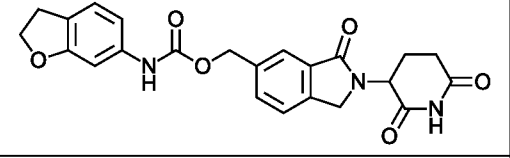
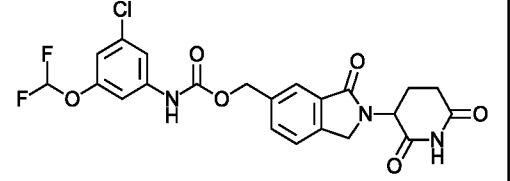
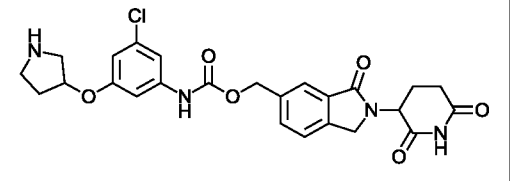
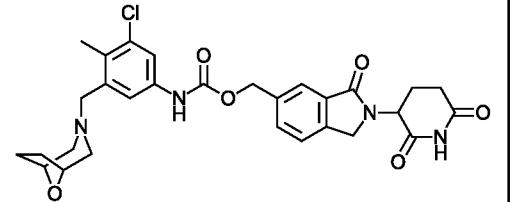
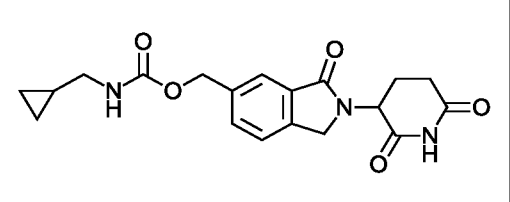
25 °C for 0.5 – 4 h. If necessary, upon completion the reaction was acidified with HCl. If the product precipitated, it was collected by filtration to afford the final carbamate compounds. Otherwise, the mixture was either concentrated to give a residue, or it was extracted and the organic layers were combined, dried over sodium sulfate, filtered, and concentrated to give a residue. The residue was purified by standard methods to afford the final carbamate compounds.

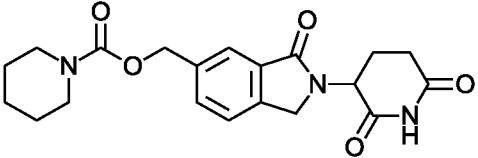
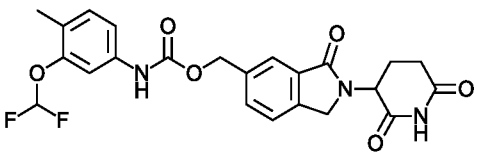
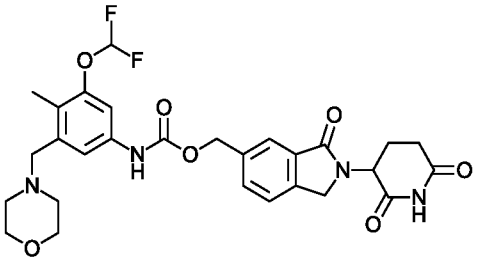
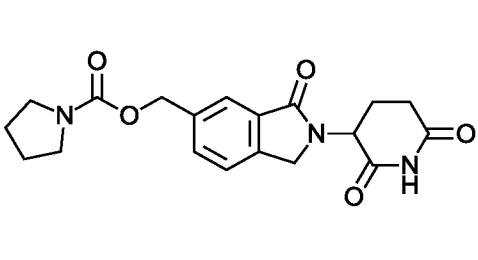
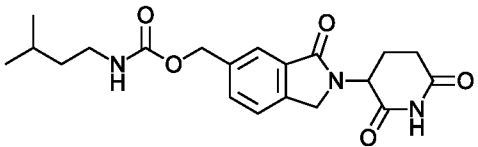
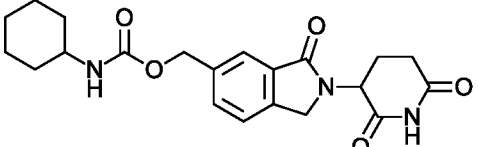
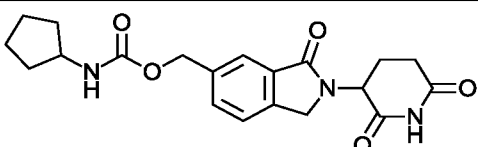
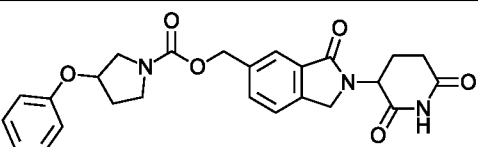
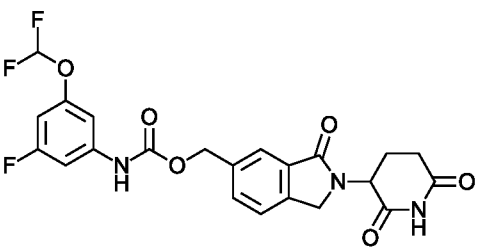
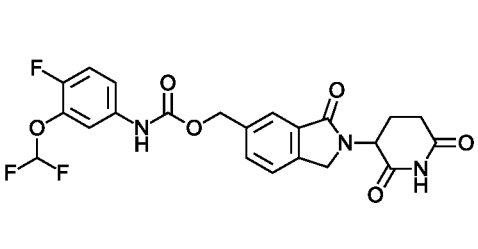
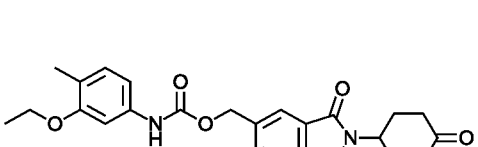
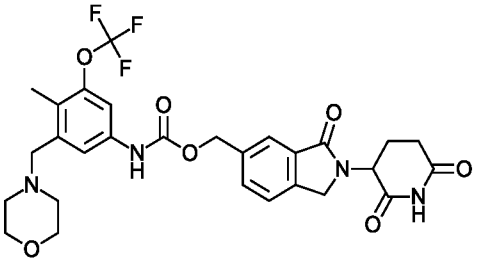
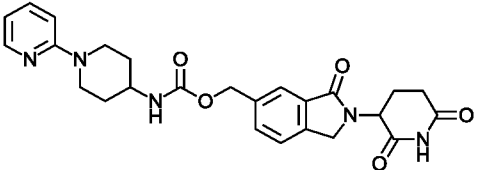
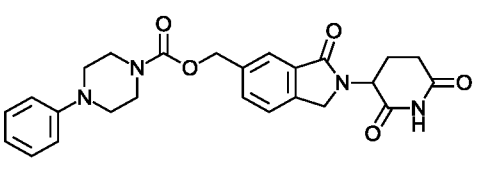
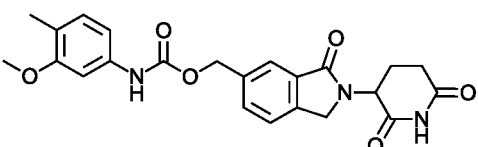
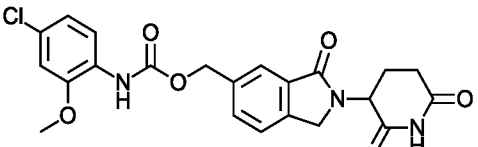
IX: Variant ii): To a solution of 3-(6-(hydroxymethyl)-1-oxoisindolin-2-yl)piperidine-2,6-dione **VIII** (1.50 g, 5.47 mmol, 1.00 eq) in dimethylformamide (15.0 mL) was added pyridine (2.21 mL, 27.3 mmol, 5.00 eq) and phenyl chloroformate (1.37 mL, 10.9 mmol, 2.00 eq) at 0 °C. The reaction was stirred at 25 °C for 12 h. The mixture was concentrated under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC to afford (2-(2,6-dioxopiperidin-3-yl)-3-oxoisindolin-5-yl)methyl phenyl carbonate. To a solution of (2-(2,6-dioxopiperidin-3-yl)-3-oxoisindolin-5-yl)methyl phenyl carbonate (1.00 eq) in dimethylformamide (0.1-0.14 M reaction) was added the amine (1.50-5.00 eq). The reaction was stirred at 25 °C for 1-36 h. The mixture was either: diluted to 0.07 M with dimethylformamide and purified by a standard method, or: diluted to 0.10 M with formic acid to give a precipitate which was filtered and dried, or: diluted to 0.10 M with formic acid and purified by a standard method, to afford the final carbamate compounds.

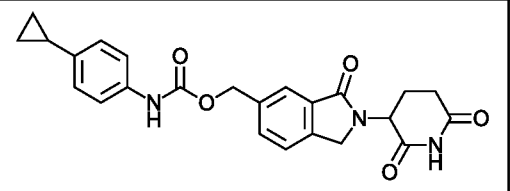
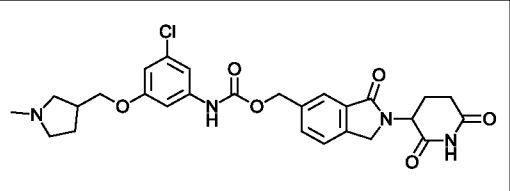
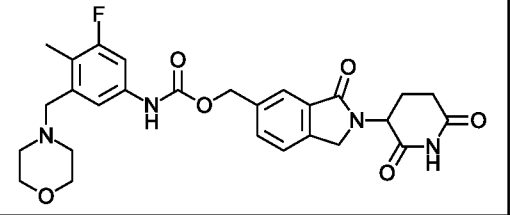
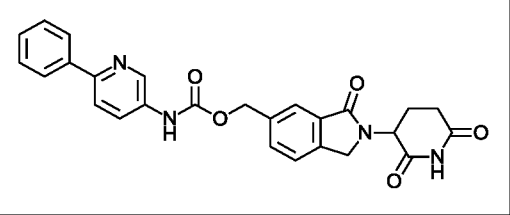
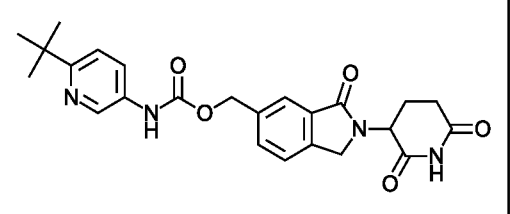
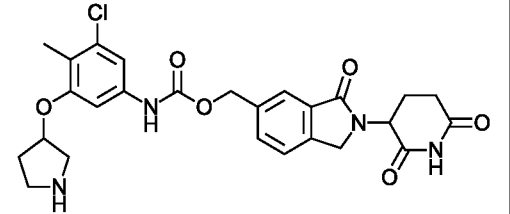
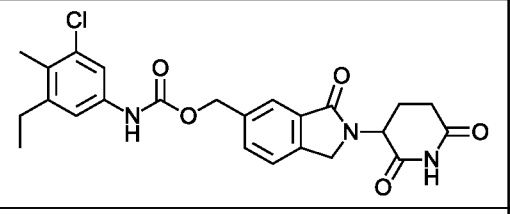
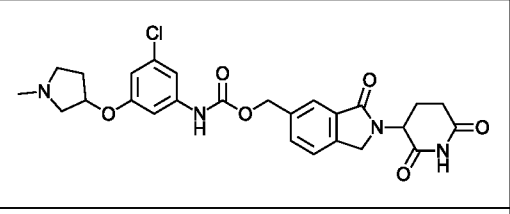
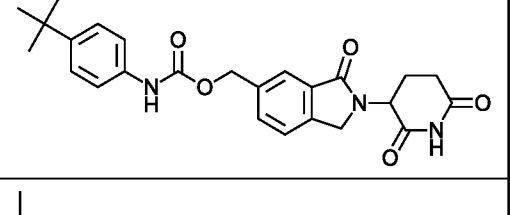
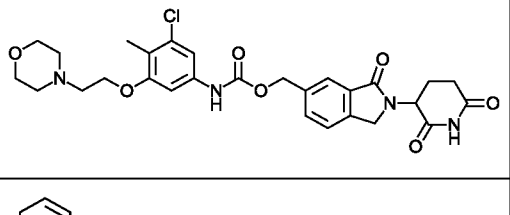
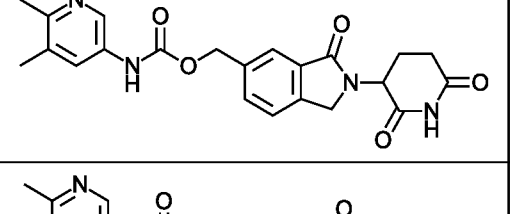
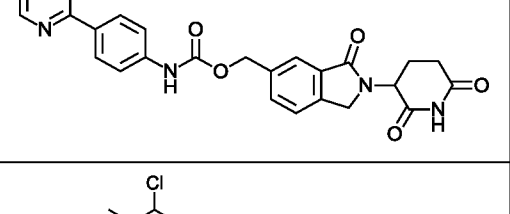
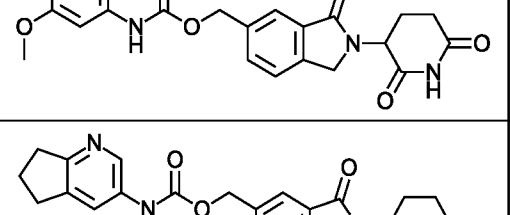
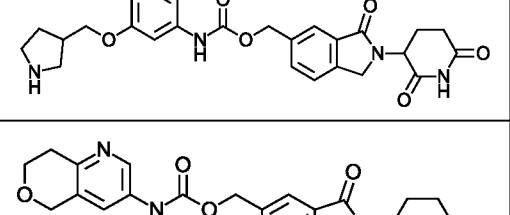
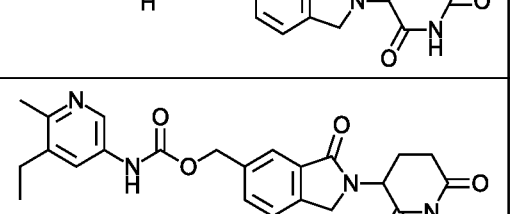
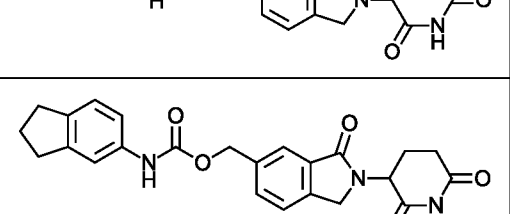
Example 2: Synthesis of specific examples

Table 1: Specific examples

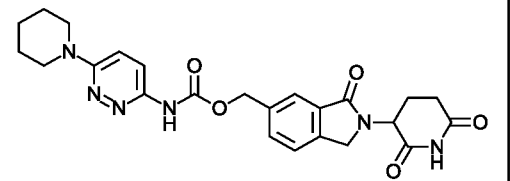
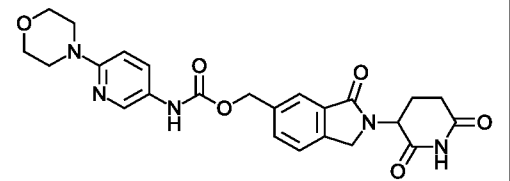
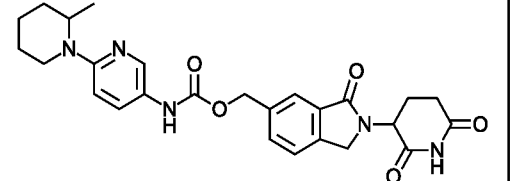
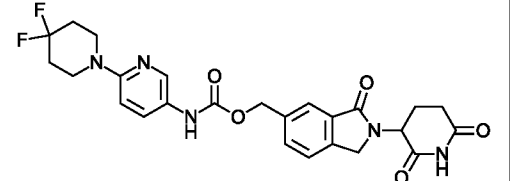
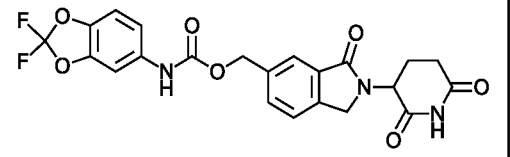
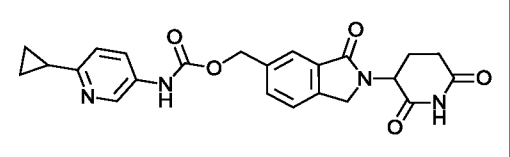
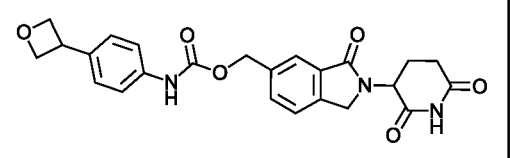
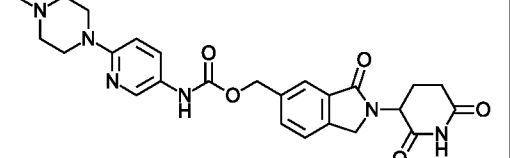
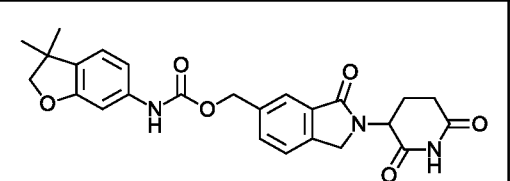
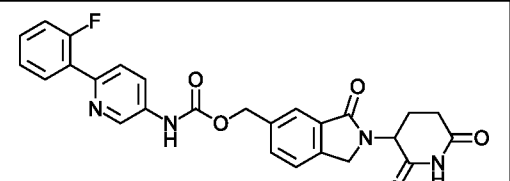
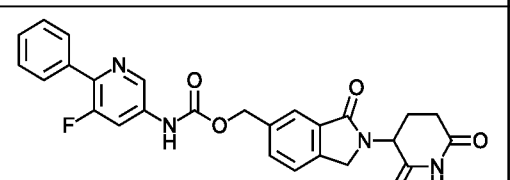
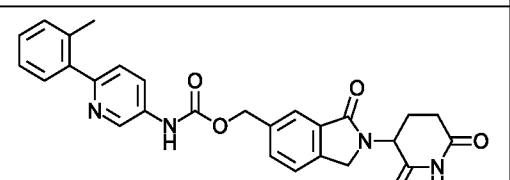
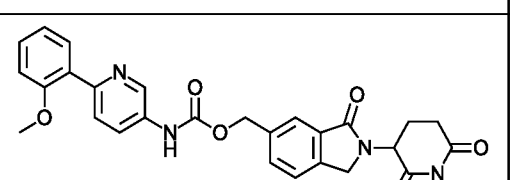
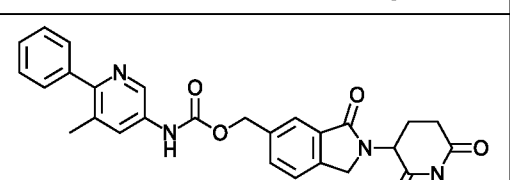
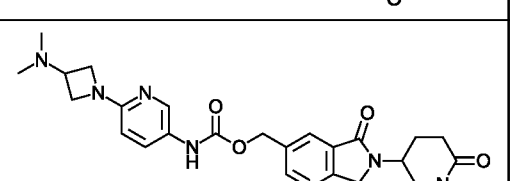
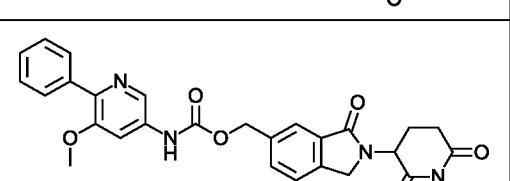
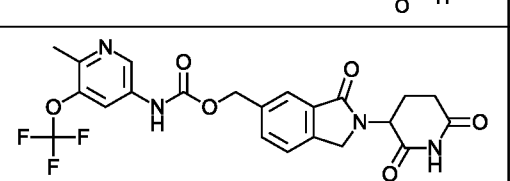
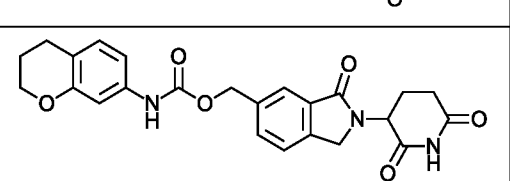
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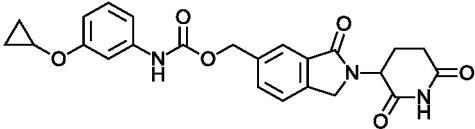
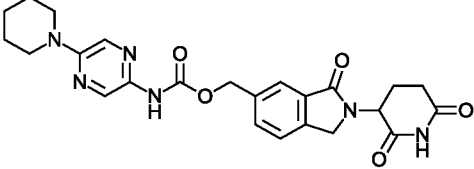
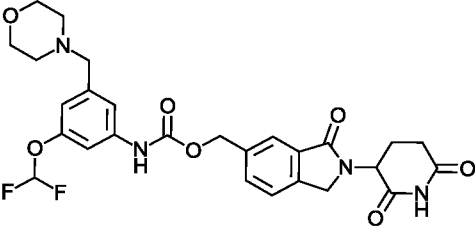
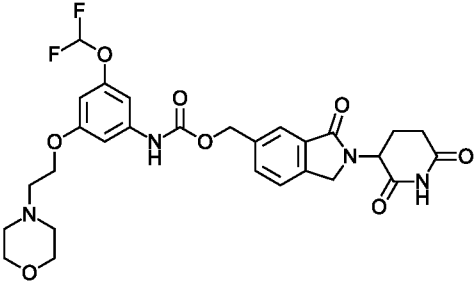
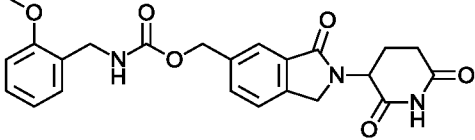
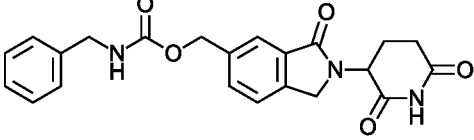
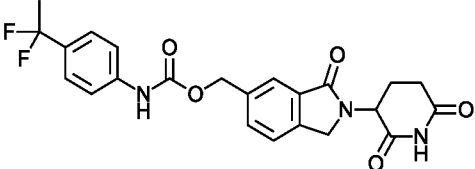
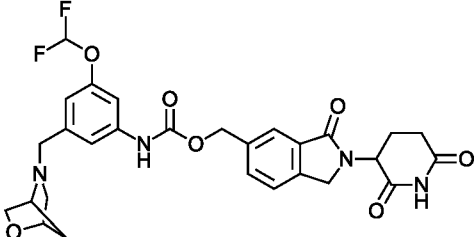
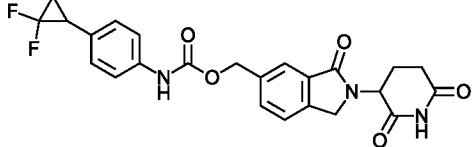
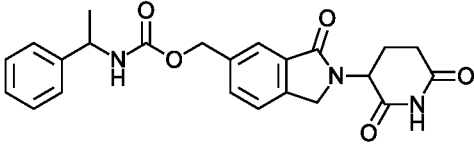
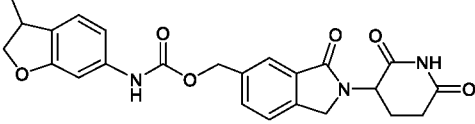
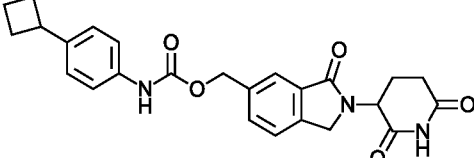
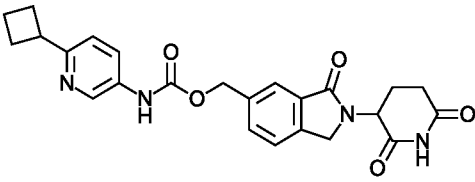
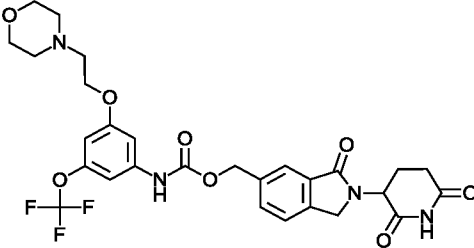
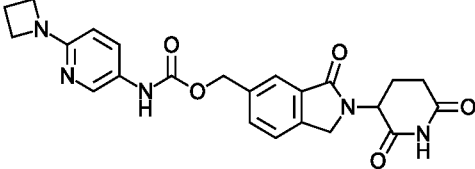
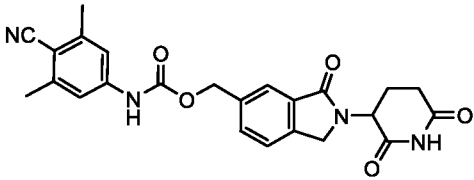
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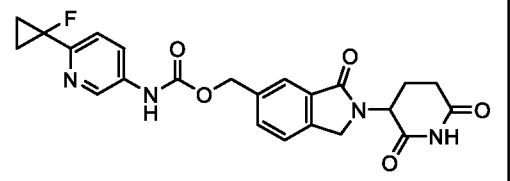
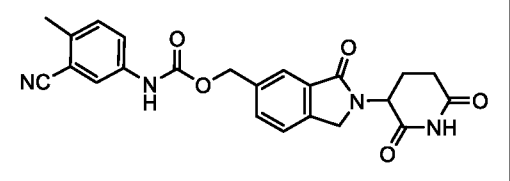
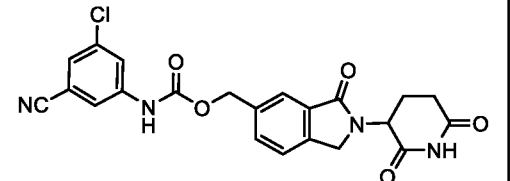
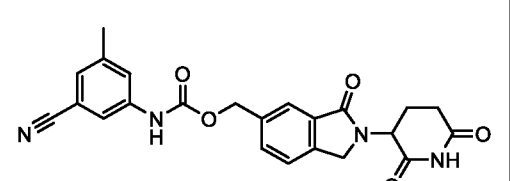
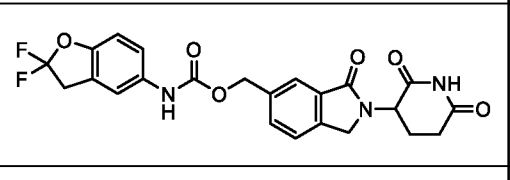
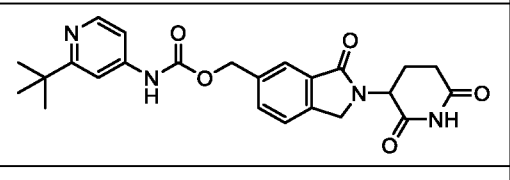
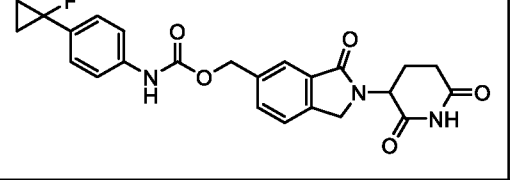
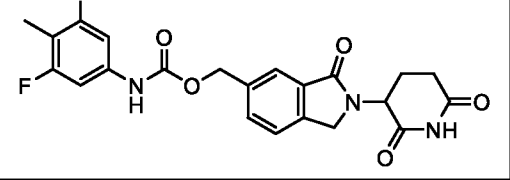
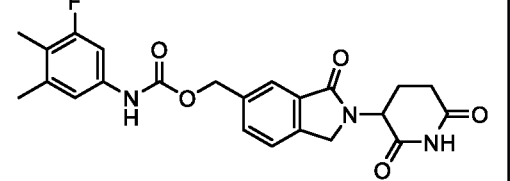
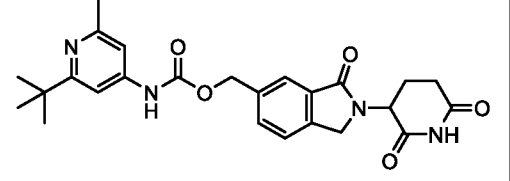
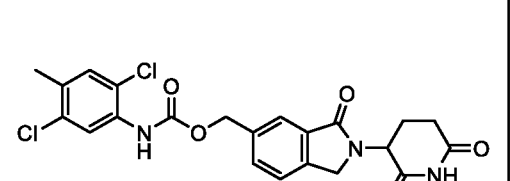
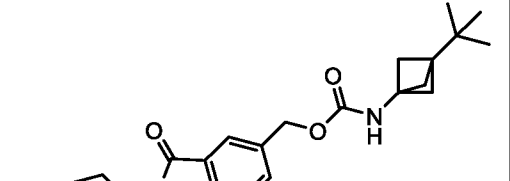
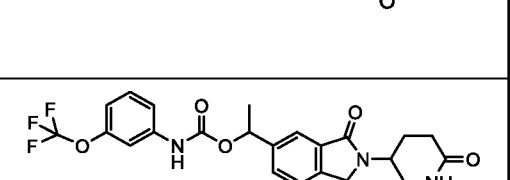
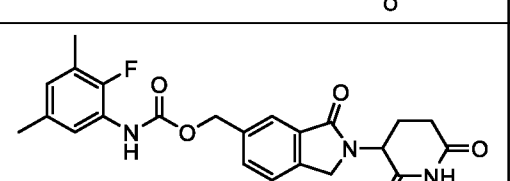
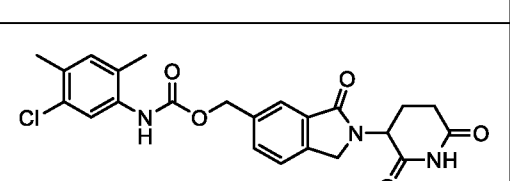
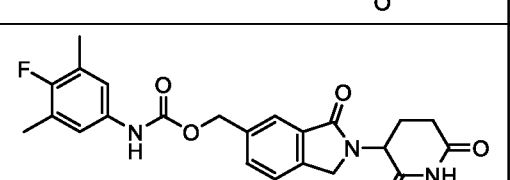
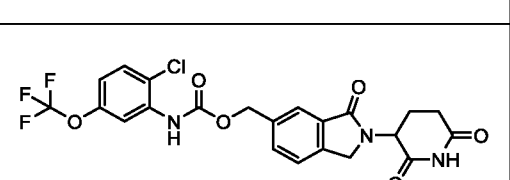
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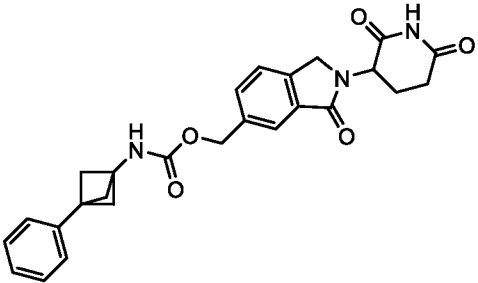
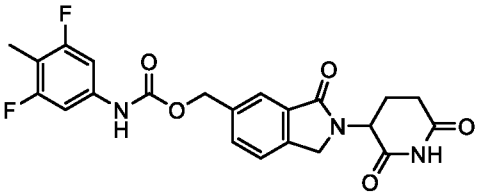
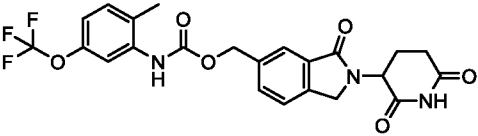
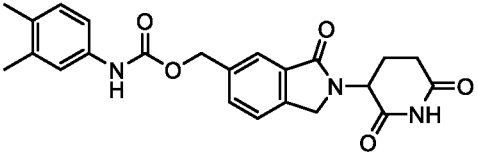
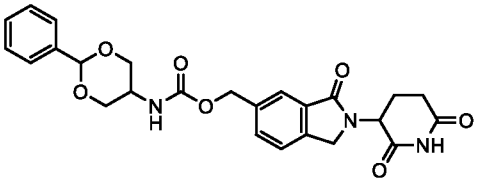
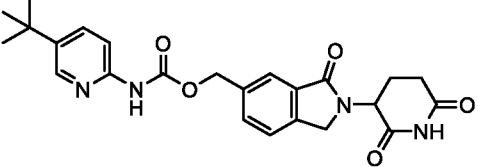
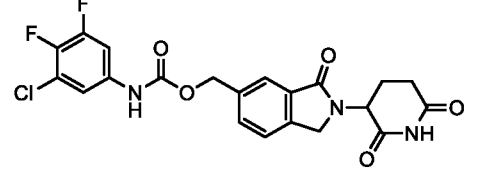
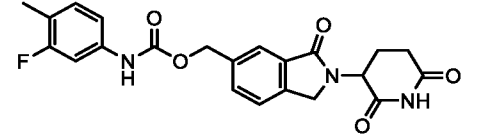
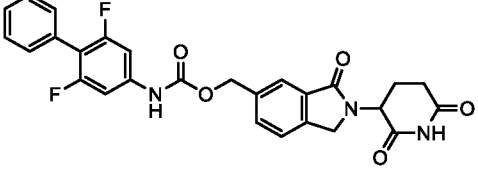
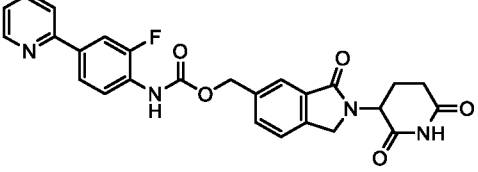
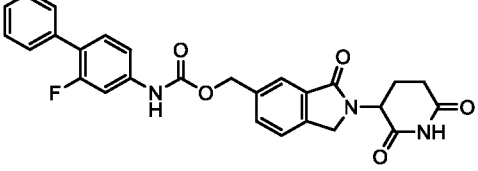
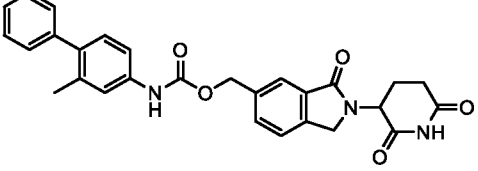
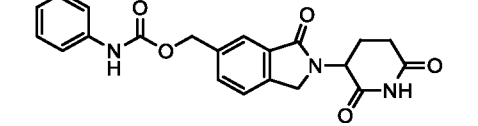
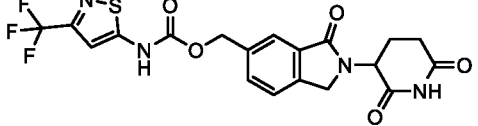
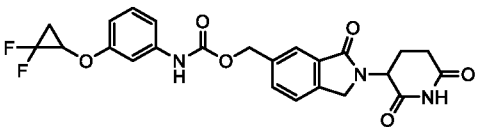
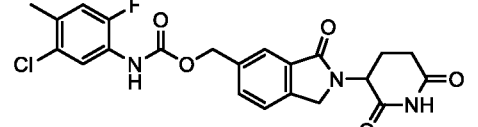
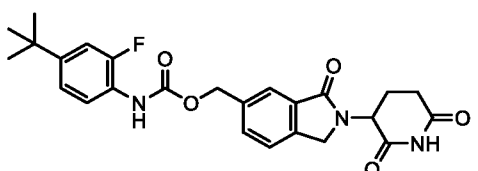
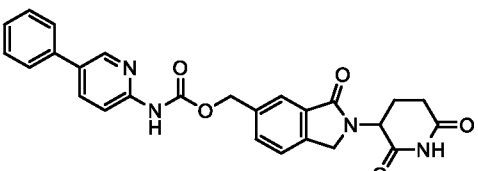
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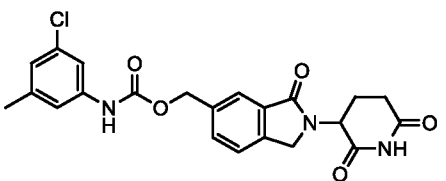
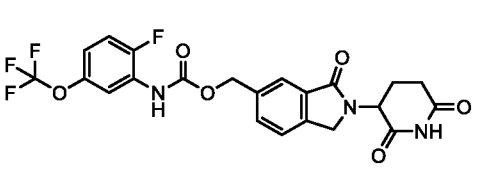
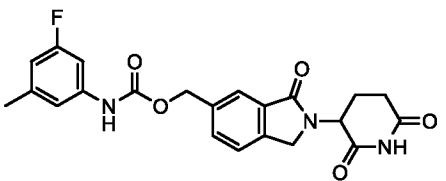
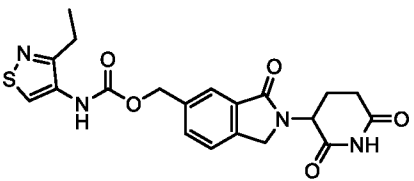
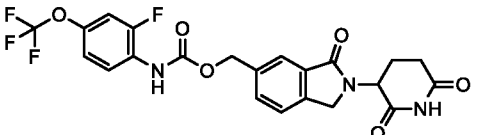
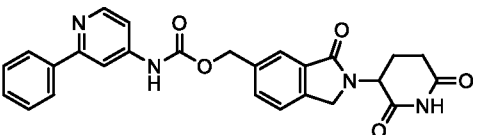
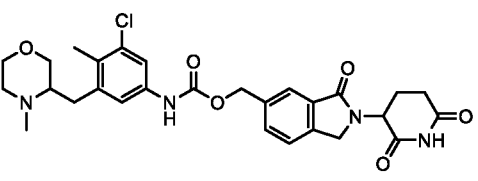
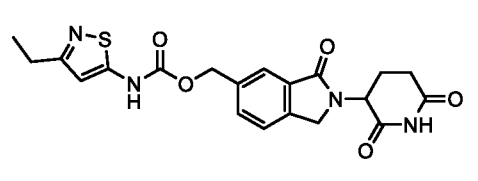
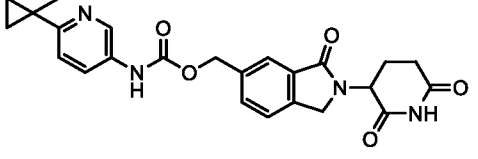
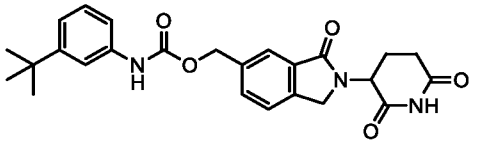
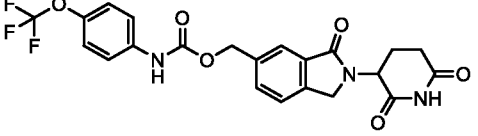
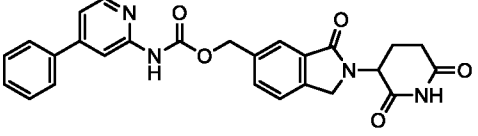
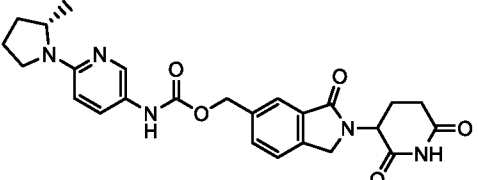
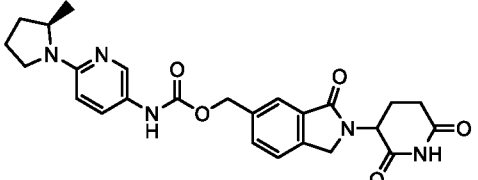
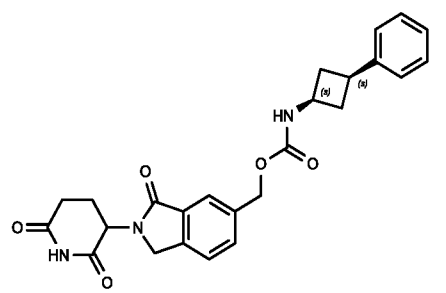
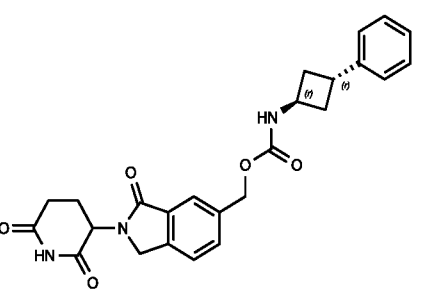
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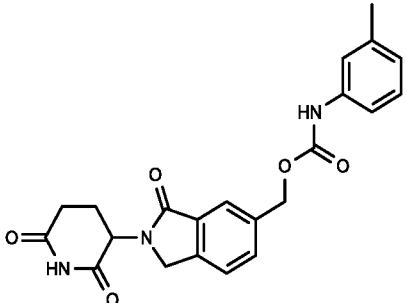
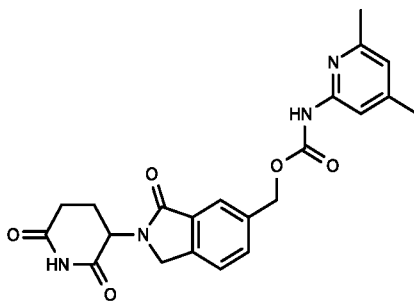
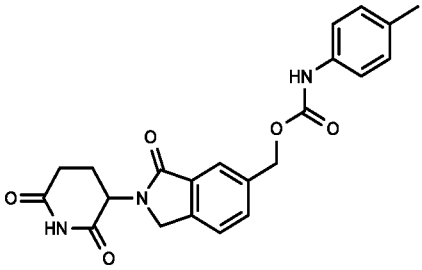
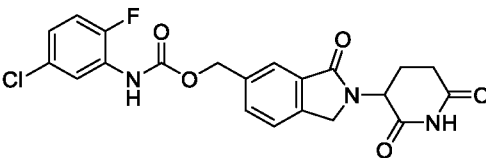
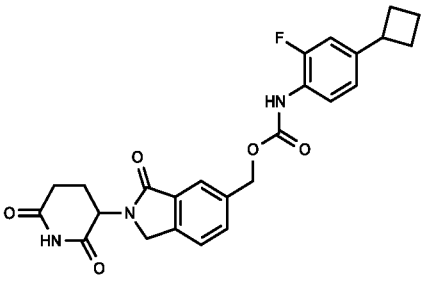
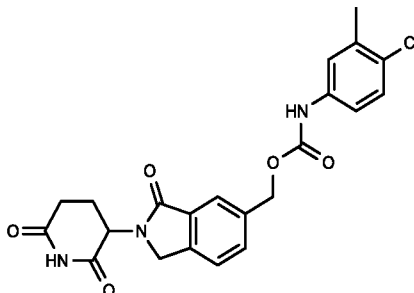
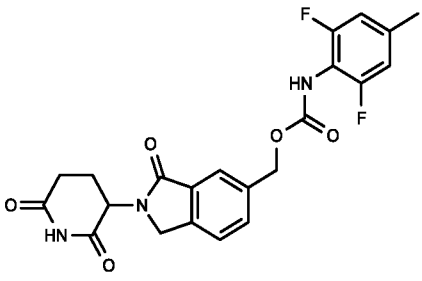
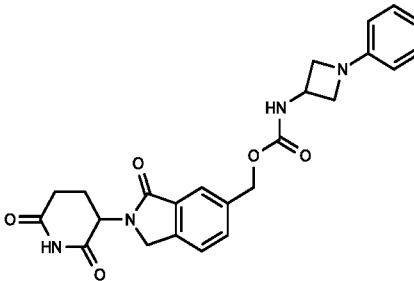
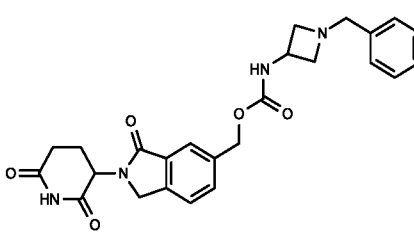
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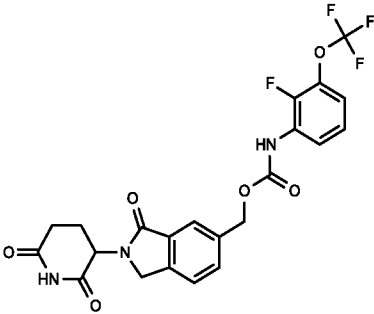
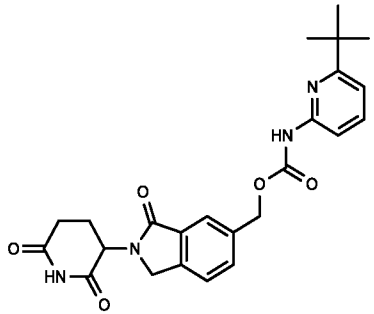
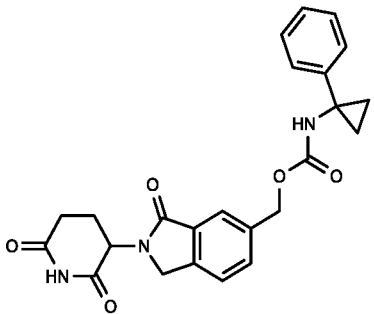
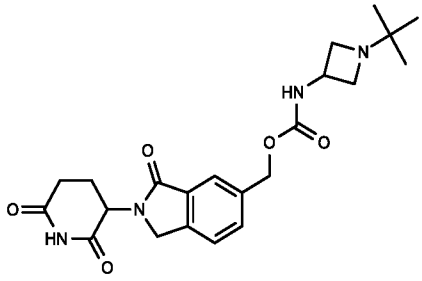
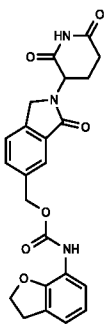
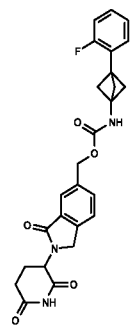
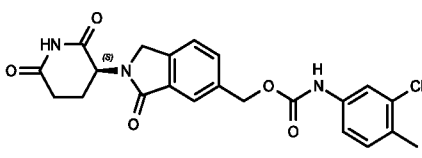
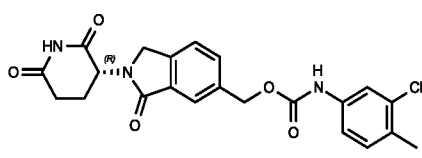
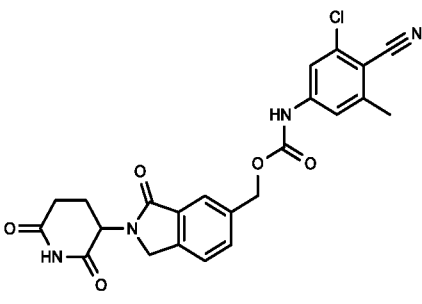
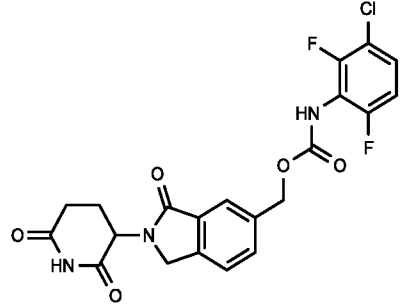
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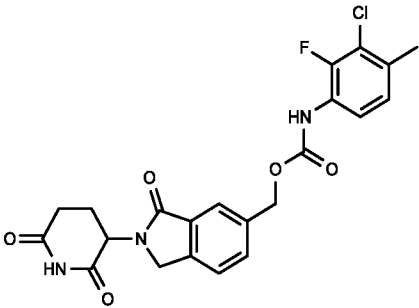
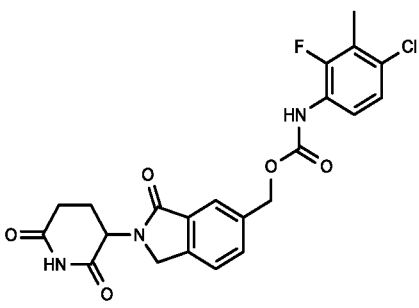
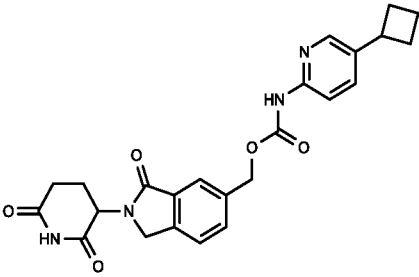
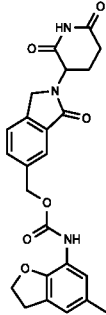
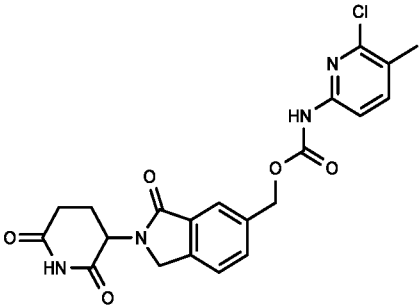
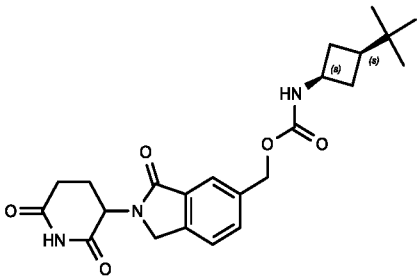
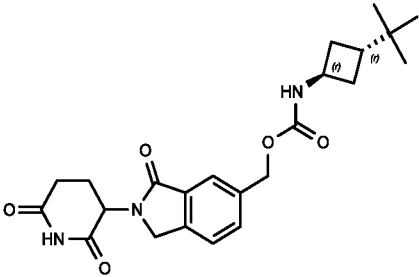
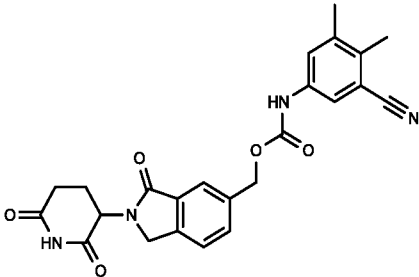
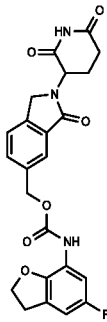
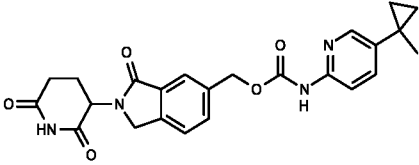
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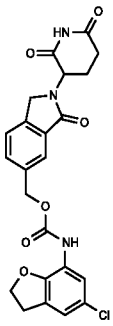
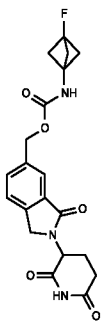
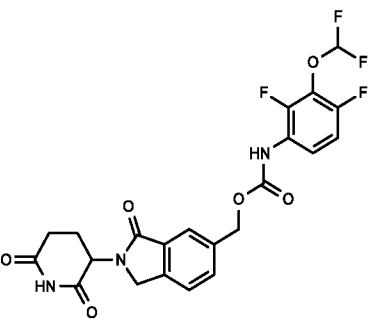
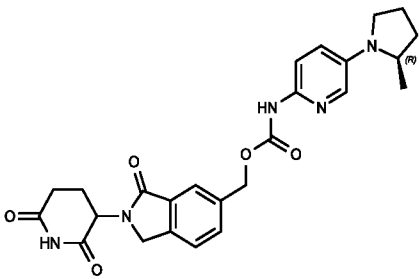
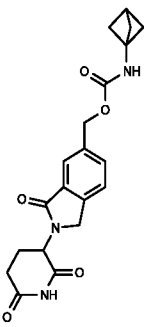
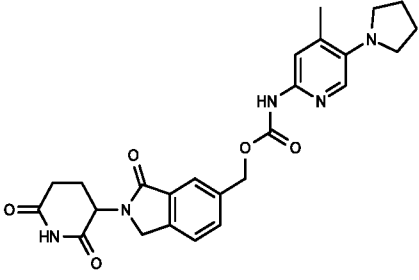
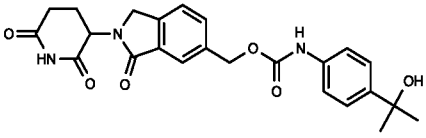
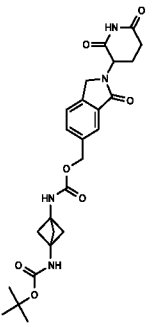
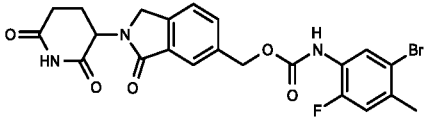
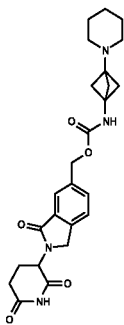
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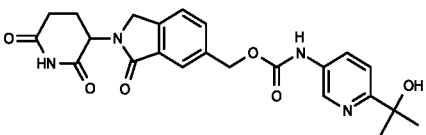
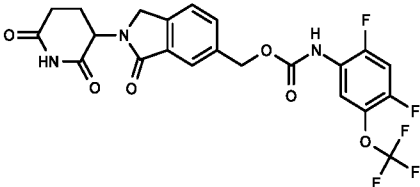
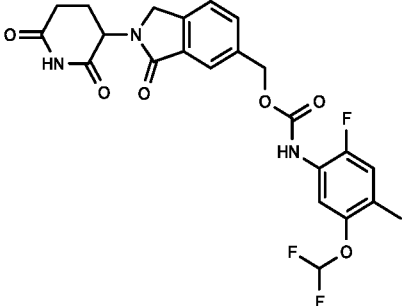
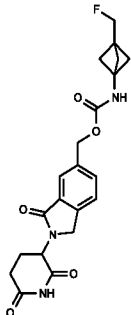
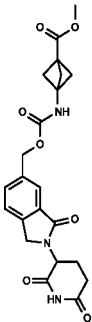
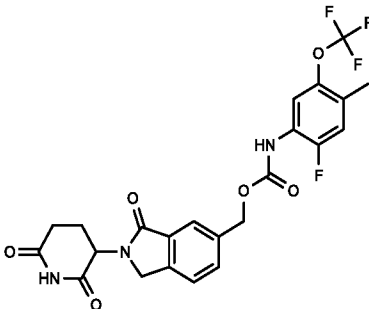
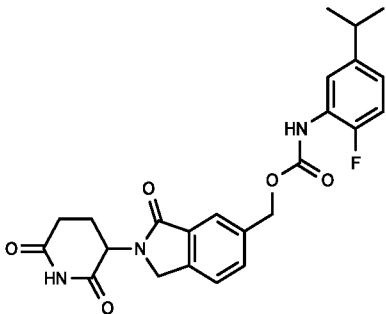
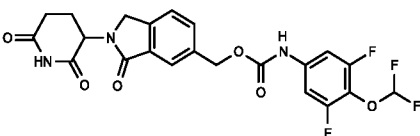
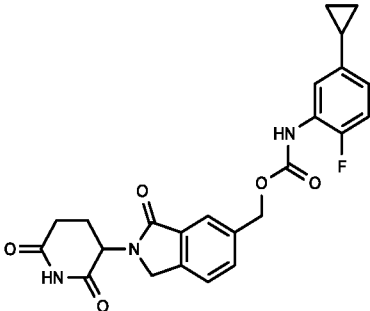
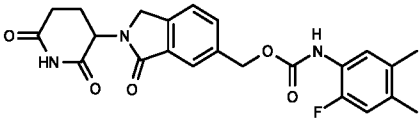
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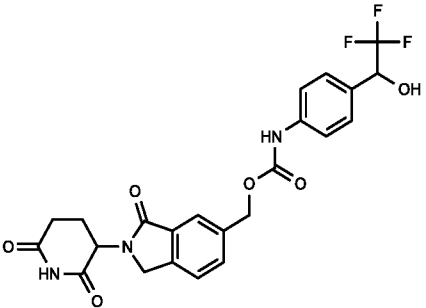
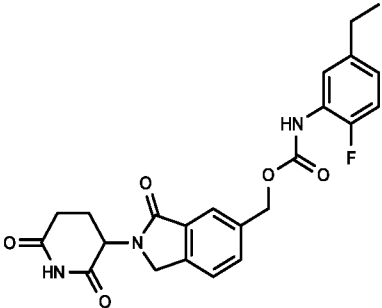
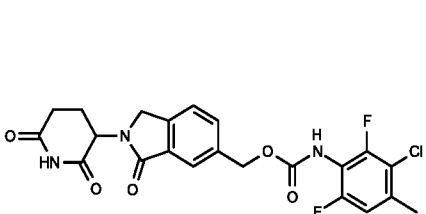
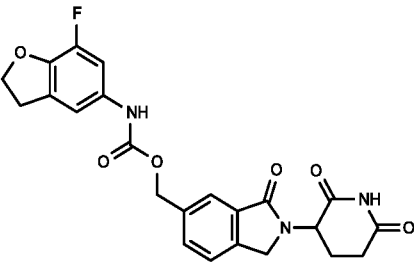
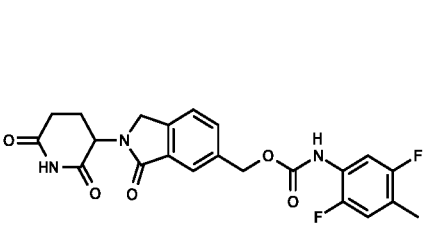
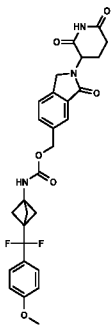
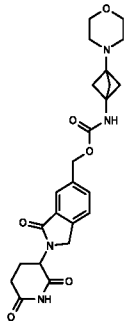
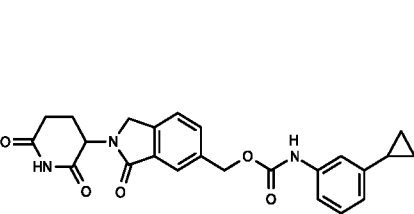
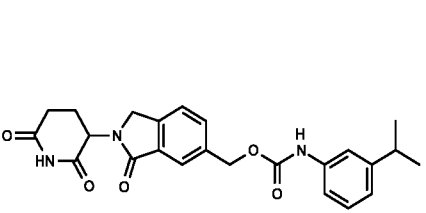
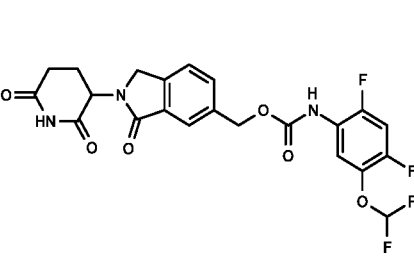
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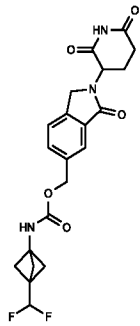
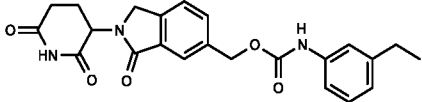
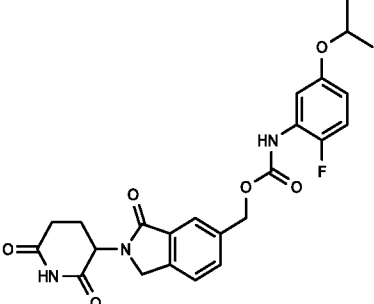
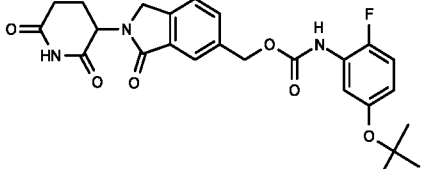
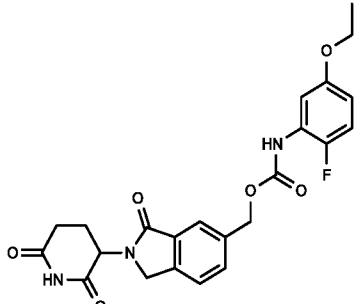
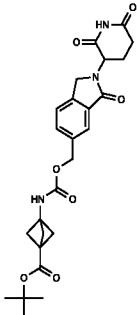
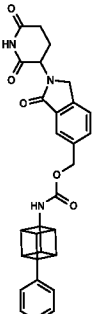
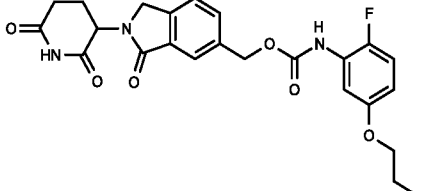
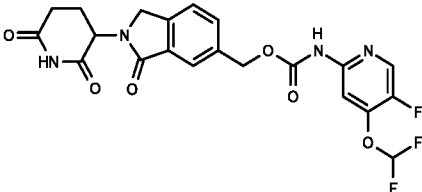
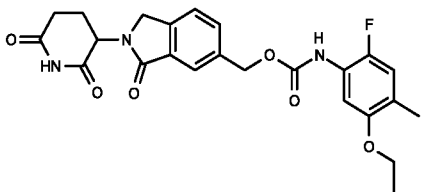
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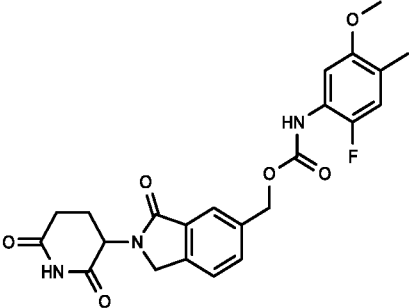
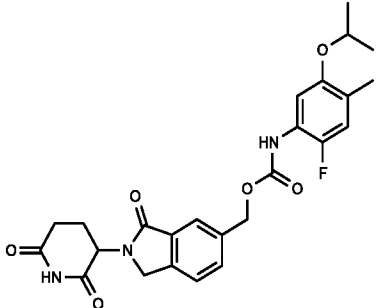
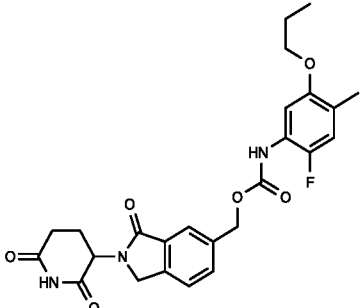
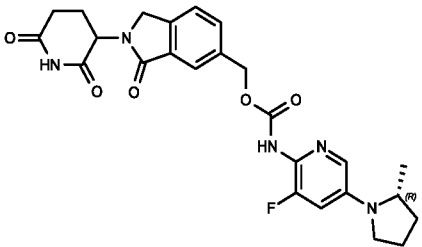
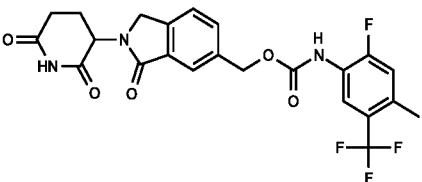
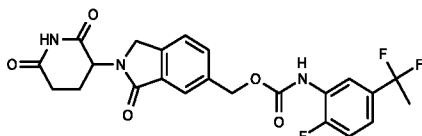
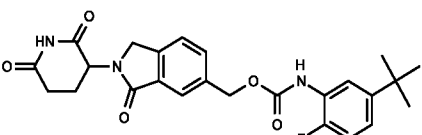
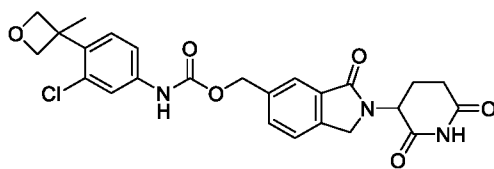
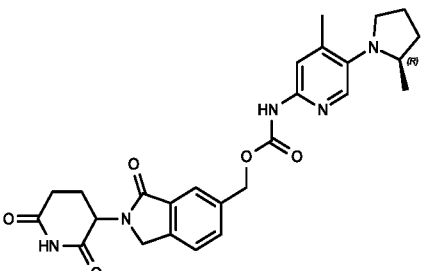
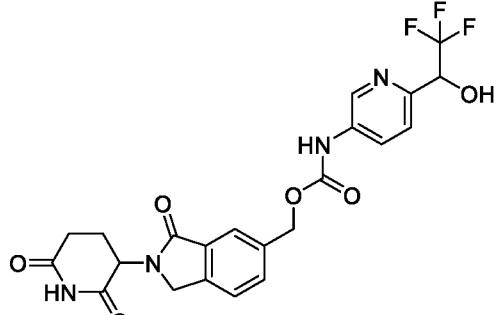
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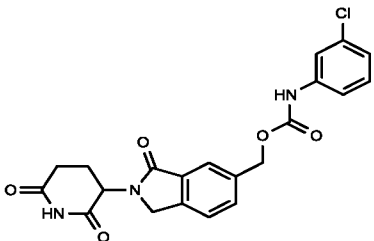
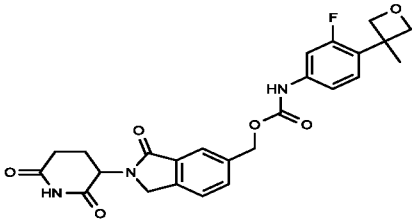
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Compound 1: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (5-chloro-2-methoxy-4-methylphenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.17 - 10.81 (m, 1H), 8.87 (s, 1H), 7.82 (s, 1H), 7.75 - 7.57 (m, 3H), 7.03 (s, 1H), 5.26 (s, 2H), 5.14 (br dd, *J* = 5.1, 13.2 Hz, 1H), 4.53 - 4.40 (m, 1H), 4.39 - 4.29 (m, 1H), 3.80 (s, 3H), 2.92 (br s, 1H), 2.65 - 2.57 (m, 1H), 2.44 - 2.38 (m, 1H), 2.29 (s, 3H), 2.07 - 1.97 (m, 1H). MS (ESI) *m/z* 472.1 [M+H]⁺

Step 1: To a solution of 4-chloro-5-methyl-2-nitrophenol (500 mg, 2.67 mmol, 1.00 eq) in dimethylformamide (3.00 mL) were added potassium carbonate (740 mg, 5.35 mmol, 2.01 eq) and methyl iodide (0.17 mL, 2.73 mmol, 1.02 eq). The reaction was stirred at 25°C for 2 h. The mixture was extracted with water/ethyl acetate (2.00 mL/2.00 mL). The organic layer was collected and concentrated to afford 1-chloro-4-methoxy-2-methyl-5-nitrobenzene (490 mg, crude) as a yellow solid.

Step 2: To a solution of 1-chloro-4-methoxy-2-methyl-5-nitrobenzene (490 mg, 2.43 mmol, 1.00 eq) in methanol (9.00 mL) and water (3.00 mL) were added iron powder (680 mg, 12.1 mmol, 5.01 eq) and ammonium chloride (1.04 g, 19.4 mmol, 8.00 eq). The reaction was stirred at 80°C for 2 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a concentrated aqueous solution. The solution was extracted with water/ethyl acetate. The organic layers were collected and concentrated under reduced pressure to afford 5-chloro-2-methoxy-4-methylaniline.

Step 3: To a solution of 5-chloro-2-methoxy-4-methylaniline (200 mg, 1.17 mmol, 1.00 eq) in acetonitrile (3.00 mL) was added pyridine (0.47 mL, 5.82 mmol, 4.99 eq), phenyl chloroformate (0.22 mL, 1.75 mmol, 1.50 eq) at 0°C. The reaction was stirred at 0°C for 2 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (5-chloro-2-methoxy-4-methylphenyl)carbamate (690 mg, crude) as an off-white solid.

Compound 2: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-chloro-4-methyl-5-(morpholinomethyl)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 9.90 (br s, 1H), 8.14 (s, 1H), 7.80 (s, 1H), 7.70 - 7.62 (m, 2H), 7.55 (s, 1H), 7.43 - 7.28 (m, 1H), 5.28 (s, 2H), 5.13 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.51 - 4.44 (m, 1H), 4.39 - 4.31 (m, 1H), 3.57 (br s, 4H), 3.41 (br s, 2H), 2.96 - 2.87 (m, 1H), 2.63 (br s, 1H), 2.46 - 2.32 (m, 5H), 2.29 (s, 3H), 2.06 - 1.98 (m, 1H). MS (ESI) *m/z* 541.2 [M+H]⁺

Step 1: To a solution of 2-methyl-5-nitro-benzoic acid (10.0 g, 55.2 mmol, 1.00 eq) in concentrated sulfuric acid (30.0 mL, 98% purity) was added 1,3-dichloro-5,5-dimethylimidazolidine-2,4-dione (13.0 g, 66.0 mmol, 1.20 eq). The mixture was stirred at 80 °C for 12 h. After cooling to room temperature, the mixture was poured into ice-water. The resulting white precipitate was collected by filtration and dried under reduced pressure to afford 3-chloro-2-methyl-5-nitro-benzoic acid.

Step 2: To a solution of 3-chloro-2-methyl-5-nitro-benzoic acid (15.0 g, 69.6 mmol, 1.00 eq) in tetrahydrofuran (100 mL) was added borane dimethyl sulfide complex (10 M, 14.0 mL, 140.0 mmol, 2.01 eq). The mixture was stirred at 20 °C for 12 h. The mixture was quenched with methanol (10.0 mL) at 0 °C and then concentrated under reduced pressure to give a residue. The residue was diluted with ethyl acetate (200 mL) and adjusted pH = 8 with aqueous sodium bicarbonate (10%, 200 mL). The organic layer was separated and concentrated under reduced pressure to afford (3-chloro-2-methyl-5-nitrophenyl)methanol.

Step 3: To a solution of (3-chloro-2-methyl-5-nitro-phenyl)methanol (11.0 g, 54.5 mmol, 1 eq) (crude) in dichloromethane (200 mL) was added carbon tetrabromide (21 g, 63.32 mmol, 1.16 eq) and triphenylphosphine (18.6 g, 70.9 mmol, 1.30 eq) at 0 °C. The mixture was stirred at 20 °C for 1 h. The mixture was concentrated under reduced pressure to give a residue. The residue was triturated with petroleum ether/ethyl acetate = 1/1 (200 mL) and filtered. The filtrate was concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8/1) to afford 1-(bromomethyl)-3-chloro-2-methyl-5-nitrobenzene.

Step 4: To a solution of 1-(bromomethyl)-3-chloro-2-methyl-5-nitro-benzene (16.0 g, 60.5 mmol, 1.00 eq) in acetonitrile (150 mL) was added morpholine (7.98 mL, 90.7 mmol, 1.50 eq), potassium carbonate (25.0 g, 181 mmol, 2.99 eq) and potassium iodide (1.00 g, 6.05 mmol, 0.100 eq). The reaction was stirred at 80 °C for 12 h. After cooling to room

temperature, the mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8/1) to give 4-(3-chloro-2-methyl-5-nitrobenzyl)morpholine.

- 5 **Step 5:** To a solution of 4-(3-chloro-2-methyl-5-nitrobenzyl)morpholine (9.70 g, 35.8 mmol, 1.00 eq) in methanol (100 mL) and water (30.0 mL) was added ammonium chloride (15.0 g, 280 mmol, 7.83 eq) and ferrous powder (10.0 g, 179 mmol, 5.00 eq). The reaction was stirred at 80 °C for 2 h. The mixture was filtered, and methanol was removed under reduced pressure. The remaining aqueous solution was extracted with ethyl acetate (2 × 100
10 mL). The combined organic layers were washed with brine (20.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-chloro-4-methyl-5-(morpholinomethyl)aniline.

- Step 6:** To a solution of 3-chloro-4-methyl-5-(morpholinomethyl)aniline (1.00 g, 4.15 mmol, 1.00 eq) and pyridine (1.01 mL, 12.4 mmol, 3.00 eq) in acetonitrile (20.0 mL) was
15 added phenyl chloroformate (0.52 mL, 4.15 mmol, 1.00 eq) at 0°C. The reaction was stirred at 20°C for 2 h. The mixture was diluted with water (20.0 mL). The resulting precipitate was collected by filtration and dried to afford phenyl (3-chloro-4-methyl-5-(morpholinomethyl)phenyl)carbamate.

- Compound 3:** General procedure A with variant i) was used for the preparation from
20 compound **VIII** employing phenyl (3-(trifluoromethoxy)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 10.15 (s, 1H), 7.81 (s, 1H), 7.72 - 7.68 (m, 1H), 7.67 - 7.62 (m, 1H), 7.59 (s, 1H), 7.45 - 7.39 (m, 2H), 7.03 - 6.96 (m, 1H), 5.30 (s, 2H), 5.13 (dd, *J* = 5.2, 13.3 Hz, 1H), 4.52 - 4.44 (m, 1H), 4.39 - 4.31 (m, 1H), 2.97 - 2.87 (m, 1H), 2.63 (br d, *J* = 2.4 Hz, 1H), 2.47 - 2.35 (m, 1H), 2.02 (dtd, *J* = 2.0, 5.1, 12.5 Hz, 1H). MS
25 (ESI) *m/z* 478.1 [M+H]⁺

- Step 1:** To a solution of 1-nitro-3-(trifluoromethoxy)benzene (1.00 g, 4.83 mmol, 1.00 eq) in methanol (15.0 mL) and water (5.00 mL) was added ammonium chloride (2.07 g, 38.6 mmol, 8.00 eq) and iron powder (1.35 g, 24.1 mmol, 5.00 eq). The reaction was stirred at 80°C for 2 h. The mixture was filtered, and the solvents were mostly removed under reduced
30 pressure to give a concentrated solution. The solution was triturated with ethyl acetate/water (20.0 mL/10.0 mL), and a drop of saturated sodium bicarbonate solution was added. The

organic layer was collected and concentrated under reduced pressure to afford 3-(trifluoromethoxy)aniline.

Step 2: To a solution of 3-(trifluoromethoxy)aniline (0.15 mL, 1.10 mmol, 1.00 eq) in acetonitrile (5.00 mL) was added pyridine (0.44 mL, 5.50 mmol, 5.00 eq). The reaction was stirred for 0.5 h, then phenyl chloroformate (0.16 mL, 1.32 mmol, 1.20 eq) was added at 0°C. The reaction was stirred for 1.5 h at 0°C. The mixture was concentrated under reduced pressure to give a residue. The residue was diluted with water (10.0 mL) and ethyl acetate (30.0 mL). The organic layer was collected and concentrated and the obtained residue was purified by standard methods to afford phenyl (3-(trifluoromethoxy)phenyl)carbamate.

Compound 4: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-(morpholinomethyl)-5-(trifluoromethoxy)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 10.11 (s, 1H), 7.80 (s, 1H), 7.71 - 7.60 (m, 2H), 7.52 - 7.37 (m, 2H), 6.91 (s, 1H), 5.29 (s, 2H), 5.18 - 5.07 (m, 1H), 4.53 - 4.29 (m, 2H), 3.62 - 3.52 (m, 4H), 3.45 (s, 2H), 2.98 - 2.85 (m, 1H), 2.60 (br d, *J* = 18.1 Hz, 1H), 2.43 - 2.38 (m, 1H), 2.34 (br s, 4H), 2.05 - 1.96 (m, 1H). MS (ESI) *m/z* 577.1 [M+H]⁺

Step 1: To a solution of 3-hydroxy-5-nitro-benzoic acid (4.50 g, 24.6 mmol, 1.00 eq) and morpholine (2.57 g, 29.5 mmol, 2.60 mL, 1.2 eq) in dichloromethane (100 mL) was added *O*-(7-azabenzotriazol-1-yl)-*N,N,N,N*-tetramethyluronium hexafluorophosphate (11.2 g, 29.5 mmol, 1.20 eq) and triethylamine (5.06 mL, 49.2 mmol, 2.00 eq). The reaction was stirred at 20°C for 12 h. The mixture was diluted with water (150 mL) and extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with brine (100 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 0/1) to afford (3-hydroxy-5-nitrophenyl)(morpholino) methanone.

Step 2: To a solution of (3-hydroxy-5-nitro-phenyl)-morpholino-methanone (2.40 g, 9.52 mmol, 1.00 eq) in toluene (200 mL) were added trimethyl(trifluoromethyl)silane (6.77 g, 47.6 mmol, 5.00 eq), silver trifluoromethanesulfonate (12.2 g, 47.6 mmol, 5.00 eq), 2-fluoropyridine (4.09 mL, 47.6 mmol, 5.00 eq), caesium fluoride (2.10 mL, 57.1 mmol, 6.00 eq), *N*-fluorobenzenesulfonimide (6.00 g, 19.0 mmol, 2.00 eq) and 1-(chloromethyl)-4-fluoro-1,4-diazoniabicyclo(2.2.2)octane bis(tetrafluoroborate) (6.74 g, 19.0 mmol, 2.00 eq). The reaction was stirred at 25°C under a nitrogen atmosphere for 12 h. The mixture was

filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was diluted with water (100 mL) and extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with brine (100 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 1/1) to afford morpholino(3-nitro-5-(trifluoromethoxy) phenyl)methanone.

Step 3: To a solution of morpholino(3-nitro-5-(trifluoromethoxy)phenyl)methanone (2.60 g, 8.12 mmol, 1.00 eq) in tetrahydrofuran (30.0 mL) was added borane dimethyl sulfide complex (10.0 M, 1.62 mL, 2.00 eq) dropwise at 0°C under nitrogen atmosphere. The reaction was stirred at 60°C for 4 h. The mixture was quenched with methanol (9.00 mL) and concentrated to give a residue. The residue was purified by reversed phase preparative HPLC to afford 4-(3-nitro-5-(trifluoromethoxy)benzyl)morpholine.

Step 4: To a solution of 4-(3-nitro-5-(trifluoromethoxy)benzyl)morpholine (1.10 g, 3.59 mmol, 1.00 eq) in methanol (50.0 mL) and water (50.0 mL) were added iron powder (1.40 g, 25.14 mmol, 7.00 eq) and ammonium chloride (1.34 g, 25.14 mmol, 7.00 eq). The reaction was stirred at 80°C for 3 h. The mixture was filtered over Celite, and the filtrate was concentrated under reduced pressure to afford 3-(morpholinomethyl)-5-(trifluoromethoxy)aniline.

Step 5: To a solution of 3-(morpholinomethyl)-5-(trifluoromethoxy)aniline (580 mg, 2.10 mmol, 1.00 eq) in acetonitrile (3.00 mL) was added phenyl chloroformate (0.39 mL, 3.15 mmol, 1.50 eq) and pyridine (0.5 mL, 6.30 mmol, 3.00 eq) at 0°C. The reaction was stirred at 25°C for 12 h. The mixture was diluted with water (100 mL) and extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated and the obtained residue was purified by standard methods to afford phenyl (3-(morpholinomethyl)-5-(trifluoromethoxy)phenyl)carbamate.

Compound 5: General procedure A with variant i) was used for the preparation from compound VIII employing phenyl (3-(difluoromethoxy)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (br s, 1H), 10.05 (s, 1H), 7.80 (s, 1H), 7.71 - 7.67 (m, 1H), 7.67 - 7.62 (m, 1H), 7.40 (br s, 1H), 7.37 (s, 1H), 7.36 - 7.28 (m, 2H), 7.19 (t, J=76 Hz, 1H), 6.81 (br d, J=7.5 Hz, 1H), 5.29 (s, 2H), 5.13 (dd, J=5.1, 13.3 Hz, 1H), 4.52 - 4.44

(m, 1H), 4.39 - 4.30 (m, 1H), 2.97 - 2.87 (m, 1H), 2.64 - 2.58 (m, 1H), 2.48 - 2.37 (m, 1H), 2.07 - 1.98 (m, 1H). MS (ESI) m/z 460.1 [M+H]⁺

Step 1: To a solution of 1-(difluoromethoxy)-3-nitrobenzene (2.00 g, 10.6 mmol, 1.00 eq) in methanol (15.0 mL) and water (5.00 mL) was added iron powder (2.95 g, 52.9 mmol, 5.00 eq) and ammonium chloride (4.53 g, 84.6 mmol, 8.00 eq). The reaction was stirred at 80°C for 2 h. The reaction solution was filtered, and the filtrate was extracted with ethyl acetate. The combined organic layers were washed with brine, dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-(difluoromethoxy)aniline.

Step 2: To a solution of 3-(difluoromethoxy)aniline (1.00 g, 6.28 mmol, 1.00 eq) and pyridine (2.54 mL, 31.4 mmol, 5.00 eq) in acetonitrile (5.00 mL) was added phenyl chloroformate (0.94 mL, 7.54 mmol, 1.20 eq). The mixture was stirred at 25°C for 3 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (3-(difluoromethoxy)phenyl)carbamate.

Compound 6: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl(5-chloro-6-methylpyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 10.18 (br s, 1H), 8.50 - 8.42 (m, 1H), 7.99 (s, 1H), 7.80 (s, 1H), 7.72 - 7.66 (m, 1H), 7.66 - 7.62 (m, 1H), 5.30 (s, 2H), 5.17 - 5.08 (m, 1H), 4.52 - 4.43 (m, 1H), 4.38 - 4.30 (m, 1H), 2.98 - 2.85 (m, 1H), 2.65 - 2.56 (m, 1H), 2.46 (s, 3H), 2.44 - 2.34 (m, 1H), 2.05 - 1.95 (m, 1H). MS (ESI) m/z 443.2 [M+H]⁺

Step 1: To a solution of 3-chloro-2-methyl-5-nitropyridine (500 mg, 2.90 mmol, 1.00 eq) in methanol (5.00 mL) and water (5.00 mL) were added iron powder (1.13 g, 20.3 mmol, 7.00 eq) and ammonium chloride (1.08 g, 20.3 mmol, 7.00 eq). The reaction was stirred at 80°C for 2 h. The mixture was filtered over Celite, and the filtrate was concentrated under reduced pressure to afford 5-chloro-6-methylpyridin-3-amine.

Step 2: To a solution of 5-chloro-6-methylpyridin-3-amine (200 mg, 1.40 mmol, 1.00 eq) in acetonitrile (2.00 mL) were added phenyl chloroformate (0.26 mL, 2.10 mmol, 1.50 eq) and pyridine (0.34 mL, 4.21 mmol, 3.00 eq). The reaction was stirred at 25°C for 12 h. The mixture was diluted with ethyl acetate (30.0 mL) and water (50.0 mL). The organic layer was separated, and the aqueous phase was extracted with ethyl acetate (3 × 100 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated and the

obtained residue was purified by standard methods to afford phenyl (5-chloro-6-methylpyridin-3-yl)carbamate.

Compound 7: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (2,6-dimethylpyridin-4-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 10.10 (s, 1H), 8.18 (s, 1H), 7.80 (s, 1H), 7.71 - 7.60 (m, 2H), 7.12 (s, 2H), 5.29 (s, 2H), 5.12 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.51 - 4.43 (m, 1H), 4.39 - 4.30 (m, 1H), 2.91 (ddd, *J* = 5.4, 13.7, 17.4 Hz, 1H), 2.64 - 2.57 (m, 1H), 2.40 (br dd, *J* = 4.6, 13.1 Hz, 1H), 2.33 (s, 6H), 2.07 - 1.97 (m, 1H). MS (ESI) *m/z* 423.1 [M+H]⁺

To a solution of 2,6-dimethylpyridin-4-amine (1.00 g, 8.19 mmol, 1.00 eq) in acetonitrile (20.0 mL) was added pyridine (3.30 mL, 40.9 mmol, 5.00 eq) and phenyl chloroformate (1.54 mL, 12.2 mmol, 1.50 eq) at 0°C. The reaction was stirred at 25°C for 0.5 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (2,6-dimethylpyridin-4-yl)carbamate.

Compound 8: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3,5-dimethylphenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.9 (br s, 1H), 9.65 (s, 1H), 7.78 (s, 1H), 7.70 - 7.59 (m, 2H), 7.09 (s, 2H), 6.64 (s, 1H), 5.25 (s, 2H), 5.13 (dd, *J* = 5.1, 13.4 Hz, 1H), 4.52 - 4.42 (m, 1H), 4.39 - 4.28 (m, 1H), 2.99 - 2.84 (m, 1H), 2.60 (td, *J* = 2.1, 15.3 Hz, 1H), 2.40 (br dd, *J* = 4.4, 13.1 Hz, 1H), 2.21 (s, 6H), 2.06 - 1.98 (m, 1H). MS (ESI) *m/z* 422.1 [M+H]⁺

To a solution of 3,5-dimethylaniline (0.51 mL, 4.13 mmol, 1.00 eq) in acetonitrile (10.00 mL) was added pyridine (1.67 mL, 20.6 mmol, 5.00 eq) and phenyl chloroformate (1.03 mL, 8.25 mmol, 2.00 eq) at 0°C in portions. The reaction was stirred at 25°C for 1 h. The mixture was concentrated under reduced pressure to give a residue, which was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 1/0 to 3/1) to afford phenyl (3,5-dimethylphenyl) carbamate.

Compound 9: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-chloro-4-fluorophenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (br s, 1H), 10.05 (br s, 1H), 7.79 (s, 1H), 7.74 - 7.61 (m, 3H), 7.44 - 7.31 (m, 2H), 5.28 (s, 2H), 5.12 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.52 - 4.41 (m, 1H), 4.39 - 4.29 (m, 1H), 2.98 - 2.85 (m, 1H), 2.60 (br dd, *J* = 2.1, 15.4 Hz, 1H), 2.42 (dt, *J* = 4.4, 13.3 Hz, 1H), 2.05 - 1.96 (m, 1H). MS (ESI) *m/z* 446.1 [M+H]⁺

To a solution of 3-chloro-4-fluoroaniline (1.00 g, 6.87 mmol, 1.00 eq) in acetonitrile (10.0 mL) was added pyridine (2.77 mL, 34.4 mmol, 5.00 eq) and phenyl chloroformate (1.72 mL, 13.7 mmol, 2.00 eq) in portions at 0°C. The reaction was stirred at 25°C for 0.5 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (3-chloro-4-fluorophenyl)carbamate.

Compound 10: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-chloro-4-methylphenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 9.93 (s, 1H), 7.80 (s, 1H), 7.74 - 7.54 (m, 3H), 7.37 - 7.19 (m, 2H), 5.28 (s, 2H), 5.13 (dd, *J* = 5.1, 13.2 Hz, 1H), 4.53 - 4.44 (m, 1H), 4.38 - 4.31 (m, 1H), 2.98 - 2.87 (m, 1H), 2.61 (br d, *J* = 17.6 Hz, 1H), 2.41 (br dd, *J* = 4.4, 13.2 Hz, 1H), 2.26 (s, 3H), 2.06 - 1.97 (m, 1H). MS (ESI) *m/z* 442.1 [M+H]⁺

Preparation of phenyl (3-chloro-4-methylphenyl)carbamate: To a solution of 3-chloro-4-methylaniline (5.00 g, 35.3 mmol, 1.00 eq) in acetonitrile (50.0 mL) was added pyridine (5.70 mL, 70.6 mmol, 2.00 eq) and phenyl chloroformate (4.87 mL, 38.8 mmol, 1.10 eq) at 0 °C. The mixture was stirred at 30 °C for 2 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (3-chloro-4-methylphenyl)carbamate.

Compound 11: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-chloro-5-(trifluoromethoxy)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 10.35 (s, 1H), 7.81 (s, 1H), 7.73 - 7.68 (m, 1H), 7.67 - 7.62 (m, 1H), 7.60 - 7.49 (m, 2H), 7.17 (s, 1H), 5.31 (s, 2H), 5.13 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.53 - 4.44 (m, 1H), 4.39 - 4.31 (m, 1H), 2.99 - 2.85 (m, 1H), 2.64 - 2.58 (m, 1H), 2.41 (dd, *J* = 4.4, 13.0 Hz, 1H), 2.07 - 1.95 (m, 1H). MS (ESI) *m/z* 332.0 [M+H]⁺

To a solution of 3-chloro-5-(trifluoromethoxy)aniline (150 mg, 708 μ mol, 1.00 eq) in acetonitrile (1.00 mL) were added pyridine (0.29 mL, 3.54 mmol, 5.00 eq) and phenyl chloroformate (0.11 mL, 850 μ mol, 1.20 eq) at 0 °C. The reaction was stirred at 0°C for 2 h. The mixture was filtered to give a solution, which was purified by standard methods to afford phenyl (3-chloro-5-(trifluoromethoxy)phenyl)carbamate.

Compound 12: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-chloro-5-fluorophenyl)carbamate. ¹H NMR (400 MHz,

DMSO- d_6) δ = 10.99 (s, 1H), 10.25 (s, 1H), 7.80 (s, 1H), 7.74 - 7.56 (m, 2H), 7.44 - 7.28 (m, 2H), 7.10 - 6.96 (m, 1H), 5.30 (s, 2H), 5.18 - 5.06 (m, 1H), 4.54 - 4.42 (m, 1H), 4.40 - 4.31 (m, 1H), 2.98 - 2.86 (m, 1H), 2.62 (br d, J = 2.6 Hz, 1H), 2.46 - 2.37 (m, 1H), 2.05 - 1.96 (m, 1H). MS (ESI) m/z 446.0 $[M+H]^+$

- 5 To a solution of 3-chloro-5-fluoroaniline (1.00 g, 6.87 mmol, 1.00 eq) in acetonitrile (20.0 mL) were added pyridine (2.77 mL, 34.3 mmol, 5.00 eq) and phenyl chloroformate (1.29 mL, 10.3 mmol, 1.50 eq) at 0°C. The reaction was stirred at 25°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (3-chloro-5-fluorophenyl)carbamate.

- 10 **Compound 13:** General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-(2-oxa-5-azabicyclo[2.2.1]heptan-5-ylmethyl)-5-chloro-4-methylphenyl)carbamate.

- ^1H NMR (400 MHz, DMSO- d_6) δ = 11.00 (s, 1H), 9.89 (br s, 1H), 8.14 (s, 1H), 7.80 (s, 1H), 7.71 - 7.62 (m, 2H), 7.54 (br s, 1H), 7.41 (d, J = 1.5 Hz, 1H), 5.27 (s, 2H), 5.13 (dd, J = 5.0, 13.3 Hz, 1H), 4.46 (s, 1H), 4.37 (s, 2H), 3.91 (s, 1H), 3.72 - 3.64 (m, 2H), 3.54 (dd, J = 1.6, 7.4 Hz, 1H), 3.46 (br s, 1H), 2.97 - 2.87 (m, 1H), 2.75 (br d, J = 9.0 Hz, 1H), 2.61 (br d, J = 17.0 Hz, 1H), 2.47 (br d, J = 10.3 Hz, 1H), 2.41 (br dd, J = 4.6, 13.0 Hz, 1H), 2.26 (s, 3H), 2.07 - 1.97 (m, 1H), 1.80 (br s, 1H), 1.61 (br d, J = 9.3 Hz, 1H). MS (ESI) m/z 553.2 $[M+H]^+$

- 20 To a solution of 3-(2-oxa-5-azabicyclo[2.2.1]heptan-5-ylmethyl)-5-chloro-4-methylaniline (350 mg, 1.38 mmol, 1.00 eq) in acetonitrile (2.00 mL) were added pyridine (0.56 mL, 6.92 mmol, 5.00 eq) and phenyl chloroformate (0.21 mL, 1.66 mmol, 1.20 eq) at 0°C. The reaction was stirred at 0°C for 2 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (3-(2-oxa-5-azabicyclo[2.2.1]heptan-5-ylmethyl)-5-chloro-4-methylphenyl)carbamate.

Compound 14: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl(5-chloro-2-methoxyphenyl)carbamate.

- ^1H NMR (400 MHz, DMSO- d_6) δ = 10.99 (br s, 1H), 8.95 (s, 1H), 7.82 (s, 1H), 7.77 (br d, J = 1.5 Hz, 1H), 7.72 - 7.66 (m, 1H), 7.65 - 7.60 (m, 1H), 7.13 - 7.08 (m, 1H), 7.06 - 7.01 (m, 1H), 5.27 (s, 2H), 5.13 (dd, J = 5.1, 13.3 Hz, 1H), 4.51 - 4.43 (m, 1H), 4.37 -

4.30 (m, 1H), 3.80 (s, 3H), 2.97 - 2.86 (m, 1H), 2.60 (td, $J = 2.1, 15.3$ Hz, 1H), 2.40 (br dd, $J = 4.5, 13.1$ Hz, 1H), 2.05 - 1.97 (m, 1H). MS (ESI) m/z 458.1 $[M+H]^+$

To a solution of 5-chloro-2-methoxyaniline (1.00 g, 6.35 mmol, 1.00 eq) in acetonitrile (10.0 mL) were added pyridine (2.56 mL, 31.7 mmol, 5.00 eq) and phenyl chloroformate (1.59 mL, 12.7 mmol, 2.00 eq) in portions at 0°C. The reaction was stirred at 25°C for 1 h. The mixture was concentrated under reduced pressure to give a residue, which was diluted with water (50.0 mL) and extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with water, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC. The desired fraction was collected, and acetonitrile was removed under reduced pressure. The residual aqueous solution was extracted with ethyl acetate (3 × 50.0 mL). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated to afford phenyl(5-chloro-2-methoxyphenyl)carbamate.

Compound 15: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl(6-(piperidin-1-yl)pyridin-3-yl)carbamate.

^1H NMR (400 MHz, DMSO- d_6) δ = 10.99 (s, 1H), 10.12 (br s, 1H), 8.19 (br s, 1H), 7.95 - 7.89 (m, 1H), 7.79 (s, 1H), 7.70 - 7.62 (m, 2H), 7.41 (br d, $J = 9.3$ Hz, 1H), 5.29 (s, 2H), 5.12 (dd, $J = 5.1, 13.3$ Hz, 1H), 4.52 - 4.44 (m, 1H), 4.39 - 4.31 (m, 1H), 3.64 (br s, 4H), 2.91 (ddd, $J = 5.4, 13.6, 17.5$ Hz, 1H), 2.63 - 2.58 (m, 1H), 2.45 - 2.35 (m, 1H), 2.06 - 1.96 (m, 1H), 1.63 (br s, 6H). MS (ESI) m/z 478.1 $[M+H]^+$

Step 1: To a solution of 2-fluoro-5-nitro-pyridine (5.00 g, 35.2 mmol, 1.00 eq) in acetonitrile (50.0 mL) were added potassium carbonate (9.73 g, 70.4 mmol, 2.00 eq) and piperidine (4.17 mL, 42.2 mmol, 1.20 eq). The reaction was stirred at 25°C for 1 h. The mixture was filtered and concentrated under reduced pressure to afford 5-nitro-2-(1-piperidyl)pyridine.

Step 2: To a solution of 5-nitro-2-(piperidin-1-yl)pyridine (5.20 g, 25.1 mmol, 1.00 eq) and ammonium chloride (6.71 g, 125 mmol, 5.00 eq) in methanol (40.0 mL) and water (10.0 mL) was added iron powder (7.01 g, 126 mmol, 5.00 eq) in portions. The reaction was stirred at 80°C for 2 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was diluted with water (150 mL) and extracted with ethyl acetate (3 × 60.0 mL). The combined organic layers were washed with

brine (60.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC. The desired fraction was collected, diluted with saturated sodium bicarbonate (150 mL), and extracted with ethyl acetate (3 × 60.0 mL). The combined organic layers were washed with
5 brine (60.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 6-(piperidin-1-yl)pyridin-3-amine.

Step 3: To a solution of 6-(piperidin-1-yl)pyridin-3-amine (300 mg, 1.69 mmol, 1.00 eq) and pyridine (0.41 mL, 5.08 mmol, 3.00 eq) in acetonitrile (3.00 mL) was added phenyl chloroformate (0.32 mL, 2.54 mmol, 1.50 eq) dropwise at 0°C. The reaction was stirred at
10 25°C for 12 h. The mixture was diluted with water (50.0 mL) and extracted with ethyl acetate (3 × 40.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC. The desired fraction was collected, diluted with saturated sodium bicarbonate (30 mL), and extracted with ethyl acetate (3 ×
15 40.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over sodium sulfate, filtered, and concentrated to afford phenyl (6-(piperidin-1-yl)pyridin-3-yl)carbamate.

Compound 16:

Step 1: To a solution of *tert*-butyl 3-(hydroxymethyl)pyrrolidine-1-carboxylate (3.00 g, 14.9
20 mmol, 1.00 eq) and triethylamine (5.19 mL, 37.3 mmol, 2.50 eq) in dichloromethane (30.0 mL) at 0°C was added methylsulfamoyl chloride (1.50 mL, 19.4 mmol, 1.30 eq) dropwise over 2 min under nitrogen atmosphere. The reaction was then stirred at 25°C for 2 h. The mixture was diluted with ethyl acetate (100 mL) and water (150 mL). The organic layer was separated, and the aqueous phase was extracted with ethyl acetate (3 × 100 mL). The
25 combined organic layers were dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford *tert*-butyl 3-(((methylsulfonyl)oxy)methyl)pyrrolidine-1-carboxylate.

Step 2: A solution of *tert*-butyl 3-(((methylsulfonyl)oxy)methyl)pyrrolidine-1-carboxylate (3.00 g, 10.8 mmol, 1.00 eq), 3-chloro-5-nitrophenol (2.05 g, 11.8 mmol, 1.10 eq) and
30 caesium carbonate (10.5 g, 32.2 mmol, 3.00 eq) in dimethylformamide (30.0 mL) was stirred at 80°C for 12 h. The mixture was diluted with ethyl acetate (100 mL) and water (100 mL). The organic layer was separated, and the aqueous phase was extracted with ethyl

acetate (3 × 80.0 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 3/1) to afford *tert*-butyl 3-((3-chloro-5-nitrophenoxy)methyl)pyrrolidine-1-carboxylate.

- 5 **Step 3:** A solution of *tert*-butyl 3-((3-chloro-5-nitrophenoxy)methyl)pyrrolidine-1-carboxylate (2.00 g, 5.61 mmol, 1.00 eq), iron powder (2.19 g, 39.2 mmol, 7.00 eq) and ammonium chloride (2.10 g, 39.2 mmol, 7.00 eq) in methanol (30.0 mL) and water (30.0 mL) was stirred at 80°C for 2 h. The mixture was filtered over Celite, and the filtrate was concentrated under reduced pressure to afford *tert*-butyl 3-((3-amino-5-chlorophenoxy)methyl)pyrrolidine-1-carboxylate.
- 10

- Step 4:** A solution of phenyl chloroformate (0.11 mL, 918 μmol, 1.50 eq), *tert*-butyl 3-((3-amino-5-chlorophenoxy)methyl)pyrrolidine-1-carboxylate (200 mg, 612 μmol, 1.00 eq) and pyridine (0.15 mL, 1.84 mmol, 3.00 eq) in acetonitrile (2.00 mL) was stirred at 25°C for 12 h. The mixture was diluted with ethyl acetate (80.0 mL) and water (80.0 mL). The organic layer was separated, and the aqueous phase was extracted with ethyl acetate (3 × 50.0 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 3/1) to afford *tert*-butyl 3-((3-chloro-5-((phenoxycarbonyl)amino)phenoxy)methyl)pyrrolidine-1-carboxylate.
- 15

- 20 **Step 5:** A solution of 3-(6-(hydroxymethyl)-1-oxoisindolin-2-yl)piperidine-2,6-dione **VIII** (80.0 mg, 292 μmol, 1.00 eq), *tert*-butyl 3-((3-chloro-5-((phenoxycarbonyl)amino)phenoxy)methyl)pyrrolidine-1-carboxylate (156 mg, 350 μmol, 1.20 eq) and sodium hydride (60% dispersion in mineral oil) (23.3 mg, 583 μmol, 2.00 eq) in dimethylformamide (2.00 mL) was stirred at 0°C for 4 h. The mixture was quenched by addition by hydrochloric acid (1 M, 5.00 mL) and the filtrate was concentrated under reduced pressure to afford *tert*-butyl 3-((3-chloro-5-(((2-(2,6-dioxopiperidin-3-yl)-3-oxoisindolin-5-yl)methoxy)carbonyl)amino)phenoxy)methyl)pyrrolidine-1-carboxylate.
- 25

- Step 6:** A solution of *tert*-butyl 3-((3-chloro-5-(((2-(2,6-dioxopiperidin-3-yl)-3-oxoisindolin-5-yl)methoxy)carbonyl)amino)phenoxy)methyl)pyrrolidine-1-carboxylate (200 mg, 319 μmol, 1.00 eq) and hydrochloric acid (12 M, 26.6 μL, 1.00 eq) in water (2.00 mL) was stirred at 25°C for 12 h. The mixture was diluted with acetonitrile (2.00 mL) and
- 30

filtered. The filtrate was purified by a standard method to afford Compound 16. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 10.04 (s, 1H), 9.12 (br d, *J* = 2.7 Hz, 2H), 7.79 (s, 1H), 7.71 - 7.61 (m, 2H), 7.15 - 7.09 (m, 2H), 6.70 (t, *J* = 2.0 Hz, 1H), 5.28 (s, 2H), 5.16 - 5.08 (m, 1H), 4.52 - 4.43 (m, 1H), 4.38 - 4.31 (m, 1H), 4.03 - 3.93 (m, 2H), 3.30 - 3.10 (m, 3H), 3.05 - 2.84 (m, 2H), 2.78 - 2.65 (m, 1H), 2.60 (br d, *J* = 16.8 Hz, 1H), 2.47 - 2.35 (m, 1H), 2.13 - 1.96 (m, 2H), 1.80 - 1.68 (m, 1H). MS (ESI) *m/z* 527.3 [M+H]⁺

Compound 17:

Step 1: To a solution of 2-(2,6-dioxo-1-((2-(trimethylsilyl)ethoxy)methyl)piperidin-3-yl)-3-oxoisindoline-5-Carbaldehyde **V** (750 mg, 1.86 mmol, 1.00 eq) in dichloromethane (10.0 mL) was added methylmagnesium bromide 3.00 M in diethyl ether (3.00 M, 0.75 mL, 1.20 eq) dropwise at -78°C. The reaction was stirred at -78°C for 2 h. The reaction was quenched with ammonium chloride (50.0 mL) to reach pH = 7, and the mixture was extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduces pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1 to 2/3) to afford 3-(6-(1-hydroxyethyl)-1-oxoisindolin-2-yl)-1-((2-(trimethylsilyl) ethoxy)methyl)piperidine-2,6-dione.

Step 2: A solution of 3-(6-(1-hydroxyethyl)-1-oxoisindolin-2-yl)-1-((2-(trimethylsilyl)ethoxy) methyl)piperidine-2,6-dione (600 mg, 1.43 mmol, 1.00 eq) in hydrochloric acid/dioxane (6 M, 6.67 mL, 27.9 eq) was stirred at 50°C for 1 h. The mixture was concentrated under reduced pressure to afford 3-(6-(1-hydroxyethyl)-1-oxoisindolin-2-yl)-1-(hydroxymethyl)piperidine-2,6-dione.

Step 3: To a solution of 3-(6-(1-hydroxyethyl)-1-oxoisindolin-2-yl)-1-(hydroxymethyl)piperidine-2,6-dione (450 mg, 1.41 mmol, 1.00 eq) in acetonitrile (10.0 mL) was added ammonium hydroxide 30% (0.20 mL, 1.56 mmol, 1.10 eq) dropwise. The reaction was stirred at 25°C for 0.5 h. The reaction was quenched with 1M HCl to reach pH = 3 and concentrated under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC to afford 3-(6-(1-hydroxyethyl)-1-oxoisindolin-2-yl)piperidine-2,6-dione.

Step 4: To a solution of 3-(6-(1-hydroxyethyl)-1-oxoisindolin-2-yl)piperidine-2,6-dione (85.0 mg, 295 μ mol, 1.00 eq) and phenyl (3-chloro-4-methylphenyl)carbamate (described

in example 1) (84.9 mg, 324 μ mol, 1.10 eq) in dimethylformamide (3.00 mL) was added sodium hydride (60% dispersion in mineral oil) (23.6 mg, 590 μ mol, 2.00 eq) in portions at 0°C. The reaction was stirred at 0°C for 0.5 h. The reaction was quenched with 1M hydrochloric acid (2.00 mL), filtered, and concentrated to give a residue. The residue was
5 purified by a standard method to afford Compound 17. ¹H NMR (400MHz, DMSO-*d*₆) δ = 11.00 (br s, 1H), 9.93 (br s, 1H), 7.77 (s, 1H), 7.71 - 7.60 (m, 2H), 7.58 (d, *J* = 1.6 Hz, 1H), 7.35 - 7.18 (m, 2H), 5.91 (q, *J* = 6.4 Hz, 1H), 5.13 (dd, *J* = 5.0, 13.3 Hz, 1H), 4.56 - 4.26 (m, 2H), 2.98 - 2.86 (m, 1H), 2.65 - 2.56 (m, 1H), 2.45 - 2.35 (m, 1H), 2.24 (s, 3H), 2.06 - 1.96 (m, 1H), 1.58 (d, *J* = 6.6 Hz, 3H). MS (ESI) *m/z* 456.1 [M+H]⁺

10 **Compound 18:** General procedure A with variant i) was used for the preparation from compound VIII employing phenyl (2,3-dihydrobenzofuran-6-yl)carbamate.

¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 9.72 (br s, 1H), 7.79 (s, 1H), 7.69 - 7.61 (m, 2H), 7.09 (d, *J* = 8.0 Hz, 1H), 6.98 (s, 1H), 6.88 (br d, *J* = 7.9 Hz, 1H), 5.25 (s, 2H), 5.13 (dd, *J* = 5.1, 13.2 Hz, 1H), 4.54 - 4.43 (m, 3H), 4.38 - 4.30 (m, 1H), 3.08 (t, *J* = 8.6
15 Hz, 2H), 2.98 - 2.85 (m, 1H), 2.63 - 2.57 (m, 1H), 2.43 - 2.33 (m, 1H), 2.06 - 1.96 (m, 1H). MS (ESI) *m/z* 436.2 [M+H]⁺

To a solution of 2,3-dihydrobenzofuran-6-amine (200 mg, 1.48 mmol, 1.00 eq) in acetonitrile (8.00 mL) were added pyridine (0.60 mL, 7.40 mmol, 5.00 eq) and phenyl chloroformate (0.37 mL, 2.96 mmol, 2.00 eq) at 0°C in portions. The reaction was stirred at
20 25°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (2,3-dihydrobenzofuran-6-yl)carbamate.

Compound 19: General procedure A with variant i) was used for the preparation from compound VIII employing phenyl (3-chloro-5-(difluoromethoxy)phenyl)carbamate.

¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 10.23 (s, 1H), 7.79 (s, 1H), 7.72 - 7.61 (m, 2H), 7.42 (t, *J* = 1.8 Hz, 1H), 7.31 (s, 1H), 7.06 (t, *J* = 4.4 Hz, 1H), 6.94 (t, *J* = 2.0 Hz, 1H), 5.29 (s, 2H), 5.12 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.51 - 4.43 (m, 1H), 4.38 - 4.30 (m, 1H), 2.97 - 2.85 (m, 1H), 2.60 (br d, *J* = 17.5 Hz, 1H), 2.40 (dd, *J* = 4.4, 13.1 Hz, 1H), 2.06 - 1.96 (m, 1H). MS (ESI) *m/z* 494.1 [M+H]⁺
25

Step 1: To a solution of 3-chloro-5-nitro-phenol (1.50 g, 8.64 mmol, 1.00 eq) and sodium 2-chloro-2,2-difluoroacetate (5.27 g, 34.6 mmol, 4.00 eq) in dimethylformamide (17.0 mL) and water (2.00 mL) was added potassium carbonate (2.39 g, 17.3 mmol, 2.00 eq).
30

The reaction was stirred at 100°C for 12 h. The mixture was filtered and concentrated under reduced pressure to give a residue. The residue was diluted with water (100 mL) and extracted with ethyl acetate (3 × 20.0 mL). The combined organic layers were washed with saturated sodium carbonate solution (50.0 mL) and brine (20.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 1-chloro-3-(difluoromethoxy)-5-nitrobenzene.

Step 2: To a solution of 1-chloro-3-(difluoromethoxy)-5-nitrobenzene (1.70 g, 7.60 mmol, 1.00 eq) in methanol (10.0 mL) and water (10.0 mL) were added iron powder (2.12 g, 38.0 mmol, 5.00 eq) and ammonium chloride (2.03 g, 38.0 mmol, 5.00 eq). The reaction was stirred at 80°C for 2 h. The mixture was concentrated under reduced pressure to give a residue. The residue was diluted with saturated sodium bicarbonate solution (20.0 mL) and extracted with ethyl acetate (3 × 20.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-chloro-5-(difluoromethoxy)aniline.

Step 3: To a solution 3-chloro-5-(difluoromethoxy)aniline (400 mg, 2.07 mmol, 1.00 eq) in acetonitrile (10.0 mL) were added pyridine (0.83 mL, 10.3 mmol, 5.00 eq) and phenyl chloroformate (0.39 mL, 3.10 mmol, 1.50 eq). The reaction was stirred at 25°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (3-chloro-5-(difluoromethoxy)phenyl)carbamate.

Compound 20:

Step 1: To a solution of 3-(6-(hydroxymethyl)-1-oxoisindolin-2-yl)piperidine-2,6-dione (120 mg, 437 µmol, 1.00 eq) and *tert*-butyl 3-(3-chloro-5-((phenoxycarbonyl)amino)phenoxy)pyrrolidine-1-carboxylate (284 mg, 656 µmol, 1.50 eq) in dimethylformamide (2.00 mL) was added sodium hydride (60% dispersion in mineral oil) (35.0 mg, 875 µmol, 2.00 eq). The reaction was stirred at 25°C for 1 h.

Step 2: A solution of *tert*-butyl 3-(3-chloro-5-(((2-(2,6-dioxopiperidin-3-yl)-3-oxoisindolin-5-yl)methoxy)carbonyl)amino)phenoxy)pyrrolidine-1-carboxylate (250 mg, 407 µmol, 1.00 eq) in hydrochloric acid (4 M, 5.00 mL, 49.0 eq) was stirred at 25°C for 12 h. The mixture was concentrated under reduced pressure to give a residue. The residue was purified by a standard method to afford Compound 20. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 10.07 (s, 1H), 9.32 - 9.13 (m, 2H), 7.80 (s, 1H), 7.75 - 7.60 (m, 2H), 7.23

- 7.09 (m, 2H), 6.75 (t, $J = 2.0$ Hz, 1H), 5.29 (s, 2H), 5.18 - 5.08 (m, 2H), 4.56 - 4.41 (m, 1H), 4.41 - 4.31 (m, 1H), 3.32 - 3.21 (m, 2H), 3.00 - 2.87 (m, 1H), 2.63 (br d, $J = 2.8$ Hz, 2H), 2.43 (dt, $J = 4.5, 13.1$ Hz, 2H), 2.25 - 2.10 (m, 2H), 2.06 - 1.97 (m, 1H). MS (ESI) m/z 513.0 $[M+H]^+$

- 5 Preparation of *tert*-butyl 3-(3-chloro-5-((phenoxycarbonyl)amino) phenoxy)pyrrolidine-1-carboxylate:

Step 1: To a solution of 3-chloro-5-nitro-phenol (5.00 g, 28.8 mmol, 1.00 eq), *tert*-butyl 3-hydroxypyrrolidine-1-carboxylate (5.93 g, 31.7 mmol, 1.10 eq) and triphenylphosphine (8.31 g, 31.7 mmol, 1.10 eq) in tetrahydrofuran (2.00 mL) was added diisopropyl azodiformate (6.16 mL, 31.7 mmol, 1.10 eq) at 0°C. The reaction was stirred at 25°C for 12
10 h. The mixture was concentrated under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC to afford *tert*-butyl 3-(3-chloro-5-nitrophenoxy)pyrrolidine-1-carboxylate.

Step 2: A mixture of *tert*-butyl 3-(3-chloro-5-nitro-phenoxy)pyrrolidine-1-carboxylate (3.00
15 g, 8.75 mmol, 100 eq), iron powder (1.47 g, 26.2 mmol, 3.00 eq) and ammonium chloride (2.34 g, 43.8 mmol, 5.00 eq) in methanol (20.0 mL) and water (10.0 mL) was stirred at 80°C for 2 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. It was added to water (80.0 mL) and saturated sodium bicarbonate (40.0 mL) and stirred for 10 min. The aqueous layer was extracted with ethyl acetate (3 ×
20 60.0 mL). The combined organic layers were washed with brine (100 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford *tert*-butyl 3-(3-amino-5-chlorophenoxy)pyrrolidine-1-carboxylate.

Compound 21: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-(8-oxa-3-azabicyclo[3.2.1]octan-3-ylmethyl)-5-
25 chloro-4-methylphenyl)carbamate. ^1H NMR (400 MHz, DMSO- d_6) $\delta = 11.05 - 10.93$ (m, 1H), 9.95 - 9.84 (m, 1H), 7.79 (s, 1H), 7.71 - 7.61 (m, 2H), 7.51 (s, 1H), 7.33 (d, $J = 1.7$ Hz, 1H), 5.27 (s, 2H), 5.12 (dd, $J = 5.2, 13.4$ Hz, 1H), 4.51 - 4.42 (m, 1H), 4.39 - 4.29 (m, 1H), 4.21 - 4.15 (m, 2H), 2.95 - 2.86 (m, 1H), 2.60 (br dd, $J = 1.7, 16.8$ Hz, 1H), 2.45 (br d, $J = 10.3$ Hz, 4H), 2.41 - 2.36 (m, 1H), 2.29 - 2.25 (m, 3H), 2.19 (br d, $J = 9.8$ Hz,
30 2H), 2.04 - 1.98 (m, 1H), 1.88 - 1.79 (m, 2H), 1.68 (br dd, $J = 4.1, 7.0$ Hz, 2H). MS (ESI) m/z 567.2 $[M+H]^+$

Step 1: To a solution of (3-chloro-2-methyl-5-nitro-phenyl)methanol (2.00 g, 9.92 mmol, 1.00 eq) in dichloromethane (30.0 mL) was added thionyl chloride (3.60 mL, 49.6 mmol, 5.00 eq) at 25°C. The reaction was stirred at 25°C for 12 h. The reaction was quenched by addition of ice water (20.0 mL) at 0°C, and the aqueous layer was extracted with ethyl acetate (3 × 20.0 mL). The combined organic layers were washed with brine (30.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 1-chloro-3-(chloromethyl)-2-methyl-5-nitrobenzene.

Step 2: To a solution of 1-chloro-3-(chloromethyl)-2-methyl-5-nitro-benzene (1.40 g, 6.36 mmol, 1.00 eq), 8-oxa-3-azabicyclo[3.2.1]octane (1.14 g, 7.63 mmol, 1.20 eq, HCl) and potassium carbonate (2.64 g, 19.1 mmol, 3.00 eq) in acetonitrile (20.0 mL) was added potassium iodide (106 mg, 0.64 mmol, 0.10 eq) at 25°C. The reaction was stirred at 80°C for 12 h. The mixture was filtered and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1 to 2/1) to afford 3-(3-chloro-2-methyl-5-nitrobenzyl)-8-oxa-3-azabicyclo[3.2.1]octane.

Step 3: To a solution of 3-(3-chloro-2-methyl-5-nitrobenzyl)-8-oxa-3-azabicyclo[3.2.1]octane (1.00 g, 3.37 mmol, 1.00 eq) in methanol (20.0 mL) were added iron powder (941 mg, 16.9 mmol, 5.00 eq), ammonium chloride (901 mg, 16.9 mmol, 5.00 eq) and water (5.00 mL) at 25°C. The reaction was stirred at 80°C for 2 h. The mixture was concentrated under reduced pressure to give a residue. Sodium bicarbonate (20.0 mL) was added, and the aqueous layer was extracted with ethyl acetate (3 × 20.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-(8-oxa-3-azabicyclo[3.2.1]octan-3-ylmethyl)-5-chloro-4-methylaniline.

Step 4: To a solution of 3-(8-oxa-3-azabicyclo[3.2.1]octan-3-ylmethyl)-5-chloro-4-methylaniline (200 mg, 749 µmol, 1.00 eq) in acetonitrile (5.00 mL) were added pyridine (0.30 mL, 3.75 mmol, 5.00 eq) and phenyl chloroformate (0.14 mL, 1.12 mmol, 1.50 eq). The reaction was stirred at 25°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (3-(8-oxa-3-azabicyclo[3.2.1]octan-3-ylmethyl)-5-chloro-4-methylphenyl)carbamate.

Compound 22: General procedure A with variant ii) was used for the preparation from compound VIII employing cyclopropylmethanamine. ¹H NMR (400 MHz, DMSO-*d*₆) δ =

10.99 (s, 1H), 7.71 (s, 1H), 7.60 (s, 2H), 7.40 (br t, $J = 5.6$ Hz, 1H), 5.16 - 5.06 (m, 3H), 4.49 - 4.42 (m, 1H), 4.36 - 4.29 (m, 1H), 2.96 - 2.85 (m, 3H), 2.65 - 2.56 (m, 1H), 2.43 - 2.37 (m, 1H), 2.06 - 1.96 (m, 1H), 0.96 - 0.85 (m, 1H), 0.43 - 0.35 (m, 2H), 0.19 - 0.09 (m, 2H). MS (ESI) m/z 372.1 $[M+H]^+$

- 5 **Compound 23:** General procedure A with variant ii) was used for the preparation from compound **VIII** employing piperidine. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) $\delta = 11.06 - 10.92$ (m, 1H), 7.69 (s, 1H), 7.64 - 7.54 (m, 2H), 5.17 (s, 2H), 5.11 (dd, $J = 5.1, 13.3$ Hz, 1H), 4.51 - 4.41 (m, 1H), 4.38 - 4.28 (m, 1H), 3.37 (br s, 4H), 2.97 - 2.85 (m, 1H), 2.60 (br d, $J = 17.6$ Hz, 1H), 2.40 (br dd, $J = 4.3, 13.0$ Hz, 1H), 2.06 - 1.95 (m, 1H), 1.59 - 1.50 (m, 2H),
10 1.48 - 1.39 (m, 4H). MS (ESI) m/z 386.1 $[M+H]^+$

Compound 24: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-(difluoromethoxy)-4-methylphenyl)carbamate. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) $\delta = 10.99$ (br s, 1H), 9.92 (br s, 1H), 7.79 (s, 1H), 7.70 - 7.61 (m, 2H), 7.41 (s, 1H), 7.19 (s, 2H), 7.09 (t, $J = 74$ Hz, 1H), 5.27 (s, 2H), 5.12 (dd, $J =$
15 5.1, 13.2 Hz, 1H), 4.52 - 4.43 (m, 1H), 4.38 - 4.30 (m, 1H), 2.96 - 2.85 (m, 1H), 2.63 - 2.57 (m, 1H), 2.40 (br dd, $J = 4.3, 13.1$ Hz, 1H), 2.15 (s, 3H), 2.04 - 1.96 (m, 1H). MS (ESI) m/z 474.1 $[M+H]^+$

Step 1: To a solution of 2-methyl-5-nitrophenol (5.00 g, 32.7 mmol, 1.00 eq) and sodium 2-chloro-2,2-difluoroacetate (12.4 g, 81.6 mmol, 2.50 eq) in dimethylformamide (50.0
20 mL) was added caesium carbonate (21.3 g, 65.3 mmol, 2.00 eq) in portions. The reaction was stirred at 100°C for 2 h. The mixture was diluted with water (800 mL) and extracted with ethyl acetate (3×100 mL). The combined organic layers were washed with brine (80.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum
25 ether/ethyl acetate = 1/0 to 10/1) to afford 2-(difluoromethoxy)-1-methyl-4-nitrobenzene.

Step 2: To a solution of 2-(difluoromethoxy)-1-methyl-4-nitrobenzene (4.85 g, 23.8 mmol, 1.00 eq) and ammonium chloride (6.39 g, 119 mmol, 5.00 eq) in methanol (40.0 mL) and water (40.0 mL) was added iron powder (4.00 g, 71.6 mmol, 3.00 eq) in portions. The reaction was stirred at 80°C for 2 h. The mixture was filtered, and the filtrate was concentrated
30 under reduced pressure to give a residue. Water (100 mL) was added, and the mixture was extracted with ethyl acetate (3×50.0 mL). The combined organic layers were washed with

brine (20 mL), dried over anhydrous sodium sulfate, filtered, and concentrated to afford 3-(difluoromethoxy)-4-methylaniline.

Step 3: To a solution of 3-(difluoromethoxy)-4-methylaniline (1.00 g, 5.78 mmol, 1.00 eq) and pyridine (1.40 mL, 17.3 mmol, 3.00 eq) in acetonitrile (10.0 mL) was added phenyl chloroformate (1.09 mL, 8.66 mmol, 1.50 eq) dropwise. The reaction was stirred at 25°C for 12 h. The mixture was diluted with water (150 mL) and extracted with ethyl acetate (3 × 50.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated and the obtained residue was purified by standard methods to afford phenyl (3-(difluoromethoxy)-4-methylphenyl)carbamate.

Compound 25: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-(difluoromethoxy)-4-methyl-5-(morpholinomethyl)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 9.89 (s, 1H), 8.21 (s, 1H), 7.78 (s, 1H), 7.70 - 7.60 (m, 2H), 7.35 (br s, 1H), 7.26 (d, *J* = 1.8 Hz, 1H), 7.25 - 6.85 (m, 1H), 5.27 (s, 2H), 5.16 - 5.08 (m, 1H), 4.51 - 4.28 (m, 2H), 3.55 (br t, *J* = 4.3 Hz, 4H), 3.39 (s, 2H), 2.98 - 2.84 (m, 1H), 2.65 - 2.56 (m, 1H), 2.45 - 2.38 (m, 1H), 2.35 (br s, 4H), 2.14 (s, 3H), 2.06 - 1.96 (m, 1H). MS (ESI) *m/z* 573.4 [M+H]⁺

Step 1: To a solution of 2-methyl-5-nitro-benzoic acid (10.0 g, 55.2 mmol, 1.00 eq) in sulfuric acid (20.0 mL) was added *N*-Iodosuccinimide (14.9 g, 66.3 mmol, 1.20 eq). The reaction was stirred at 60°C for 2 h. The mixture was diluted with ice water (200 mL) and the resulting precipitate was collected by filtration. The filter cake was washed with water (100 mL) and dried under vacuum to afford 3-iodo-2-methyl-5-nitro-benzoic acid.

Step 2: To a solution of 3-iodo-2-methyl-5-nitro-benzoic acid (5.00 g, 16.3 mmol, 1.00 eq), copper iodide (310 mg, 1.63 mmol, 0.100 eq), and quinolin-8-ol (0.56 mL, 3.26 mmol, 0.200 eq) in water (3.00 mL) and dimethylsulfoxide (3.00 mL) was added potassium hydroxide (3.65 g, 65.1 mmol, 4.00 eq). The reaction was stirred at 100°C for 12 h. The mixture was diluted with water (50.0 mL) and extracted with ethyl acetate (2 × 50.0 mL). The combined organic layers were washed with water (50.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-hydroxy-2-methyl-5-nitro-benzoic acid.

Step 3: To a solution of 3-hydroxy-2-methyl-5-nitro-benzoic acid (3.20 g, 16.2 mmol, 1.00 eq) and morpholine (1.71 mL, 19.5 mmol, 1.20 eq) in dichloromethane (100 mL) were added triethylamine (2.26 mL, 16.2 mmol, 1.00 eq) and *O*-(7-azabenzotriazol-1-yl)-*N,N,N,N*-tetramethyluroniumhexafluorophosphate (7.41 g, 19.5 mmol, 1.20 eq) at 20°C.

5 The reaction was stirred at 20°C for 12 h. The mixture was concentrated under reduced pressure to afford a residue. The residue was diluted with water (100 mL) and extracted with ethyl acetate (100 mL). The organic layer was washed with water (100 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum
10 ether/ethyl acetate = 1/1 to 0/1) to afford (3-hydroxy-2-methyl-5-nitro-phenyl)-morpholino-methanone.

Step 4: A solution of (3-hydroxy-2-methyl-5-nitro-phenyl)-morpholino-methanone (2.00 g, 7.51 mmol, 1.00 eq), potassium carbonate (2.08 g, 15.0 mmol, 2.00 eq) and sodium 2-chloro-2,2-difluoroacetate (4.58 g, 30.0 mmol, 4.00 eq) in dimethylformamide (24.0 mL)
15 and water (3.00 mL) was stirred at 100°C for 12 h. The mixture was diluted with water (150 mL) and extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with brine (50.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 3/1) to afford (3-(difluoromethoxy)-2-
20 methyl-5-nitrophenyl)(morpholino)methanone.

Step 5: To a solution of (3-(difluoromethoxy)-2-methyl-5-nitrophenyl)(morpholino)methanone (1.70 g, 5.38 mmol, 1.00 eq) in tetrahydrofuran (3.00 mL) was added borane dimethyl sulfide complex (10 M, 1.08 mL, 2.00 eq) dropwise at 0°C under nitrogen atmosphere. The reaction was stirred at 60°C for 4 h. The reaction was
25 quenched by addition with methanol (5.00 mL) and the solvents were removed under reduced pressure to afford 4-(3-(difluoromethoxy)-2-methyl-5-nitrobenzyl)morpholine.

Step 6: A solution of 4-(3-(difluoromethoxy)-2-methyl-5-nitrobenzyl)morpholine (1.50 g, 4.96 mmol, 1.00 eq), iron powder (1.94 g, 34.7 mmol, 7.00 eq) and ammonium chloride (1.86 g, 34.7 mmol, 7.00 eq) in methanol (5.00 mL) and water (5.00 mL) was stirred at
30 80°C for 2 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to afford 3-(difluoromethoxy)-4-methyl-5-(morpholinomethyl)aniline.

Step 7: To a solution of 3-(difluoromethoxy)-4-methyl-5-(morpholinomethyl)aniline (500 mg, 1.84 mmol, 1.00 eq) in acetonitrile (5.00 mL) were added pyridine (0.45 mL, 5.51 mmol, 3.00 eq) and phenyl chloroformate (0.28 mL, 2.20 mmol, 1.20 eq). The reaction was stirred at 25°C for 2 h. The mixture was diluted with ethyl acetate (80.0 mL) and water (80.0 mL). The organic layer was separated, and the aqueous phase was extracted with ethyl acetate (3 × 50.0 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated and the obtained residue was purified by standard methods to afford phenyl (3-(difluoromethoxy)-4-methyl-5-(morpholinomethyl)phenyl) carbamate.

Compound 26: General procedure A with variant ii) was used for the preparation from compound **VIII** employing pyrrolidine. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 7.70 (s, 1H), 7.65 - 7.58 (m, 2H), 5.17 (s, 2H), 5.12 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.51 - 4.41 (m, 1H), 4.37 - 4.27 (m, 1H), 3.31 - 3.25 (m, 4H), 2.98 - 2.86 (m, 1H), 2.60 (br d, *J* = 17.5 Hz, 1H), 2.43 - 2.32 (m, 1H), 2.05 - 1.97 (m, 1H), 1.86 - 1.76 (m, 4H). MS (ESI) *m/z* 372.2 [M+H]⁺

Compound 27: General procedure A with variant ii) was used for the preparation from compound **VIII** employing 3-methylbutan-1-amine. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 7.70 (s, 1H), 7.66 - 7.55 (m, 2H), 7.28 (br t, *J* = 5.4 Hz, 1H), 5.22 - 5.06 (m, 3H), 4.52 - 4.42 (m, 1H), 4.38 - 4.28 (m, 1H), 3.06 - 2.98 (m, 2H), 2.97 - 2.86 (m, 1H), 2.64 - 2.57 (m, 1H), 2.44 - 2.36 (m, 1H), 2.06 - 1.97 (m, 1H), 1.63 - 1.50 (m, 1H), 1.30 (q, *J* = 6.9 Hz, 2H), 0.86 (d, *J* = 6.6 Hz, 6H). MS (ESI) *m/z* 388.2 [M+H]⁺

Compound 28: General procedure A with variant ii) was used for the preparation from compound **VIII** employing cyclohexanamine. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 7.72 (s, 1H), 7.61 (s, 2H), 7.25 (br d, *J* = 7.9 Hz, 1H), 5.18 - 5.08 (m, 3H), 4.50 - 4.42 (m, 1H), 4.37 - 4.29 (m, 1H), 3.30 - 3.22 (m, 1H), 2.98 - 2.86 (m, 1H), 2.61 (br dd, *J* = 2.1, 15.6 Hz, 1H), 2.44 - 2.34 (m, 1H), 2.06 - 1.95 (m, 1H), 1.76 (br d, *J* = 11.7 Hz, 2H), 1.71 - 1.61 (m, 2H), 1.54 (br d, *J* = 12.8 Hz, 1H), 1.31 - 1.07 (m, 5H). MS (ESI) *m/z* 400.2 [M+H]⁺

Compound 29: General procedure A with variant ii) was used for the preparation from compound **VIII** employing cyclopentanamine. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.98 (br s, 1H), 7.71 (s, 1H), 7.60 (s, 2H), 7.31 (br d, *J* = 7.1 Hz, 1H), 5.19 - 5.07 (m, 3H), 4.50 - 4.41 (m, 1H), 4.37 - 4.28 (m, 1H), 3.85 - 3.74 (m, 1H), 2.98 - 2.85 (m, 1H), 2.65 - 2.57

(m, 1H), 2.43 - 2.34 (m, 1H), 2.05 - 1.95 (m, 1H), 1.83 - 1.71 (m, 2H), 1.65 - 1.54 (m, 2H), 1.52 - 1.35 (m, 4H). MS (ESI) m/z 386.1 $[M+H]^+$

Compound 30: General procedure A with variant ii) was used for the preparation from compound **VIII** employing 3-phenoxy pyrrolidine. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ = 11.00 (s, 1H), 7.77 - 7.68 (m, 1H), 7.68 - 7.56 (m, 2H), 7.37 - 7.20 (m, 2H), 7.05 - 6.84 (m, 3H), 5.30 - 5.08 (m, 3H), 5.07 - 4.98 (m, 1H), 4.54 - 4.40 (m, 1H), 4.38 - 4.27 (m, 1H), 3.72 - 3.57 (m, 1H), 3.55 - 3.41 (m, 3H), 2.97 - 2.87 (m, 1H), 2.65 - 2.58 (m, 1H), 2.41 (br dd, J = 4.5, 12.8 Hz, 1H), 2.19 - 1.99 (m, 3H). MS (ESI) m/z 464.1 $[M+H]^+$

Step 1: To a solution of *tert*-butyl 3-hydroxypyrrolidine-1-carboxylate (3.00 g, 16.0 mmol, 1.00 eq) and triethylamine (5.58 mL, 40.0 mmol, 2.50 eq) in dichloromethane (30.0 mL) was added methanesulfonyl chloride (1.74 mL, 22.4 mmol, 1.40 eq) dropwise at 0°C. The reaction was stirred at 25°C for 2 h. The mixture was diluted with water (150 mL) and extracted with ethyl acetate (3 $\times$ 80.0 mL). The combined organic layers were washed with brine (60.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford *tert*-butyl 3-((methylsulfonyl)oxy)pyrrolidine-1-carboxylate.

Step 2: To a solution of *tert*-butyl 3-((methylsulfonyl)oxy)pyrrolidine-1-carboxylate (1.00 g, 3.77 mmol, 1.00 eq) and phenol (0.40 mL, 4.52 mmol, 1.20 eq) in dimethylformamide (10.0 mL) was added caesium carbonate (3.68 g, 11.3 mmol, 3.00 eq) in one portion. The reaction was stirred at 80°C for 12 h. The mixture was diluted with water (50.0 mL) and extracted with ethyl acetate (3 $\times$ 60.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 20/1 to 5/1) and then by reversed phase preparative HPLC to afford *tert*-butyl 3-phenoxy pyrrolidine-1-carboxylate.

Step 3: A solution of *tert*-butyl 3-phenoxy pyrrolidine-1-carboxylate (460 mg, 1.75 mmol, 1.00 eq) in 4 M hydrochloric acid/dioxane (4.00 mL) was stirred at 25°C for 1 h and concentrated to afford 3-phenoxy pyrrolidine.

Compound 31: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-(difluoromethoxy)-5-fluorophenyl) carbamate. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ = 11.00 (br s, 1H), 10.25 (s, 1H), 7.80 (s, 1H), 7.72 - 7.62 (m, 2H), 7.24 (t, J = 73.2 Hz, 1H), 7.23 - 7.19 (m, 1H), 7.16 (s, 1H), 6.76 (td, J = 2.2, 9.7 Hz,

1H), 5.30 (s, 2H), 5.13 (dd, $J = 5.1, 13.3$ Hz, 1H), 4.51 - 4.45 (m, 1H), 4.38 - 4.32 (m, 1H), 2.95 - 2.86 (m, 1H), 2.64 - 2.60 (m, 1H), 2.46 - 2.36 (m, 1H), 2.05 - 1.98 (m, 1H). MS (ESI) m/z 478.1 $[M+H]^+$

Step 1: To a solution of methanol (3.00 mL, 74.1 mmol, 3.93 eq) in *N*-methyl-pyrrolidone (10.0 mL) was added sodium hydride (60% dispersion in mineral oil) (830 mg, 20.7 mmol, 1.10 eq). The reaction was stirred at 0°C for 1 h, then 1,3-difluoro-5-nitro-benzene (3.00 g, 18.9 mmol, 1.00 eq) was added. The reaction was stirred at 25°C for another 11 h. The reaction was quenched with 1M hydrochloric acid (40.0 mL) and extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with brine (15.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1 to 1/1) to afford 1-fluoro-3-methoxy-5-nitro-benzene.

Step 2: To a solution of 1-fluoro-3-methoxy-5-nitro-benzene (2.50 g, 14.6 mmol, 1.00 eq) in dichloromethane (15.0 mL) was added boron tribromide (11.0 g, 43.8 mmol, 4.22 mL, 3.00 eq) at -78°C. The reaction was stirred at -78°C for 1 h, and then at 25°C for 11 h. The reaction was quenched with methanol (30.0 mL) and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1 to 5/1) to afford 3-fluoro-5-nitro-phenol.

Step 3: A solution of 3-fluoro-5-nitro-phenol (0.500 g, 3.18 mmol, 1.00 eq), sodium 2-chloro-2,2-difluoro-acetate (1.46 g, 9.55 mmol, 3.00 eq) and potassium carbonate (879 mg, 6.37 mmol, 2.00 eq) in dimethylformamide (10.0 mL) and water (2.00 mL) was stirred at 100°C for 12 h. The mixture was poured into water (20.0 mL). The aqueous phase was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with brine (30.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1 to 5/1) to afford 1-(difluoromethoxy)-3-fluoro-5-nitrobenzene.

Step 4: A mixture of 1-(difluoromethoxy)-3-fluoro-5-nitrobenzene (700 mg, 3.38 mmol, 1.00 eq), ferrous powder (566 mg, 10.1 mmol, 3.00 eq) and ammonium chloride (904 mg, 16.9 mmol, 5.00 eq) in methanol (6.00 mL) and water (3.00 mL) was stirred at 80°C for 1 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to afford 3-(difluoromethoxy)-5-fluoroaniline.

Step 5: To a solution of 3-(difluoromethoxy)-5-fluoroaniline (300 mg, 1.69 mmol, 1.00 eq) in acetonitrile (20.0 mL) were added pyridine (0.68 mL, 8.42 mmol, 4.97 eq) and phenyl chloroformate (0.25 mL, 2.00 mmol, 1.18 eq) at 0°C. The reaction was stirred at 25°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (3-(difluoromethoxy)-5-fluorophenyl)carbamate.

Compound 32: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-(difluoromethoxy)-4-fluorophenyl) carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 10.04 (s, 1H), 7.80 (s, 1H), 7.71 - 7.67 (m, 1H), 7.67 - 7.63 (m, 1H), 7.58 (br d, *J* = 6.6 Hz, 1H), 7.37 - 7.27 (m, 2H), 7.21 (t, *J* = 73.2 Hz, 1H), 5.29 (s, 2H), 5.13 (br d, *J* = 8.2 Hz, 1H), 4.46 (s, 1H), 4.40 - 4.30 (m, 1H), 2.92 (br d, *J* = 1.6 Hz, 1H), 2.64 - 2.59 (m, 1H), 2.46 - 2.37 (m, 1H), 2.06 - 1.98 (m, 1H). MS (ESI) *m/z* 478.1 [M+H]⁺

Step 1: To a solution of 2-fluoro-5-nitrophenol (500 mg, 3.18 mmol, 1.00 eq) and methyl 2-chloro-2,2-difluoroacetate (2.43 g, 15.9 mmol, 5.00 eq) in dimethylformamide (20.0 mL) and water (3.00 mL) was added potassium carbonate (880 mg, 6.37 mmol, 2.00 eq). The reaction was stirred at 100°C for 12 h. Water (50.0 mL) was added, and the aqueous layer was extracted with ethyl acetate (3 × 20.0 mL). The organic layers were gathered, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 20/1 to 10/1) to afford 2-(difluoromethoxy)-1-fluoro-4-nitrobenzene.

Step 2: To a solution of 2-(difluoromethoxy)-1-fluoro-4-nitrobenzene (400 mg, 1.93 mmol, 1.00 eq) in methanol (9.00 mL) and water (3.00 mL) were added ammonium chloride (516 mg, 9.66 mmol, 5.00 eq) and ferrous powder (539 mg, 9.66 mmol, 5.00 eq). The reaction was stirred at 80°C for 2 h. The mixture was filtered and concentrated under reduced pressure to afford 3-(difluoromethoxy)-4-fluoroaniline.

Step 3: To a solution of 3-(difluoromethoxy)-4-fluoroaniline (110 mg, 621 μmol, 1.00 eq) in acetonitrile (2.00 mL) were added pyridine (0.25 mL, 3.11 mmol, 5.00 eq) and phenyl chloroformate (0.08 mL, 0.68 mmol, 1.10 eq) at 0°C. The reaction was stirred at 0°C for 0.5 h. The mixture was filtered, and the filtrate was concentrated and the obtained residue was purified by standard methods to afford phenyl (3-(difluoromethoxy)-4-fluorophenyl)carbamate.

Compound 33: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-ethoxy-4-methylphenyl) carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (br s, 1H), 9.68 (br s, 1H), 7.79 (s, 1H), 7.69 - 7.65 (m, 1H), 7.65 - 7.61 (m, 1H), 7.14 (br s, 1H), 7.00 (d, *J* = 8.2 Hz, 1H), 6.90 (br d, *J* = 7.9 Hz, 1H), 5.25 (s, 2H), 5.12 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.50 - 4.43 (m, 1H), 4.38 - 4.29 (m, 1H), 3.95 (q, *J* = 6.8 Hz, 2H), 2.96 - 2.86 (m, 1H), 2.63 - 2.56 (m, 1H), 2.40 (br dd, *J* = 4.5, 13.1 Hz, 1H), 2.07 - 2.05 (m, 3H), 2.01 (dt, *J* = 2.1, 6.2 Hz, 1H), 1.33 (t, *J* = 6.9 Hz, 3H). MS (ESI) *m/z* 452.2 [M+H]⁺

Step 1: To a solution of 2-methyl-5-nitrophenol (1.00 g, 6.53 mmol, 1.00 eq) and iodoethane (0.57 mL, 7.18 mmol, 1.10 eq) in dimethylformamide (10.0 mL) was added potassium carbonate (2.71 g, 19.6 mmol, 3.00 eq) under nitrogen. The reaction was stirred at 40°C for 2 h under nitrogen atmosphere. The mixture was poured into water (20.0 mL) and extracted with ethyl acetate (3 × 20.0 mL). The combined organic layers were gathered, washed with brine (10.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 1/0 to 10/1) to afford 2-ethoxy-1-methyl-4-nitrobenzene.

Step 2: To a solution of 2-ethoxy-1-methyl-4-nitrobenzene (0.900 g, 4.97 mmol, 1.00 eq) in methanol (10.0 mL) and water (10.0 mL) were added iron powder (1.39 g, 24.8 mmol, 5.00 eq) and ammonium chloride (1.33 g, 24.8 mmol, 5.00 eq). The reaction was stirred at 80°C for 2 h. The mixture was concentrated under reduced pressure to give a slurry. The slurry was poured into saturated sodium bicarbonate solution (20.0 mL) and extracted with ethyl acetate (3 × 20.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-ethoxy-4-methylaniline.

Step 3: To a solution of 3-ethoxy-4-methylaniline (500 mg, 3.31 mmol, 1.00 eq) in acetonitrile (5.00 mL) were added pyridine (1.33 mL, 16.5 mmol, 5.00 eq) and phenyl chloroformate (0.50 mL, 3.97 mmol, 1.20 eq) at 0°C. The reaction was stirred at 25°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (3-ethoxy-4-methylphenyl)carbamate.

Compound 34: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (4-methyl-3-(morpholinomethyl)-5-

(trifluoromethoxy)phenyl) carbamate. ^1H NMR (400 MHz, DMSO-d_6) δ = 11.00 (s, 1H), 10.26 (br s, 1H), 10.20 (br s, 1H), 7.80 (s, 1H), 7.74 - 7.62 (m, 3H), 7.58 (br s, 1H), 5.31 (s, 2H), 5.12 (dd, J = 5.1, 13.3 Hz, 1H), 4.52 - 4.30 (m, 4H), 3.94 (br d, J = 12.1 Hz, 2H), 3.75 (br t, J = 11.6 Hz, 2H), 3.30 - 3.15 (m, 3H), 2.99 - 2.84 (m, 1H), 2.61 (br d, J = 17.0 Hz, 1H), 2.43 (br dd, J = 8.7, 13.3 Hz, 2H), 2.35 - 2.30 (m, 3H), 2.07 - 1.98 (m, 1H). MS (ESI) m/z 591.1 $[\text{M}+\text{H}]^+$

Step 1: To a solution of 2-methyl-5-nitro-benzoic acid (10.0 g, 55.2 mmol, 1.00 eq) in sulfuric acid (20.0 mL) was added N-Iodosuccinimide (14.9 g, 66.3 mmol, 1.20 eq). The reaction was stirred at 60°C for 2 h. The mixture was diluted with ice water (200 mL) and filtered. The filter cake was washed with water (100 mL) and dried under vacuum to afford 3-iodo-2-methyl-5-nitro-benzoic acid.

Step 2: To a solution of 3-iodo-2-methyl-5-nitro-benzoic acid (5.00 g, 16.3 mmol, 1.00 eq), copper iodide (310 mg, 1.63 mmol, 0.10 eq) and quinolin-8-ol (563 μL , 3.26 mmol, 0.20 eq) in water (3.00 mL) and dimethylsulfoxide (3.00 mL) was added a solution of potassium hydroxide (3.65 g, 65.1 mmol, 4.00 eq). The reaction was stirred at 100°C for 12 h. The mixture was diluted with water (50.0 mL) and extracted with ethyl acetate (2×50.0 mL). The combined organic layers were washed with water (50.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-hydroxy-2-methyl-5-nitro-benzoic acid.

Step 3: To a solution of 3-hydroxy-2-methyl-5-nitro-benzoic acid (3.20 g, 16.2 mmol, 1.00 eq) and morpholine (1.71 mL, 19.5 mmol, 1.20 eq) in dichloromethane (100 mL) were added triethylamine (2.26 mL, 16.2 mmol, 1.00 eq) and O-(7-azabenzotriazol-1-yl)-N,N,N,N-tetramethyluroniumhexafluorophosphate (7.41 g, 19.5 mmol, 1.20 eq) at 20°C. The reaction was stirred at 20°C for 12 h. The mixture was concentrated under reduced pressure to give a residue. The residue was diluted with water (100 mL) and extracted with ethyl acetate (100 mL). The organic layer was washed with water (100 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 1/1 to 0/1) to afford (3-hydroxy-2-methyl-5-nitro-phenyl)-morpholino-methanone.

Step 4: To a solution of (3-hydroxy-2-methyl-5-nitro-phenyl)-morpholino-methanone (1.30 g, 4.88 mmol, 1.00 eq), silver trifluoromethanesulfonate (6.27 g, 24.4 mmol, 5.00 eq), 1-

(chloromethyl)-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (3.46 g, 9.77 mmol, 2.00 eq), N-fluorobenzenesulfonimide (3.08 g, 9.77 mmol, 2.00 eq) and caesium fluoride (4.45 g, 29.3 mmol, 1.08 mL, 6.00 eq) in toluene (130 mL) were added trimethyl(trifluoromethyl)silane (3.47 g, 24.4 mmol, 5.00 eq) and 2-fluoropyridine (2.10 mL, 24.4 mmol, 5.00 eq) under nitrogen. The reaction was stirred at 20°C for 12 h under nitrogen. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was diluted with water (100 mL) and extracted with ethyl acetate (100 mL). The organic layer was washed with water (20.0 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 1/0 to 2/1) to afford (2-methyl-5-nitro-3-(trifluoromethoxy)phenyl)(morpholino)methanone.

Step 5: To a solution of (2-methyl-5-nitro-3-(trifluoromethoxy)phenyl)-morpholino-methanone (900 mg, 2.69 mmol, 1.00 eq) in tetrahydrofuran (15.0 mL) was added borane dimethyl sulfide complex (10.0 M, 539 μ L, 2.00 eq) at 0°C. The reaction was stirred at 60°C for 30 min. The mixture was quenched with methanol (2.00 mL) and concentrated under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC to afford 4-(2-methyl-5-nitro-3-(trifluoromethoxy)benzyl)morpholine.

Step 6: To a solution of 4-(2-methyl-5-nitro-3-(trifluoromethoxy)benzyl)morpholine (400 mg, 1.25 mmol, 1.00 eq) in methanol (5.00 mL) and water (5.00 mL) was added iron powder (488 mg, 8.74 mmol, 7.00 eq) and ammonium chloride (468 mg, 8.74 mmol, 7.00 eq). The reaction was stirred at 80°C for 2 h. The mixture was diluted with saturated sodium carbonate (1.00 mL) and extracted with ethyl acetate (2 $\times$ 10.0 mL). The combined organic layers were washed with water (5.00 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 3/1 to 1/1) to afford 4-methyl-3-(morpholinomethyl)-5-(trifluoromethoxy)aniline.

Step 7: To a solution of 4-methyl-3-(morpholinomethyl)-5-(trifluoromethoxy)aniline (100 mg, 344 μ mol, 1.00 eq) and potassium carbonate (57.1 mg, 413 μ mol, 1.20 eq) in acetone (1.00 mL) was added phenyl chloroformate (47 μ L, 379 μ mol, 1.10 eq) at 25°C. The reaction was stirred at 25°C for 1 h. The mixture was diluted with water (6.00 mL) and extracted with ethyl acetate (10.0 mL). The organic layer was dried over anhydrous sodium sulfate, filtered,

and the filtrate was concentrated to afford phenyl (4-methyl-3-(morpholinomethyl)-5-(trifluoromethoxy)phenyl)carbamate.

Compound 35: General procedure A with variant ii) was used for the preparation from compound **VIII** employing 1-(pyridin-2-yl)piperidin-4-amine. ¹H NMR (400 MHz, DMSO-*d*₆)

5 δ = 11.00 (s, 1H), 8.35 - 8.27 (m, 1H), 8.09 (dd, *J* = 1.4, 4.9 Hz, 1H), 7.72 (s, 1H), 7.61 (s, 2H), 7.53 - 7.47 (m, 1H), 7.36 (br d, *J* = 7.5 Hz, 1H), 6.83 (d, *J* = 8.4 Hz, 1H), 6.59 (dd, *J* = 5.0, 6.8 Hz, 1H), 5.17 - 5.08 (m, 3H), 4.50 - 4.43 (m, 1H), 4.37 - 4.30 (m, 1H), 4.20 (br d, *J* = 13.1 Hz, 2H), 3.58 (br s, 1H), 2.92 (br s, 3H), 2.63 - 2.58 (m, 1H), 2.43 - 2.38 (m, 1H), 2.04 - 1.98 (m, 1H), 1.80 (br d, *J* = 10.3 Hz, 2H), 1.41 - 1.30 (m, 2H). MS
10 (ESI) *m/z* 478.2 [M+H]⁺

Step 1: A solution of 2-fluoropyridine (1.79 mL, 20.8 mmol, 1.00 eq), *tert*-butyl piperidin-4-ylcarbamate (5.00 g, 25.0 mmol, 1.20 eq) and potassium carbonate (5.75 g, 41.6 mmol, 2.00 eq) in dimethylacetamide (20.0 mL) was stirred at 120°C for 12 h. The mixture was poured into water (20.0 mL) and extracted with ethyl acetate (3 × 20.0 mL). The combined
15 organic layers were washed with brine (10.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5/1 to 3/1) to afford *tert*-butyl (1-(pyridin-2-yl)piperidin-4-yl)carbamate.

Step 2: A solution of *tert*-butyl (1-(pyridin-2-yl)piperidin-4-yl)carbamate (1.27 g, 4.58
20 mmol, 1.00 eq) and hydrochloric acid/ethyl acetate (8.00 mL) in ethyl acetate (24.0 mL) was stirred at 25°C for 2 h. The mixture was concentrated and the obtained residue was purified by standard methods and filtered to afford 1-(pyridin-2-yl)piperidin-4-amine.

Compound 36: General procedure A with variant ii) was used for the preparation from compound **VIII** employing 1-phenylpiperazine. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s,
25 1H), 7.74 (s, 1H), 7.69 - 7.59 (m, 2H), 7.27 - 7.18 (m, 2H), 6.95 (d, *J* = 7.9 Hz, 2H), 6.81 (t, *J* = 7.3 Hz, 1H), 5.22 (s, 2H), 5.12 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.52 - 4.42 (m, 1H), 4.39 - 4.29 (m, 1H), 3.55 (br s, 4H), 3.17 - 3.09 (m, 4H), 2.92 (ddd, *J* = 5.4, 13.7, 17.4 Hz, 1H), 2.63 - 2.58 (m, 1H), 2.44 - 2.35 (m, 1H), 2.06 - 1.98 (m, 1H). MS (ESI) *m/z* 463.2 [M+H]⁺

30 **Compound 37:** General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-methoxy-4-methylphenyl)carbamate. ¹H NMR (400

MHz, DMSO- d_6) δ = 11.00 (br s, 1H), 9.71 (br s, 1H), 7.80 (s, 1H), 7.71 - 7.67 (m, 1H), 7.66 - 7.61 (m, 1H), 7.17 (s, 1H), 7.01 (d, J = 8.2 Hz, 1H), 6.93 (s, 1H), 5.27 (s, 2H), 5.16 - 5.10 (m, 1H), 4.46 (s, 1H), 4.37 (s, 1H), 3.73 (s, 3H), 2.97 - 2.86 (m, 1H), 2.58 (br s, 1H), 2.43 - 2.35 (m, 1H), 2.07 (s, 3H), 2.03 (br s, 1H). MS (ESI) m/z 438.1 $[M+H]^+$

- 5 To a solution of 3-methoxy-4-methylaniline (500 mg, 3.64 mmol, 1.00 eq) in acetonitrile (5.00 mL) were added pyridine (1.47 mL, 18.2 mmol, 5.00 eq) and phenyl chloroformate (0.91 mL, 7.29 mmol, 2.00 eq) at 0°C. The reaction was stirred at 0°C for 1 h. The mixture was concentrated under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC. The desired fraction was collected and concentrated under
10 reduced pressure to give concentrated solution. The solution was diluted with water/ethyl acetate (40.0 ml/80.0 ml). The organic layer was separated, dried over anhydrous sodium sulfate, filtered, and concentrated by standard methods to afford phenyl (3-methoxy-4-methylphenyl)carbamate.

- Compound 38:** General procedure A with variant i) was used for the preparation from
15 compound **VIII** employing phenyl (4-chloro-2-methoxyphenyl)carbamate. ^1H NMR (400 MHz, DMSO- d_6) δ = 11.08 - 10.95 (m, 1H), 8.86 (s, 1H), 7.81 (s, 1H), 7.71 - 7.61 (m, 3H), 7.10 (d, J = 2.3 Hz, 1H), 6.98 (dd, J = 2.3, 8.6 Hz, 1H), 5.26 (s, 2H), 5.18 - 5.10 (m, 1H), 4.51 - 4.44 (m, 1H), 4.39 - 4.30 (m, 1H), 3.83 (s, 3H), 2.97 - 2.88 (m, 1H), 2.62 - 2.59 (m, 1H), 2.41 (br dd, J = 4.4, 12.9 Hz, 1H), 2.06 - 1.98 (m, 1H). MS (ESI) m/z 458.1
20 $[M+H]^+$

- To a solution of 4-chloro-2-methoxyaniline (1.00 g, 6.35 mmol, 1.00 eq) in acetonitrile (5.00 mL) were added pyridine (2.57 mL, 31.8 mmol, 5.01 eq) and phenyl chloroformate (0.88 mL 7.03 mmol, 1.11 eq) at 0°C. The reaction was stirred at 0°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford
25 phenyl (4-chloro-2-methoxyphenyl)carbamate.

- Compound 39:** General procedure A with variant i) was used for the preparation with from compound **VIII** employing phenyl (4-cyclopropylphenyl)carbamate. ^1H NMR (400 MHz, DMSO- d_6) δ = 10.99 (s, 1H), 9.68 (br s, 1H), 7.78 (s, 1H), 7.71 - 7.59 (m, 2H), 7.34 (br d, J = 8.4 Hz, 2H), 6.98 (d, J = 8.6 Hz, 2H), 5.25 (s, 2H), 5.18 - 5.08 (m, 1H), 4.53 - 4.43
30 (m, 1H), 4.37 - 4.29 (m, 1H), 2.99 - 2.85 (m, 1H), 2.65 - 2.56 (m, 1H), 2.47 - 2.34 (m, 1H), 2.05 - 1.97 (m, 1H), 1.89 - 1.79 (m, 1H), 0.92 - 0.84 (m, 2H), 0.62 - 0.55 (m, 2H). MS (ESI) m/z 434.3 $[M+H]^+$

To a solution of 4-cyclopropylaniline (500 mg, 3.75 mmol, 1.00 eq) in acetonitrile (5.00 mL) was added pyridine (0.91 mL, 11.3 mmol, 3.00 eq) and phenyl chloroformate (0.56 mL, 4.50 mmol, 1.20 eq). The reaction was stirred at 25°C for 2 h. The mixture was diluted with ethyl acetate (50.0 mL) and water (50.0 mL). The organic layer was separated, and the aqueous phase was extracted with ethyl acetate (3 × 100 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated and the obtained residue was purified by standard methods to afford phenyl (4-cyclopropylphenyl)carbamate.

Compound 40: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-chloro-5-((1-methylpyrrolidin-3-yl)methoxy)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 9.99 (s, 1H), 8.15 (s, 1H), 7.79 (s, 1H), 7.70 - 7.61 (m, 2H), 7.13 (s, 1H), 7.06 (s, 1H), 6.67 (t, *J* = 1.9 Hz, 1H), 5.28 (s, 2H), 5.12 (dd, *J* = 5.2, 13.1 Hz, 1H), 4.52 - 4.43 (m, 1H), 4.38 - 4.30 (m, 1H), 3.85 (br dd, *J* = 4.7, 7.0 Hz, 2H), 2.96 - 2.88 (m, 1H), 2.74 - 2.68 (m, 1H), 2.62 (br s, 1H), 2.58 (br s, 2H), 2.55 - 2.52 (m, 2H), 2.43 - 2.38 (m, 1H), 2.35 (s, 3H), 2.04 - 1.91 (m, 2H), 1.53 (br dd, *J* = 6.3, 12.5 Hz, 1H). MS (ESI) *m/z* 541.2 [M+H]⁺

Step 1: To a solution of *tert*-butyl 3-(hydroxymethyl)pyrrolidine-1-carboxylate (3.00 g, 14.9 mmol, 1.00 eq) and triethylamine (3.77 g, 37.3 mmol, 5.19 mL, 2.50 eq) in dichloromethane (30.0 mL) at 0°C was added methylsulfamoyl chloride (1.50 mL, 19.4 mmol, 1.30 eq) dropwise under nitrogen atmosphere. The reaction was stirred at 25°C for 2 h. The mixture was diluted with ethyl acetate (100 mL) and water (150 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 100 mL). The organic layers were gathered, dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford *tert*-butyl 3-(((methylsulfonyl)oxy)methyl)pyrrolidine-1-carboxylate.

Step 2: To a solution of *tert*-butyl 3-(((methylsulfonyl)oxy)methyl)pyrrolidine-1-carboxylate (3.00 g, 10.8 mmol, 1.00 eq) in dimethylformamide (30.0 mL) was added 3-chloro-5-nitrophenol (2.05 g, 11.8 mmol, 1.10 eq) and cesium carbonate (10.5 g, 32.2 mmol, 3.00 eq). The reaction was stirred at 80°C for 12 h. The mixture was diluted with ethyl acetate (100 mL) and water (100 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 80.0 mL). The organic layers were gathered, dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The

residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 3/1) to afford *tert*-butyl 3-((3-chloro-5-nitrophenoxy)methyl)pyrrolidine-1-carboxylate.

Step 3: To a solution of *tert*-butyl 3-((3-chloro-5-nitrophenoxy)methyl)pyrrolidine-1-carboxylate (1.10 g, 3.08 mmol, 1.00 eq) in ethyl acetate (5.00 mL) was added hydrochloric acid in ethyl acetate (4 M, 10 mL). The reaction was stirred at 25°C for 2 h. The mixture was concentrated under reduced pressure to afford 3-((3-chloro-5-nitrophenoxy)methyl)pyrrolidine.

Step 4: To a solution of 3-((3-chloro-5-nitrophenoxy)methyl)pyrrolidine (1.50 g, 5.84 mmol, 1.00 eq) in 2,2,2-trifluoroethanol (10.0 mL) was added paraformaldehyde (0.80 mL, 29.2 mmol, 5.00 eq). The reaction was stirred at 60°C for 0.5 h. Sodium borohydride (442 mg, 11.7 mmol, 2.00 eq) was added in portions, and the reaction was stirred at 60°C for 1 h. The reaction was quenched with saturated ammonium chloride solution (10.0 mL) and concentrated under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC to afford 3-((3-chloro-5-nitrophenoxy)methyl)-1-methylpyrrolidine.

Step 5: To a solution of 3-((3-chloro-5-nitrophenoxy)methyl)-1-methylpyrrolidine (1.20 g, 4.43 mmol, 1.00 eq) in methanol (6.00 mL) and water (6.00 mL) was added ammonium chloride (1.66 g, 31.0 mmol, 7.00 eq) and iron powder (1.73 g, 31.0 mmol, 7.00 eq). The reaction was stirred at 80°C for 2 h. The mixture was filtered over Celite, and the filtrate was concentrated under reduced pressure to afford 3-chloro-5-((1-methylpyrrolidin-3-yl)methoxy)aniline.

Step 6: To a solution of phenyl chloroformate (0.28 mL, 2.24 mmol, 1.20 eq) in acetonitrile (5.00 mL) was added pyridine (0.45 mL, 5.61 mmol, 3.00 eq) and 3-chloro-5-((1-methylpyrrolidin-3-yl)methoxy)aniline (450 mg, 1.87 mmol, 1.00 eq). The reaction was stirred at 25°C for 2 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (3-chloro-5-((1-methylpyrrolidin-3-yl)methoxy)phenyl)carbamate.

Compound 41: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-fluoro-4-methyl-5-(morpholinomethyl)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 10.90 (br s, 1H), 10.12 (s, 1H), 7.79 (s, 1H), 7.71 - 7.61 (m, 2H), 7.50 (s, 1H), 7.36 (br

d, $J = 11.7$ Hz, 1H), 5.29 (s, 2H), 5.11 (dd, $J = 5.1, 13.3$ Hz, 1H), 4.51 - 4.43 (m, 1H), 4.38 - 4.29 (m, 3H), 3.90 - 3.81 (m, 4H), 3.34 - 3.14 (m, 4H), 2.97 - 2.86 (m, 1H), 2.60 (br d, $J = 17.7$ Hz, 1H), 2.46 - 2.36 (m, 1H), 2.29 (d, $J = 1.7$ Hz, 3H), 2.09 - 1.94 (m, 1H). MS (ESI) m/z 525.3 $[M+H]^+$

- 5 **Step 1:** To a solution of 3-fluoro-2-methylbenzoic acid (10.0 g, 64.9 mmol, 1.00 eq) in sulfuric acid (100 mL) was added potassium nitrate (7.22 g, 71.4 mmol, 1.10 eq) in portions at 0°C. The reaction was stirred at 0°C for 1 h. The mixture was poured into water (100 mL) and the resulting precipitate was collected by filtration. The filter cake was dried under vacuum, then added to water (100 mL) and extracted with ethyl acetate (3 × 80.0 mL). The
10 combined organic layers were washed with brine (60.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-fluoro-2-methyl-5-nitrobenzoic acid.

- Step 2:** To a solution of 3-fluoro-2-methyl-5-nitrobenzoic acid (11.0 g, 55.2 mmol, 1.00 eq) in tetrahydrofuran (100 mL) was added borane dimethyl sulfide complex (10 M, 11.0 mL,
15 2.00 eq) at 0°C. The reaction was stirred at 25°C for 12 h. The mixture was poured into methanol (200 mL) and concentrated under reduced pressure to give a residue. Water (150 mL) was added, and the pH was adjusted to pH = 10 by addition of 15% sodium hydroxide solution. The aqueous layer was extracted with ethyl acetate (3 × 80.0 mL). The combined organic layers were washed with brine (50.0 mL), dried over sodium sulfate, filtered, and
20 concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 4/1) to afford (3-fluoro-2-methyl-5-nitrophenyl)methanol.

- Step 3:** To a solution of (3-fluoro-2-methyl-5-nitrophenyl)methanol (870 mg, 4.70 mmol, 1.00 eq) in dichloromethane (10.0 mL) was added thionyl chloride (1.70 mL, 23.5 mmol,
25 5.00 eq) dropwise at 0°C. The reaction was stirred at 25°C for 12 h. The mixture was concentrated under reduced pressure to afford 1-(chloromethyl)-3-fluoro-2-methyl-5-nitrobenzene.

- Step 4:** To a solution of 1-(chloromethyl)-3-fluoro-2-methyl-5-nitrobenzene (950 mg, 4.67 mmol, 1.00 eq) and triethylamine (1.62 mL, 11.7 mmol, 2.50 eq) in acetonitrile (10.0 mL)
30 was added morpholine (0.51 mL, 5.83 mmol, 1.25 eq) dropwise. The reaction was stirred at 25°C for 12 h. The mixture was concentrated under reduced pressure to give a residue. The residue was diluted with water (80.0 mL) and extracted with ethyl acetate (3 × 60.0 mL).

The combined organic layers were washed with brine (40.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 4/1) to afford 4-(3-fluoro-2-methyl-5-nitrobenzyl)morpholine.

- 5 **Step 5:** To a solution of 4-(3-fluoro-2-methyl-5-nitrobenzyl)morpholine (1.00 g, 3.93 mmol, 1.00 eq) and ammonium chloride (1.05 g, 19.7 mmol, 5.00 eq) in methanol (8.00 mL) and water (2.00 mL) was added iron powder (1.10 g, 19.7 mmol, 5.00 eq) in portions. The reaction was stirred at 80°C for 2 h. The mixture was filtered, and the filtrate was diluted with water (80.0 mL) and extracted with ethyl acetate (3 × 60.0 mL). The combined organic
10 layers were washed with brine (40.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-fluoro-4-methyl-5-(morpholinomethyl)aniline.

- Step 6:** To a solution of 3-fluoro-4-methyl-5-(morpholinomethyl)aniline (300 mg, 1.34 mmol, 1.00 eq) and pyridine (0.54 mL, 6.69 mmol, 5.00 eq) in acetonitrile (5.00 mL) was
15 added phenyl chloroformate (0.20 mL, 1.61 mmol, 1.20 eq) dropwise at 0°C. The reaction was stirred at 25°C for 12 h. The mixture was diluted with water (50.0 mL) and extracted with ethyl acetate (3 × 40.0 mL). The combined organic layers were washed with brine (30.0 mL), dried over sodium sulfate, filtered, and concentrated and the obtained residue was purified by standard methods to afford phenyl (3-fluoro-4-methyl-5-
20 (morpholinomethyl)phenyl)carbamate.

- Compound 42:** General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-phenylpyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 10.23 (br s, 1H), 8.75 (s, 1H), 8.06 - 7.95 (m, 4H), 7.82 (s, 1H), 7.73 - 7.68 (m, 1H), 7.67 - 7.62 (m, 1H), 7.51 - 7.45 (m, 2H), 7.44 - 7.39 (m, 1H),
25 5.33 (s, 2H), 5.13 (dd, *J* = 5.1, 13.2 Hz, 1H), 4.51 - 4.45 (m, 1H), 4.38 - 4.32 (m, 1H), 2.97 - 2.86 (m, 1H), 2.60 (br d, *J* = 17.2 Hz, 1H), 2.41 (br dd, *J* = 4.4, 12.9 Hz, 1H), 2.05 - 1.97 (m, 1H). MS (ESI) *m/z* 471.2 [M+H]⁺

- To a solution of 6-phenylpyridin-3-amine (300 mg, 1.76 mmol, 1.00 eq) and pyridine (0.71 mL, 8.81 mmol, 5.00 eq) in acetonitrile (5.00 mL) was added phenyl chloroformate (0.26
30 mL, 2.12 mmol, 1.20 eq) in portions at 0°C. The reaction was stirred at 25°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (6-phenylpyridin-3-yl)carbamate.

Compound 43: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-(*tert*-butyl)pyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.01 (s, 1H), 10.80 - 10.56 (m, 1H), 8.91 - 8.80 (m, 1H), 8.29 (br d, *J* = 8.5 Hz, 1H), 7.87 (br d, *J* = 8.6 Hz, 1H), 7.82 (s, 1H), 7.73 - 7.69 (m, 1H), 7.68 - 7.63 (m, 1H), 5.35 (s, 2H), 5.13 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.53 - 4.43 (m, 1H), 4.38 - 4.32 (m, 1H), 2.97 - 2.87 (m, 1H), 2.66 - 2.57 (m, 1H), 2.47 - 2.35 (m, 1H), 2.06 - 1.97 (m, 1H), 1.45 - 1.37 (m, 9H). MS (ESI) *m/z* 451.2 [M+H]⁺

To a solution of 6-(*tert*-butyl)pyridin-3-amine (150 mg, 1.00 mmol, 1.00 eq) and pyridine (0.40 mL, 5.00 mmol, 5.00 eq) in acetonitrile (5.00 mL) was added phenyl chloroformate (0.15 mL, 1.20 mmol, 1.20 eq). The reaction was stirred at 25°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (6-(*tert*-butyl)pyridin-3-yl)carbamate.

Compound 44:

Step 1: A solution of 3-chloro-2-methyl-5-nitrophenol (260 mg, 1.39 mmol, 1.00 eq), *tert*-butyl 3-((methylsulfonyl)oxy)pyrrolidine-1-carboxylate (441 mg, 1.66 mmol, 1.20 eq) and potassium carbonate (575 mg, 4.16 mmol, 3.00 eq) in dimethylformamide (10.0 mL) was stirred at 80°C for 4 h. The mixture was poured into water (20.0 mL) and extracted with ethyl acetate (3 × 20.0 mL). The combined organic layers were washed with brine (10.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 1/0 to 5/1) to afford *tert*-butyl 3-(3-chloro-2-methyl-5-nitrophenoxy)pyrrolidine-1-carboxylate.

Step 2: To a mixture of *tert*-butyl 3-(3-chloro-2-methyl-5-nitrophenoxy)pyrrolidine-1-carboxylate (430 mg, 1.21 mmol, 1.00 eq), iron powder (337 mg, 6.03 mmol, 5.00 eq) and ammonium chloride (322 g, 6.03 mmol, 5.00 eq) in methanol (10.0 mL) was added water (10.0 mL) at 25°C. The reaction was stirred at 80°C for 2 h. The mixture was concentrated under reduced pressure to give a residue. The residue was added to saturated sodium bicarbonate (20.0 mL) and extracted with ethyl acetate (3 × 20.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford *tert*-butyl 3-(5-amino-3-chloro-2-methylphenoxy)pyrrolidine-1-carboxylate.

Step 3: To a solution of *tert*-butyl 3-(5-amino-3-chloro-2-methylphenoxy)pyrrolidine-1-carboxylate (170 mg, 520 μ mol, 1.00 eq) and pyridine (0.21 mL, 2.60 mmol, 5.00 eq) in acetonitrile (5.00 mL) was added phenyl chloroformate (78.0 μ L, 623 μ mol, 1.20 eq) in portions at 0°C. The reaction was stirred at 25°C for 1 h. The mixture was concentrated under reduced pressure to give a residue, which was purified by reversed phase preparative HPLC to afford *tert*-butyl 3-(3-chloro-2-methyl-5-((phenoxycarbonyl)amino)phenoxy)pyrrolidine-1-carboxylate.

Step 4: To a solution of 3-(6-(hydroxymethyl)-1-oxoisindolin-2-yl)piperidine-2,6-dione **VIII** (100 mg, 365 μ mol, 1.00 eq) and *tert*-butyl 3-(3-chloro-2-methyl-5-((phenoxycarbonyl)amino)phenoxy)pyrrolidine-1-carboxylate (179 mg, 401 μ mol, 1.10 eq) in dimethylformamide (3.00 mL) was added sodium hydride (60% dispersion in mineral oil) (30.0 mg, 750 μ mol, 2.06 eq) in portions at 0°C. The reaction was stirred at 25°C for 1 h. The reaction was quenched with hydrochloric acid (1 M, 0.50 mL), and the solvents were removed under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC to afford *tert*-butyl 3-(3-chloro-5-(((2-(2,6-dioxopiperidin-3-yl)-3-oxoisindolin-5-yl)methoxy)carbonyl)amino)-2-methylphenoxy)pyrrolidine-1-carboxylate.

Step 5: To a solution of *tert*-butyl 3-(3-chloro-5-(((2-(2,6-dioxopiperidin-3-yl)-3-oxoisindolin-5-yl)methoxy)carbonyl)amino)-2-methylphenoxy)pyrrolidine-1-carboxylate (120 mg, 191 μ mol, 1.00 eq) in ethyl acetate (10.0 mL) was added hydrochloric acid/ethyl acetate (4 M, 4.62 mL, 96.5 eq). The reaction was stirred at 25°C for 1 h. The mixture was concentrated to give a residue, and purified by a standard method to afford Compound 44 (hydrochloride). ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 9.95 (br s, 1H), 9.54 (br s, 1H), 9.49 - 9.38 (m, 1H), 7.79 (s, 1H), 7.70 - 7.62 (m, 2H), 7.25 - 7.11 (m, 2H), 5.28 (s, 2H), 5.12 (dd, *J* = 5.1, 13.2 Hz, 1H), 5.02 (br s, 1H), 4.52 - 4.44 (m, 1H), 4.38 - 4.31 (m, 1H), 3.51 - 3.43 (m, 2H), 3.37 - 3.31 (m, 2H), 3.27 (br dd, *J* = 6.9, 9.9 Hz, 1H), 2.97 - 2.85 (m, 1H), 2.60 (br d, *J* = 16.9 Hz, 1H), 2.40 (br dd, *J* = 4.5, 13.1 Hz, 1H), 2.23 - 2.16 (m, 1H), 2.14 (s, 3H), 2.06 - 1.95 (m, 1H). MS (ESI) *m/z* 527.2 [M+H]⁺

Compound 45: General procedure A with variant i) was used for the preparation with from compound **VIII** employing phenyl (3-chloro-5-ethyl-4-methylphenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 9.85 (s, 1H), 7.79 (s, 1H), 7.70 - 7.61 (m, 2H), 7.46 (s, 1H), 7.22 (d, *J* = 1.9 Hz, 1H), 5.27 (s, 2H), 5.12 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.50 - 4.44 (m, 1H), 4.37 - 4.31 (m, 1H), 2.99 - 2.86 (m, 1H), 2.65 - 2.61 (m, 1H), 2.60 - 2.56

(m, 2H), 2.46 - 2.36 (m, 1H), 2.22 (s, 3H), 2.06 - 1.98 (m, 1H), 1.11 (t, $J = 7.5$ Hz, 3H).
MS (ESI) m/z 470.2 $[M+H]^+$

Step 1: To a solution of 2-chloro-1-methyl-4-nitrobenzene (0.60 mL, 2.91 mmol, 1.00 eq) in sulfuric acid (5.00 mL, 98% purity) was added *N*-iodosuccinimide (787 mg, 3.50 mmol, 1.20 eq) in portions. The reaction was stirred at 60°C for 1 h. The mixture was quenched with sodium carbonate (10%, 100 mL) and extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with brine (50.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 1/0 to 10/1) to afford 1-chloro-3-iodo-2-methyl-5-nitrobenzene.

Step 2: To a solution of 1-chloro-3-iodo-2-methyl-5-nitrobenzene (760 mg, 2.55 mmol, 1.00 eq) in toluene (15.0 mL) were added diisopropylethylamine (1.34 mL, 7.66 mmol, 3.00 eq), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (187 mg, 256 μ mol, 0.10 eq) and potassium vinyltrifluoroborate (685 mg, 5.11 mmol, 2.00 eq) in portions under nitrogen. The reaction was stirred at 110°C for 12 h. The mixture was concentrated under reduced pressure to give a residue, which was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 1/0 to 10/1) to afford 1-chloro-2-methyl-5-nitro-3-vinylbenzene.

Step 3: To a solution of 1-chloro-2-methyl-5-nitro-3-vinylbenzene (370 mg, 1.87 mmol, 1.00 eq) in tetrahydrofuran (6.00 mL) and ethyl acetate (6.00 mL) were added zinc chloride (12.7 μ L, 271 μ mol, 0.140 eq) and palladium on activated carbon (10%) (wetted with ca. 55% water) (50.0 mg) in portions under H_2 (15 Psi). The reaction was stirred at 25°C for 1 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 20/1 to 5/1) to afford 3-chloro-5-ethyl-4-methylaniline.

Step 4: To a solution of 3-chloro-5-ethyl-4-methylaniline (125 mg, 737 μ mol, 1.00 eq) in acetonitrile (8.00 mL) were added pyridine (0.30 mL, 3.72 mmol, 5.04 eq) and phenyl chloroformate (0.11 mL, 886 μ mol, 1.20 eq) in portions at 0°C. The reaction was stirred at 25°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (3-chloro-5-ethyl-4-methylphenyl)carbamate.

Compound 46: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-chloro-5-((1-methylpyrrolidin-3-yl)oxy)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 9.99 (s, 1H), 8.15 (s, 1H), 7.79 (s, 1H), 7.70 - 7.62 (m, 2H), 7.15 (s, 1H), 6.99 (s, 1H), 6.60 (s, 1H), 5.28 (s, 2H), 5.12 (dd, *J* = 5.0, 13.2 Hz, 1H), 4.82 (br d, *J* = 5.4 Hz, 1H), 4.50 - 4.44 (m, 1H), 4.37 - 4.31 (m, 1H), 2.97 - 2.88 (m, 2H), 2.77 (br d, *J* = 5.5 Hz, 1H), 2.72 (br d, *J* = 6.1 Hz, 2H), 2.62 (br d, *J* = 1.5 Hz, 1H), 2.58 (br s, 2H), 2.29 (s, 3H), 2.04 - 1.98 (m, 1H), 1.80 - 1.71 (m, 1H). MS (ESI) *m/z* 527.2 [M+H]⁺

Step 1: To a solution of *tert*-butyl 3-(3-chloro-5-nitro-phenoxy)pyrrolidine-1-carboxylate (2.00 g, 5.83 mmol, 1.00 eq) in ethyl acetate (10.0 mL) was added hydrochloric acid in ethyl acetate (4 M, 20.0 mL, 13.7 eq). The reaction was stirred at 25°C for 1 h. The mixture was concentrated under reduced pressure to afford 3-(3-chloro-5-nitrophenoxy)pyrrolidine.

Step 2: To a solution of 3-(3-chloro-5-nitrophenoxy)pyrrolidine (1.00 g, 4.12 mmol, 1.00 eq) in methanol (6.00 mL) was added paraformaldehyde 37% purity (6.00 mL, 80.6 mmol, 19.60 eq), acetic acid (0.23 mL, 4.11 mmol, 1.00 eq) and sodium cyanoborohydride (1.29 g, 20.6 mmol, 5.00 eq) in portions. The reaction was stirred at 25°C for 1 h. The mixture was concentrated under reduced pressure to give a residue. The residue was purified first by silica gel column chromatography (petroleum ether/ethyl acetate to ethyl acetate/methanol = 3/1 to 0/1), then by reversed phase preparative HPLC, to afford 3-(3-chloro-5-nitrophenoxy)-1-methylpyrrolidine.

Step 3: To a solution of 3-(3-chloro-5-nitrophenoxy)-1-methylpyrrolidine (460 mg, 1.79 mmol, 1.00 eq) in methanol (15.0 mL) and water (8.00 mL) was added iron powder (300 mg, 5.37 mmol, 3.00 eq) and ammonium chloride (479 mg, 8.95 mmol, 5.00 eq) in portions. The reaction was stirred at 80°C for 1 h. The mixture was concentrated under reduced pressure to give a residue, which was diluted with water (50.0 mL) and extracted with ethyl acetate (3 × 20.0 mL). The combined organic layers were washed with water, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-chloro-5-((1-methylpyrrolidin-3-yl)oxy)aniline.

Step 4: To a solution of 3-chloro-5-((1-methylpyrrolidin-3-yl)oxy)aniline (290 mg, 1.28 mmol, 1.00 eq) in acetonitrile (5.00 mL) was added pyridine (0.52 mL, 6.39 mmol, 5.00 eq) and phenyl chloroformate (0.19 mL, 1.54 mmol, 1.20 eq) in portions. The reaction was stirred at 25°C for 1 h. The mixture was concentrated and the obtained residue was purified

by standard methods to afford phenyl (3-chloro-5-((1-methylpyrrolidin-3-yl)oxy) phenyl) carbamate.

Compound 47: General procedure A with variant i) was used for the preparation from compound **VIII** employing (4-(tert-butyl)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆)
5 δ = 10.99 (s, 1H), 9.70 (br s, 1H), 7.79 (s, 1H), 7.72 - 7.60 (m, 2H), 7.38 (br d, *J* = 8.7 Hz, 2H), 7.32 - 7.25 (m, 2H), 5.26 (s, 2H), 5.16 - 5.08 (m, 1H), 4.52 - 4.43 (m, 1H), 4.39 - 4.28 (m, 1H), 2.98 - 2.85 (m, 1H), 2.64 - 2.63 (m, 1H), 2.65 - 2.56 (m, 1H), 2.47 - 2.33 (m, 1H), 2.07 - 1.97 (m, 1H), 1.24 (s, 9H). MS (ESI) *m/z* 450.2 [M+H]⁺

To a solution of phenyl carbamate (0.63 mL, 5.03 mmol, 1.50 eq) and pyridine (0.81 mL,
10 10.1 mmol, 3.00 eq) in acetonitrile (5.00 mL) was added 4-(tert-butyl)aniline (0.53 mL, 3.35 mmol, 1.00 eq). The reaction was stirred at 25°C for 12 h. The mixture was diluted with ethyl acetate (50.0 mL) and water (50.0 mL). The organic layer was separated, and the aqueous phase was extracted with ethyl acetate (3 × 50.0 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated and the obtained residue was
15 purified by standard methods to afford phenyl (4-(tert-butyl)phenyl)carbamate.

Compound 48: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-chloro-4-methyl-5-(2-morpholinoethoxy)phenyl) carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 9.89 (s, 1H), 8.20 (s, 1H), 7.79 (s, 1H), 7.71 - 7.60 (m, 2H), 7.14 (br d, *J* = 19.5 Hz, 2H), 5.27 (s, 2H), 5.13 (dd, *J* =
20 5.1, 13.3 Hz, 1H), 4.51 - 4.43 (m, 1H), 4.38 - 4.30 (m, 1H), 4.03 (t, *J* = 5.7 Hz, 2H), 3.58 - 3.55 (m, 4H), 2.96 - 2.87 (m, 1H), 2.72 (t, *J* = 5.6 Hz, 2H), 2.60 (br d, *J* = 17.5 Hz, 1H), 2.47 (br d, *J* = 4.6 Hz, 4H), 2.35 (br d, *J* = 4.5 Hz, 1H), 2.12 (s, 3H), 2.05 - 1.97 (m, 1H). MS (ESI) *m/z* 571.2 [M+H]⁺

Step 1: A solution of 2-chloro-1-methyl-4-nitrobenzene (12.1 mL, 58.3 mmol, 1.00 eq) and
25 *N*-iodosuccinimide (14.4 g, 64.1 mmol, 1.10 eq) in sulfuric acid (100 mL) was stirred at 60°C for 2 h. The reaction was quenched by addition of ice water (200 mL) at 0°C. The aqueous layer was extracted with ethyl acetate (3 × 50.0 mL). The combined organic layers were washed with brine (100 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column
30 chromatography (petroleum ether/ethyl acetate = 1/0) to afford 1-chloro-3-iodo-2-methyl-5-nitrobenzene.

Step 2: A solution of 1-chloro-3-iodo-2-methyl-5-nitrobenzene (7.80 g, 26.2 mmol, 1.00 eq), potassium hydroxide (4.41 g, 78.7 mmol, 3.00 eq), tris(dibenzylidenethyl acetate)cetone)dipalladium(0) (1.20 g, 1.31 mmol, 0.05 eq) and 2-di-tert-butylphosphino-2',4',6'-triisopropylbiphenyl (557 mg, 1.31 mmol, 0.050 eq) in dioxane (80.0 mL) and water (16.0 mL) was stirred at 80°C for 12 h under nitrogen atmosphere. The mixture was acidified to pH ~ 4 and concentrated under reduced pressure to give a residue. Brine (200 mL) was added, and the aqueous layer was extracted with ethyl acetate (3 × 50.0 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 1/0 to 17/3) to afford 3-chloro-2-methyl-5-nitrophenol.

Step 3: A suspension of 3-chloro-2-methyl-5-nitrophenol (500 mg, 2.67 mmol, 1.00 eq), 4-(2-chloroethyl) morpholine (479 mg, 3.20 mmol, 1.20 eq), potassium carbonate (553 mg, 4.00 mmol, 1.50 eq) and potassium iodide (133 mg, 0.80 mmol, 0.30 eq) in dimethylformamide (5.00 mL) was stirred at 80°C for 1 h. The mixture was poured into brine (50.0 mL) and extracted with ethyl acetate (3 × 15.0 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 4-(2-(3-chloro-2-methyl-5-nitrophenoxy)ethyl)morpholine.

Step 4: To a solution of 4-(2-(3-chloro-2-methyl-5-nitrophenoxy)ethyl)morpholine (570 mg, 1.90 mmol, 1.00 eq) in methanol (5.00 mL) and water (1.00 mL) were added iron powder (529 mg, 9.48 mmol, 5.00 eq) and ammonium chloride (507 mg, 9.48 mmol, 5.00 eq). The reaction was stirred at 80°C for 12 h under nitrogen. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was treated with brine (5.00 mL) and saturated aqueous sodium bicarbonate (5.00 mL). The aqueous layer was extracted with ethyl acetate (3 × 10.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-chloro-4-methyl-5-(2-morpholinoethoxy)aniline.

Step 5: To a solution of 3-chloro-4-methyl-5-(2-morpholinoethoxy)aniline (300 mg, 1.11 mmol, 1.00 eq) in acetonitrile (10.0 mL) were added pyridine (0.45 mL, 5.54 mmol, 5.00 eq) and phenyl chloroformate (0.17 mL, 1.33 mmol, 1.20 eq) at 0°C. The reaction was stirred at 25°C for 1 h. The mixture was concentrated and the obtained residue was purified by

standard methods to afford phenyl (3-chloro-4-methyl-5-(2-morpholinoethoxy)phenyl)carbamate.

Compound 49: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-ethyl-5-methylpyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.11 - 10.94 (m, 1H), 10.81 - 10.66 (m, 1H), 8.67 (d, *J* = 1.6 Hz, 1H), 8.20 (br s, 1H), 7.82 (s, 1H), 7.74 - 7.59 (m, 2H), 5.35 (s, 2H), 5.19 - 5.02 (m, 1H), 4.53 - 4.44 (m, 1H), 4.40 - 4.27 (m, 1H), 3.04 - 2.90 (m, 3H), 2.61 (br d, *J* = 16.5 Hz, 1H), 2.43 (s, 3H), 2.42 - 2.35 (m, 1H), 2.07 - 1.97 (m, 1H), 1.24 (t, *J* = 7.6 Hz, 3H). MS (ESI) *m/z* 437.1 [M+H]⁺

Step 1: To a solution of 2-chloro-3-methyl-5-nitropyridine (2.00 g, 11.6 mmol, 1.00 eq), ethylboronic acid (2.14 g, 29.0 mmol, 2.50 eq) and potassium carbonate (4.81 g, 34.8 mmol, 3.00 eq) in dioxane (20.0 mL) was added tetrakis(triphenylphosphine)palladium(0) (1.34 g, 1.16 mmol, 0.100 eq) at 20°C. The reaction was stirred at 110°C under nitrogen for 12 h. The mixture was concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 1/0 to 20/1) to afford 2-ethyl-3-methyl-5-nitropyridine.

Step 2: A mixture of 2-ethyl-3-methyl-5-nitropyridine (800 mg, 4.81 mmol, 1.00 eq), iron powder (806 mg, 14.4 mmol, 3.00 eq) and ammonium chloride (1.29 g, 24.0 mmol, 5.00 eq) in methanol (8.00 mL) and water (4.00 mL) was stirred at 80°C for 1 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was added to water (100 mL) and the solution was stirred for 10 min, then extracted with ethyl acetate (3 × 50.0 mL). The combined organic layers were washed with brine (100 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 6-ethyl-5-methylpyridin-3-amine.

Step 3: To a solution of 6-ethyl-5-methylpyridin-3-amine (300 mg, 2.20 mmol, 1 eq) and pyridine (0.89 mL, 11.0 mmol, 5.00 eq) in acetonitrile (5.00 mL) was added phenyl chloroformate (0.41 mL, 3.30 mmol, 1.50 eq). The reaction was stirred at 25°C for 1 h. The mixture was concentrated under reduced pressure to give a residue. The residue was added to water (80.0 mL) and stirred for 10 min, then extracted with ethyl acetate (3 × 40.0 mL). The combined organic layers were washed with brine (80.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated and the obtained residue was purified by standard methods to afford phenyl (6-ethyl-5-methylpyridin-3-yl)carbamate.

Compound 50: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (4-(pyridin-2-yl)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 10.01 (s, 1H), 8.62 (d, *J* = 4.1 Hz, 1H), 8.29 (s, 1H), 8.03 (d, *J* = 8.8 Hz, 2H), 7.93 - 7.88 (m, 1H), 7.87 - 7.79 (m, 2H), 7.73 - 7.69 (m, 1H), 7.67 - 7.63 (m, 1H), 7.60 (d, *J* = 8.6 Hz, 2H), 7.29 (dd, *J* = 5.3, 6.7 Hz, 1H), 5.30 (s, 2H), 5.13 (dd, *J* = 5.0, 13.3 Hz, 1H), 4.53 - 4.44 (m, 1H), 4.41 - 4.30 (m, 1H), 2.96 - 2.86 (m, 1H), 2.65 - 2.58 (m, 1H), 2.41 (dq, *J* = 4.4, 13.2 Hz, 1H), 2.06 - 1.99 (m, 1H). MS (ESI) *m/z* 471.2 [M+H]⁺

Step 1: To a solution of (4-nitrophenyl)boronic acid (1.41 g, 8.44 mmol, 1.00 eq) and 2-bromopyridine (1.20 mL, 12.7 mmol, 1.50 eq) in ethanol (35.0 mL) were added potassium carbonate (2.33 g, 16.9 mmol, 2.00 eq) and tetrakis(triphenylphosphine)palladium(0) (1.95 g, 1.69 mmol, 0.20 eq) in one portion. The reaction was stirred at 90°C under nitrogen for 12 h. The mixture was diluted with water (30.0 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with brine (2 × 10.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1 to 2/1) to afford 2-(4-nitrophenyl)pyridine.

Step 2: To a solution of 2-(4-nitrophenyl)pyridine (600 mg, 3.00 mmol, 1.00 eq) in methanol (6.00 mL) and water (3.00 mL) were added ferrous powder (502 mg, 8.99 mmol, 3.00 eq) and ammonium chloride (802 mg, 15.0 mmol, 5.00 eq). The reaction was stirred at 80°C for 2 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was diluted with water (30.0 mL) and extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with brine (2 × 10.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 4-(2-pyridyl)aniline.

Step 3: To a solution of 4-(pyridin-2-yl)aniline (200 mg, 1.18 mmol, 1.00 eq) and pyridine (0.28 mL, 3.53 mmol, 3.00 eq) in acetonitrile (3.00 mL) was added phenyl chloroformate (0.22 mL, 1.76 mmol, 1.50 eq) dropwise at 0°C. The reaction was stirred at 25°C for 12 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (4-(pyridin-2-yl)phenyl)carbamate.

Compound 51: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl(5-methoxy-6-methylpyridin-3-yl)carbamate. ¹H NMR

(400 MHz, DMSO- d_6) δ = 10.99 (s, 1H), 10.70 (br s, 1H), 8.34 (s, 1H), 7.98 (s, 1H), 7.81 (s, 1H), 7.73 - 7.62 (m, 2H), 5.35 (s, 2H), 5.12 (dd, J = 5.1, 13.3 Hz, 1H), 4.51 - 4.45 (m, 1H), 4.37 - 4.30 (m, 1H), 3.93 (s, 3H), 2.97 - 2.86 (m, 1H), 2.60 (br d, J = 17.6 Hz, 1H), 2.50 - 2.49 (m, 3H), 2.40 (dq, J = 4.4, 13.2 Hz, 1H), 2.07 - 1.95 (m, 1H). MS (ESI) m/z 439.1 $[M+H]^+$

Step 1: To a solution of 2-chloro-3-methoxy-5-nitro-pyridine (3.00 g, 15.9 mmol, 1.00 eq), methylboronic acid (1.90 g, 31.8 mmol, 2.00 eq) and potassium carbonate (6.60 g, 47.7 mmol, 3.00 eq) in dioxane (30.0 mL) was added tetrakis(triphenylphosphine)palladium(0) (1.84 g, 1.59 mmol, 0.10 eq) at 25°C. The reaction was stirred at 110°C for 12 h under nitrogen. The mixture was concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 1/0 to 30/1) to afford 3-methoxy-2-methyl-5-nitropyridine.

Step 2: A mixture of 3-methoxy-2-methyl-5-nitropyridine (500 mg, 2.97 mmol, 1.00 eq), iron powder (498 mg, 8.92 mmol, 3.00 eq), and ammonium chloride (795 mg, 14.9 mmol, 5.00 eq) in methanol (4.00 mL) and water (2.00 mL) was stirred at 80°C for 1 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was added to water (80.0 mL) and stirred for 10 min. The solution was extracted with ethyl acetate (3 $\times$ 50.0 mL). The combined organic layers were washed with brine (80.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 5-methoxy-6-methylpyridin-3-amine.

Step 3: To a solution of 5-methoxy-6-methylpyridin-3-amine (200 mg, 1.45 mmol, 1.00 eq), and pyridine (0.58 mL, 7.24 mmol, 5.00 eq) in acetonitrile (4.00 mL) was added phenyl chloroformate (0.22 mL, 1.74 mmol, 1.20 eq) dropwise at 0°C. The reaction was stirred at 25°C for 12 h. The mixture was concentrated under reduced pressure to give a residue. The residue was diluted with water (50.0 mL) and extracted with ethyl acetate (3 $\times$ 40.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over sodium sulfate, filtered, and concentrated and the obtained residue was purified by standard methods to afford phenyl (5-methoxy-6-methylpyridin-3-yl)carbamate.

Compound 52:

Step 1: To a solution of 2-chloro-1-methyl-4-nitrobenzene (10.0 g, 58.3 mmol, 12.1 mL, 1.00 eq) in sulfuric acid (100 mL) was added *N*-iodosuccinimide (14.4 g, 64.1 mmol, 1.10

eq) in portions. The reaction was stirred at 60°C for 2 h. The mixture was poured into water (300 mL) and extracted with ethyl acetate (3 × 80.0 mL). The combined organic layers were washed with brine (50 mL) and dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 1-chloro-3-iodo-2-methyl-5-nitrobenzene.

5 **Step 2:** To a solution of 1-chloro-3-iodo-2-methyl-5-nitrobenzene (7.00 g, 23.5 mmol, 1.00 eq) and potassium hydroxide (3.96 g, 70.6 mmol, 3.00 eq) in dioxane (70.0 mL) and water (10.0 mL) were added tris(dibenzylideneacetone)dipalladium(0) (2.15 g, 2.35 mmol, 0.10 eq) and 2-di-*tert*-butylphosphino-2,4,6-triisopropylbiphenyl (999 mg, 2.35 mmol, 0.10 eq) under nitrogen. The reaction was stirred at 80°C for 12 h. The mixture was diluted with water
10 (300 mL) and extracted with ethyl acetate (3 × 80.0 mL). The combined organic layers were washed with brine (50.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 1/0 to 10/1) to afford 3-chloro-2-methyl-5-nitrophenol.

15 **Step 3:** To a solution of 3-chloro-2-methyl-5-nitrophenol (1.00 g, 5.33 mmol, 1.00 eq) and *tert*-butyl 3-(((methylsulfonyl)oxy)methyl)pyrrolidine-1-carboxylate (1.64 g, 5.86 mmol, 1.10 eq) in dimethylformamide (10.0 mL) was added potassium carbonate (2.21 g, 15.9 mmol, 3.00 eq) in portions. The reaction was stirred at 80°C for 12 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The
20 residue was purified by reversed phase preparative HPLC to afford *tert*-butyl 3-((3-chloro-2-methyl-5-nitrophenoxy)methyl)pyrrolidine-1-carboxylate.

Step 4: To a solution of *tert*-butyl 3-((3-chloro-2-methyl-5-nitrophenoxy)methyl)pyrrolidine-1-carboxylate (400 mg, 1.08 mmol, 1.00 eq) and ammonium chloride (289 mg, 5.39 mmol, 5.00 eq) in methanol (4.00 mL) and water (4.00
25 mL) was added iron powder (181 mg, 3.24 mmol, 3.00 eq) in portions. The reaction was stirred at 80°C for 2 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was diluted with water (100 mL) and extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with
30 reduced pressure to afford *tert*-butyl 3-((5-amino-3-chloro-2-methylphenoxy)methyl)pyrrolidine-1-carboxylate.

Step 5: To a solution of *tert*-butyl 3-((5-amino-3-chloro-2-methylphenoxy)methyl)pyrrolidine-1-carboxylate (200 mg, 587 μ mol, 1.00 eq) and pyridine (0.14 mL, 1.76 mmol, 3.00 eq) in acetonitrile (5.00 mL) was added phenyl chloroformate (0.11 mL, 880 μ mol, 1.50 eq) dropwise at 0°C. The reaction was stirred at 25°C for 12 h. The mixture was concentrated under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC to afford *tert*-butyl 3-((3-chloro-2-methyl-5-((phenoxycarbonyl)amino)phenoxy)methyl)pyrrolidine-1-carboxylate.

Step 6: To a solution of 3-(6-(hydroxymethyl)-1-oxoisindolin-2-yl)piperidine-2,6-dione **VIII** (100 mg, 365 μ mol, 1.00 eq) and *tert*-butyl 3-((3-chloro-2-methyl-5-((phenoxycarbonyl)amino)phenoxy)methyl)pyrrolidine-1-carboxylate (168 mg, 365 μ mol, 1.00 eq) in dimethylformamide (1.00 mL) was added sodium hydride (60% dispersion in mineral oil) (29.2 mg, 729 μ mol, 2.00 eq) in portions at 0°C. The reaction was stirred at 25°C for 1 h. The mixture was quenched slowly with 1M hydrochloric acid (2.00 mL) and concentrated under reduced pressure to afford *tert*-butyl 3-((3-chloro-5-(((2-(2,6-dioxopiperidin-3-yl)-3-oxoisindolin-5-yl)methoxy)carbonyl)amino)-2-methylphenoxy)methyl)pyrrolidine-1-carboxylate.

Step 7: A solution of *tert*-butyl 3-((3-chloro-5-(((2-(2,6-dioxopiperidin-3-yl)-3-oxoisindolin-5-yl)methoxy)carbonyl)amino)-2-methylphenoxy)methyl)pyrrolidine-1-carboxylate (200 mg, 312 μ mol, 1.00 eq) in hydrochloric acid/ethyl acetate (3 M, 5.00 mL) was stirred at 25°C for 1 h. The mixture was concentrated to give a residue. The residue was purified by a standard method to afford Compound 52. ^1H NMR (400 MHz, DMSO- d_6) δ = 11.00 (s, 1H), 9.95 (s, 1H), 9.24 (br d, J = 3.5 Hz, 2H), 7.79 (s, 1H), 7.71 - 7.62 (m, 2H), 7.17 (br d, J = 13.4 Hz, 2H), 5.28 (s, 2H), 5.13 (dd, J = 5.1, 13.3 Hz, 1H), 4.54 - 4.30 (m, 2H), 4.03 - 3.90 (m, 2H), 3.48 - 3.40 (m, 1H), 3.28 - 3.15 (m, 2H), 3.08 - 2.99 (m, 1H), 2.97 - 2.86 (m, 1H), 2.75 (td, J = 7.2, 14.4 Hz, 1H), 2.61 (br d, J = 17.6 Hz, 1H), 2.41 (dq, J = 4.5, 13.2 Hz, 1H), 2.14 (s, 3H), 2.13 - 2.06 (m, 1H), 2.06 - 1.97 (m, 1H), 1.85 - 1.73 (m, 1H). MS (ESI) m/z 541.2 $[\text{M}+\text{H}]^+$

Compound 53: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl *N*-(6,7-dihydro-5*H*-cyclopenta[b]pyridin-3-yl)carbamate. ^1H NMR (400 MHz, DMSO- d_6) δ = 11.01 (s, 1H), 10.59 - 10.34 (m, 1H), 8.67 - 8.54 (m, 1H), 8.18 - 8.01 (m, 1H), 7.86 - 7.77 (m, 1H), 7.73 - 7.69 (m, 1H), 7.67 - 7.63 (m, 1H), 5.33 (s, 2H), 5.13 (dd, J = 5.2, 13.4 Hz, 1H), 4.53 - 4.44 (m, 1H), 4.39 - 4.32 (m, 1H),

3.02 (br dd, $J = 7.5, 18.5$ Hz, 4H), 2.96 - 2.89 (m, 1H), 2.66 - 2.57 (m, 1H), 2.41 (dd, $J = 4.4, 13.2$ Hz, 1H), 2.23 - 2.11 (m, 2H), 2.06 - 1.98 (m, 1H). MS (ESI) m/z 435.1 $[M+H]^+$

Step 1: To a solution of 3-nitro-6,7-dihydro-5*H*-cyclopenta[b]pyridine (600 mg, 3.65 mmol, 1.00 eq) in methanol (6.00 mL) and water (3.00 mL) were added ferrous powder (612 mg, 11.0 mmol, 3.00 eq) and ammonium chloride (977 mg, 18.3 mmol, 5.00 eq). The reaction was stirred at 80°C for 2 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. Water (30.0 mL) was added to the residue, and the mixture was extracted with ethyl acetate (3×30.0 mL). The combined organic phases were washed with brine (2×10.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 6,7-dihydro-5*H*-cyclopenta[b]pyridin-3-amine.

Step 2: To a solution of 6,7-dihydro-5*H*-cyclopenta[b]pyridin-3-amine (350 mg, 2.61 mmol, 1.00 eq) and phenyl chloroformate (0.49 mL, 3.91 mmol, 1.50 eq) in methanol (3.00 mL) was added pyridine (0.63 mL, 7.83 mmol, 3.00 eq) in one portion. The reaction was stirred at 25°C for 2 h. The mixture was diluted with water (30.0 mL) and extracted with ethyl acetate (3×30.0 mL). The combined organic phases were washed with brine (2×10.0 mL), dried over sodium sulfate, filtered, and concentrated and the obtained residue was purified by standard methods to afford phenyl (6,7-dihydro-5*H*-cyclopenta[b]pyridin-3-yl)carbamate.

Compound 54: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (7,8-dihydro-5*H*-pyrano[4,3-*b*]pyridin-3-yl)carbamate. ^1H NMR (400 MHz, DMSO- d_6) $\delta = 10.99$ (s, 1H), 10.72 (s, 1H), 8.69 (s, 1H), 8.11 (s, 1H), 7.81 (s, 1H), 7.74 - 7.63 (m, 2H), 5.34 (s, 2H), 5.12 (dd, $J = 5.2, 13.2$ Hz, 1H), 4.81 (s, 2H), 4.51 - 4.44 (m, 1H), 4.37 - 4.31 (m, 1H), 3.98 (t, $J = 5.6$ Hz, 2H), 3.05 (s, 2H), 2.97 - 2.85 (m, 1H), 2.60 (d, $J = 17.6$ Hz, 1H), 2.40 (dq, $J = 4.4, 13.2$ Hz, 1H), 2.07 - 1.97 (m, 1H). MS (ESI) m/z 451.1 $[M+H]^+$

To a solution of 7,8-dihydro-5*H*-pyrano[4,3-*b*]pyridin-3-amine (140 mg, 0.93 mmol, 1.00 eq) in acetonitrile (3.00 mL) were added phenyl chloroformate (0.13 mL, 1.03 mmol, 1.10 eq) and pyridine (0.23 mL, 2.80 mmol, 3.00 eq). The reaction was stirred at 25°C for 2 h. The mixture was diluted with water 10.0 mL and ethyl acetate (10.0 mL). The aqueous layer was extracted with ethyl acetate (3×10.0 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated and the obtained residue was purified by standard methods to afford phenyl (7,8-dihydro-5*H*-pyrano[4,3-*b*] pyridin-3-yl)carbamate.

Compound 55: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (5-ethyl-6-methylpyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 9.85 (br s, 1H), 8.34 (s, 1H), 8.15 (s, 1H), 7.80 (s, 1H), 7.74 - 7.61 (m, 3H), 5.28 (s, 2H), 5.13 (dd, *J* = 5.2, 13.2 Hz, 1H), 4.53 - 4.43 (m, 1H), 4.40 - 4.30 (m, 1H), 2.96 - 2.88 (m, 1H), 2.63 - 2.59 (m, 1H), 2.57 (d, *J* = 7.8 Hz, 2H), 2.46 - 2.41 (m, 1H), 2.38 (s, 3H), 2.06 - 1.98 (m, 1H), 1.14 (t, *J* = 7.4 Hz, 3H). MS (ESI) *m/z* 437.3 [M+H]⁺

Step 1: To a solution of 3-bromo-2-methyl-5-nitropyridine (900 mg, 4.15 mmol, 1.00 eq), ethylboronic acid (919 mg, 12.4 mmol, 3.00 eq) and potassium carbonate (1.72 g, 12.4 mmol, 3.00 eq) in dioxane (10.0 mL) was added tetrakis(triphenylphosphine)palladium(0) (479 mg, 415 μ mol, 0.100 eq) under nitrogen. The reaction was stirred at 110°C for 12 h under nitrogen atmosphere. The mixture was concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 20/1 to 5/1) to afford 3-ethyl-2-methyl-5-nitropyridine.

Step 2: A mixture of 3-ethyl-2-methyl-5-nitropyridine (600 mg, 3.61 mmol, 1.00 eq), iron powder (605 mg, 10.8 mmol, 3.00 eq) and ammonium chloride (579 mg, 10.8 mmol, 3.00 eq) in methanol (10.0 mL) and water (10.0 mL) was stirred at 80°C for 2 h. The mixture was concentrated under reduced pressure to give a residue. The residue was added to a saturated sodium bicarbonate solution (20.0 mL) and extracted with ethyl acetate (3 $\times$ 20.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 5-ethyl-6-methylpyridin-3-amine.

Step 3: To a solution of 5-ethyl-6-methylpyridin-3-amine (350 mg, 2.57 mmol, 1.00 eq) and pyridine (0.62 mL, 7.71 mmol, 3.00 eq) in acetonitrile (5.00 mL) was added phenyl chloroformate (0.48 mL, 3.85 mmol, 1.50 eq) at 25°C. The reaction was stirred at 25°C for 2 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (5-ethyl-6-methylpyridin-3-yl)carbamate.

Compound 56: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (2,3-dihydro-1*H*-inden-5-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 9.66 (br s, 1H), 7.79 (s, 1H), 7.73 - 7.61 (m, 2H), 7.47 - 7.30 (m, 1H), 7.20 (br d, *J* = 8.0 Hz, 1H), 7.14 - 7.06 (m, 1H), 5.26 (s, 2H), 5.13 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.55 - 4.43 (m, 1H), 4.39 - 4.31 (m, 1H), 2.92 (ddd, *J* = 5.4, 13.6,

17.5 Hz, 1H), 2.80 (td, $J = 7.2, 12.7$ Hz, 4H), 2.61 (br d, $J = 17.6$ Hz, 1H), 2.41 (dd, $J = 4.3, 13.1$ Hz, 1H), 2.06 - 1.89 (m, 3H). MS (ESI) m/z 434.1 $[M+H]^+$

To a solution of 2,3-dihydro-1*H*-inden-5-amine (300 mg, 2.25 mmol, 1.00 eq) and pyridine (0.91 mL, 11.3 mmol, 5.00 eq) in acetonitrile (6.00 mL) was added phenyl chloroformate (0.42 mL, 3.38 mmol, 1.50 eq). The reaction was stirred at 25°C for 1 h. The mixture concentrated under reduced pressure to give a residue. The residue was added to water (100 mL) and stirred for 10 min. The aqueous solution was extracted with ethyl acetate (3 × 40.0 mL). The combined organic layers were washed with brine (100 mL), dried over anhydrous sodium sulfate, filtered, and concentrated and the obtained residue was purified by standard methods to afford phenyl (2,3-dihydro-1*H*-inden-5-yl)carbamate.

Compound 57: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-fluoro-5-(trifluoromethoxy)phenyl)carbamate. ^1H NMR (400 MHz, DMSO- d_6) $\delta = 10.99$ (br s, 1H), 10.35 (s, 1H), 7.80 (s, 1H), 7.71 - 7.67 (m, 1H), 7.67 - 7.61 (m, 1H), 7.39 - 7.31 (m, 2H), 6.99 (br d, $J = 8.8$ Hz, 1H), 5.30 (s, 2H), 5.13 (dd, $J = 5.1, 13.3$ Hz, 1H), 4.52 - 4.42 (m, 1H), 4.38 - 4.30 (m, 1H), 2.98 - 2.85 (m, 1H), 2.63 - 2.57 (m, 1H), 2.43 - 2.35 (m, 1H), 2.06 - 1.97 (m, 1H). MS (ESI) m/z 496.3 $[M+H]^+$

To a solution of 3-fluoro-5-(trifluoromethoxy)aniline (200 mg, 1.03 mmol, 1.00 eq) and pyridine (0.25 mL, 3.10 mmol, 3.02 eq) in acetonitrile (10.0 mL) was added phenyl chloroformate (0.15 mL, 1.23 mmol, 1.20 eq) in portions at 0°C. The reaction was stirred at 25°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (3-fluoro-5-(trifluoromethoxy)phenyl)carbamate.

Compound 58: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (4-(1-methylcyclopropyl)phenyl)carbamate. ^1H NMR (400 MHz, DMSO- d_6) $\delta = 11.00$ (s, 1H), 9.71 (br s, 1H), 7.79 (s, 1H), 7.70 - 7.66 (m, 1H), 7.66 - 7.60 (m, 1H), 7.37 (br d, $J = 8.4$ Hz, 2H), 7.17 - 7.09 (m, 2H), 5.26 (s, 2H), 5.13 (dd, $J = 5.1, 13.3$ Hz, 1H), 4.52 - 4.43 (m, 1H), 4.39 - 4.29 (m, 1H), 2.96 - 2.87 (m, 1H), 2.62 (br d, $J = 2.0$ Hz, 1H), 2.43 - 2.35 (m, 1H), 2.05 - 1.98 (m, 1H), 1.34 (s, 3H), 0.80 - 0.73 (m, 2H), 0.73 - 0.66 (m, 2H). MS (ESI) m/z 448.2 $[M+H]^+$

Step 1: To freshly distilled dichloromethane (50.0 mL) was added diethylzinc (1 M in toluene, 40.6 mL, 4.00 eq). The solution was cooled to -40°C, and diiodomethane (40.6 mL, 4.00

eq) in dichloromethane (10.0 mL) was added slowly. The mixture was stirred at -40°C for 30 min, then trifluoroacetic acid (0.15 mL, 2.03 mmol, 0.20 eq) and *N,N*-dimethylacetamide (1.05 mL, 10.1 mmol, 1.00 eq) in dichloromethane (10.0 mL) were added. The reaction was stirred at -15°C for 0.5 h, then 1-bromo-4-(prop-1-en-2-yl)benzene (2.00 g, 10.1 mmol, 1.00 eq) in dichloromethane (10.0 mL) was added at 0°C. The mixture was stirred at 25°C for 12 h. The reaction was quenched with ice-water (50.0 mL) at 0°C. The organic layer was separated and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether 100%) to afford 1-bromo-4-(1-methylcyclopropyl)benzene.

Step 2: To a solution of 1-bromo-4-(1-methylcyclopropyl)benzene (2.00 g, 9.47 mmol, 1.00 eq) (crude) in *tert*-amyl alcohol (100 mL) were added *tert*-butyl carbamate (2.00 g, 17.1 mmol, 1.80 eq), methanesulfonato(2-di-*t*butylphosphino-2,4,6-tri-*i*propyl-1,1-biphenyl)(2-amino-1,1-biphenyl-2-yl)palladium(II) (600 mg, 755 μ mol, 0.0800 eq) and sodium *tert*-butoxide (2 M in tetrahydrofuran, 14.0 mL, 2.96 eq). The reaction was stirred at 90°C for 3 h under nitrogen. The mixture was diluted with ethyl acetate (200 mL) and water (200 mL). The organic layer was separated and concentrated under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC to afford *tert*-butyl (4-(1-methylcyclopropyl)phenyl) carbamate.

Step 3: To a solution of *tert*-butyl (4-(1-methylcyclopropyl)phenyl) carbamate (520 mg, 2.10 mmol, 1.00 eq) in ethyl acetate (10.0 mL) was added hydrogen chloride/ethyl acetate (4 M, 10 mL, 19.0 eq). The reaction was stirred at 25°C for 1 h. The mixture was concentrated under reduced pressure to afford 4-(1-methylcyclopropyl)aniline.

Step 4: To a solution of 4-(1-methylcyclopropyl)aniline (200 mg, 1.09 mmol, 1.00 eq, hydrochloric acid) in acetonitrile (50.0 mL) were added pyridine (0.50 mL, 6.19 mmol, 5.69 eq) and phenyl chloroformate (187 mg, 1.20 mmol, 1.10 eq) at 0°C. The reaction was stirred at 25°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (4-(1-methylcyclopropyl)phenyl)carbamate.

Compound 59: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (4-(trifluoromethoxy)pyridin-2-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (br s, 1H), 10.80 (s, 1H), 8.38 (d, *J* = 5.6 Hz, 1H), 7.82 (s, 2H), 7.74 - 7.59 (m, 2H), 7.08 (br d, *J* = 5.5 Hz, 1H), 5.32 (s, 2H), 5.13 (br dd, *J* = 5.0,

13.4 Hz, 1H), 4.50 - 4.43 (m, 1H), 4.38 - 4.31 (m, 1H), 2.95 - 2.88 (m, 1H), 2.62 (br d, J = 2.1 Hz, 1H), 2.44 - 2.35 (m, 1H), 2.06 - 1.97 (m, 1H). MS (ESI) m/z 479.1 $[M+H]^+$

To a solution of 4-(trifluoromethoxy)pyridin-2-amine (300 mg, 1.68 mmol, 1.00 eq) and pyridine (0.68 mL, 8.42 mmol, 5.00 eq) in acetonitrile (3.00 mL) was added phenyl chloroformate (0.25 mL, 2.02 mmol, 1.20 eq) dropwise at 0°C. The reaction was stirred at 25°C for 3 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (4-(trifluoromethoxy)pyridin-2-yl)carbamate.

Compound 60: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-(pyrrolidin-1-yl)pyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO- d_6) δ = 11.00 (s, 1H), 9.43 (br s, 1H), 8.16 (s, 1H), 8.09 (br s, 1H), 7.77 (s, 1H), 7.64 (q, J = 7.7 Hz, 2H), 7.57 (br d, J = 9.4 Hz, 1H), 6.40 (d, J = 8.9 Hz, 1H), 5.23 (s, 2H), 5.12 (dd, J = 5.1, 13.3 Hz, 1H), 4.50 - 4.42 (m, 1H), 4.37 - 4.30 (m, 1H), 3.33 (br d, J = 6.7 Hz, 4H), 2.93 - 2.86 (m, 1H), 2.63 - 2.58 (m, 1H), 2.43 - 2.36 (m, 1H), 2.04 - 1.98 (m, 1H), 1.94 - 1.89 (m, 4H). MS (ESI) m/z 464.2 $[M+H]^+$

Step 1: To a solution of 2-chloro-5-nitropyridine (2.00 g, 12.6 mmol, 1.00 eq) in dimethylformamide (10.0 mL) were added pyrrolidine (1.58 mL, 18.9 mmol, 1.50 eq) and potassium carbonate (5.23 g, 37.8 mmol, 3.00 eq). The reaction was stirred at 60°C for 1 h. After cooling to room temperature, the mixture was poured into ice-water (200 mL). The resulting yellow precipitate was collected by filtration and dried under reduced pressure to afford 5-nitro-2-(pyrrolidin-1-yl)pyridine.

Step 2: To a solution of 5-nitro-2-(pyrrolidin-1-yl)pyridine (2.40 g, 12.4 mmol, 1.00 eq) in methanol (240 mL) was added palladium on carbon (100 mg, 10% weight on C). The reaction was stirred at 25°C for 1 h under hydrogen (15 Psi). The mixture was filtered, and the filtrate was concentrated under reduced pressure to afford 6-(pyrrolidin-1-yl)pyridin-3-amine.

Step 3: To a solution of 6-(pyrrolidin-1-yl)pyridin-3-amine (1.50 g, 9.19 mmol, 1.00 eq) in acetonitrile (15.0 mL) were added pyridine (3.71 mL, 45.9 mmol, 5.00 eq) and phenyl chloroformate (1.50 mL, 11.9 mmol, 1.30 eq). The reaction was stirred at 25°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (6-(pyrrolidin-1-yl)pyridin-3-yl)carbamate.

Compound 61: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (4-fluoro-3-(trifluoromethoxy)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (br s, 1H), 10.16 (br s, 1H), 7.84 - 7.62 (m, 4H), 7.50 - 7.38 (m, 2H), 5.30 (br s, 2H), 5.14 (br dd, *J* = 4.6, 13.2 Hz, 1H), 4.54 - 4.30 (m, 2H), 3.06 - 2.84 (m, 1H), 2.612 (br d, *J* = 16.8 Hz, 1H), 2.46 - 2.38 (m, 1H), 2.08 - 1.96 (m, 1H). MS (ESI) *m/z* 496.1 [M+H]⁺

To a solution of 4-fluoro-3-(trifluoromethoxy)aniline (400 mg, 2.05 mmol, 1.00 eq) and phenyl chloroformate (0.28 mL, 2.26 mmol, 1.10 eq) in acetonitrile (3.00 mL) was added pyridine (0.50 mL, 6.15 mmol, 3.00 eq) in one portion. The reaction was stirred at 25°C for 2 h. The mixture was diluted with water (30.0 mL) and extracted with ethyl acetate (3 × 30.0 mL). The combined organic phases were washed with brine (2 × 10.0 mL), dried over sodium sulfate, filtered, and concentrated and the obtained residue was purified by standard methods to afford phenyl (4-fluoro-3-(trifluoromethoxy)phenyl)carbamate.

Compound 62: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (4-(3-methyloxetan-3-yl)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.03 (s, 1H), 9.82 (br s, 1H), 7.83 (s, 1H), 7.74 - 7.65 (m, 2H), 7.48 (br d, *J* = 8.5 Hz, 2H), 7.21 (d, *J* = 8.6 Hz, 2H), 5.30 (s, 2H), 5.16 (dd, *J* = 5.2, 13.3 Hz, 1H), 4.80 (d, *J* = 5.5 Hz, 2H), 4.55 - 4.48 (m, 3H), 4.40 (s, 1H), 2.95 (s, 1H), 2.66 (br s, 1H), 2.44 (br dd, *J* = 4.5, 12.9 Hz, 1H), 2.08 - 2.01 (m, 1H), 1.63 (s, 3H). MS (ESI) *m/z* 464.2 [M+H]⁺

Step 1: To a solution of diethyl 2-methylmalonate (13.6 g, 78.0 mmol, 13.3 mL, 1.10 eq) in dimethylformamide (80.0 mL) was added sodium hydride (60% dispersion in mineral oil) (3.40 g, 85.0 mmol, 1.20 eq) slowly at 0°C. The reaction was stirred at 0°C for 0.5 h, then 1-fluoro-4-nitrobenzene (10.0 g, 70.8 mmol, 7.52 mL, 1.00 eq) was added. The mixture was stirred at 25°C for 3 h. Water (200 mL) was added, and the mixture was extracted with ethyl acetate (3 × 50.0 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1 to 8/1) to afford diethyl 2-methyl-2-(4-nitrophenyl)malonate.

Step 2: To a solution of diethyl 2-methyl-2-(4-nitrophenyl)malonate (7.00 g, 23.7 mmol, 1.00 eq) in tetrahydrofuran (15.0 mL) was added lithium aluminium hydride (953 mg, 25.1 mmol, 1.06 eq) slowly at 0°C under nitrogen. The reaction was stirred at 0°C for 3 h. The

mixture was then partitioned between dichloromethane and 1 M hydrochloric acid. The organic layer was separated, and the aqueous layer was extracted with dichloromethane (3 × 50.0 mL). The combined organic layers were concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1 to 0/1) to afford 2-methyl-2-(4-nitrophenyl)propane-1,3-diol.

Step 3: To a solution of 2-methyl-2-(4-nitrophenyl)propane-1,3-diol (200 mg, 947 μmol, 1.00 eq) in tetrahydrofuran (10.0 mL) was added *n*-butyllithium (2.5 M in hexane, 0.46 mL, 1.21 eq) and tosyl chloride (271 mg, 1.42 mmol, 1.50 eq) at 0°C. The reaction was stirred at 25°C for 1 h. After cooling to 0°C, *n*-butyllithium (2.5 M in hexane, 0.46 mL, 1.21 eq) was added. The reaction was stirred at 65°C for another 2 h. The reaction was quenched with saturated ammonium chloride (10 mL) and extracted with ethyl acetate (50.0 mL). The organic layer was separated and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 3/1) to afford 3-methyl-3-(4-nitrophenyl)oxetane.

Step 4: To a solution of 3-methyl-3-(4-nitrophenyl)oxetane (56.0 mg, 290 μmol, 1.00 eq) in ethyl acetate (5.00 mL) was added wet palladium on carbon (10% weight on C) (20.0 mg). The reaction was stirred at 25°C for 2 h under hydrogen (15.0 Psi). The mixture was filtered, and the filtrate was concentrated under reduced pressure to afford 4-(3-methyloxetan-3-yl)aniline.

Step 5: To a solution of 4-(3-methyloxetan-3-yl)aniline (60.0 mg, 368 μmol, 1.00 eq) in acetonitrile (3.00 mL) was added pyridine (0.15 mL, 1.84 mmol, 5.00 eq) and phenyl chloroformate (0.07 mL, 551 μmol, 1.50 eq) at 0°C. The reaction was stirred at 0°C for 0.5 h. The mixture was filtered, and the filtrate was concentrated and the obtained residue was purified by standard methods to afford phenyl (4-(3-methyloxetan-3-yl)phenyl)carbamate.

Compound 63: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (2-ethylpyridin-4-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.37 (br d, *J* = 10.6 Hz, 1H), 11.00 (s, 1H), 8.54 (d, *J* = 6.7 Hz, 1H), 7.85 - 7.80 (m, 2H), 7.77 - 7.70 (m, 2H), 7.69 - 7.64 (m, 1H), 5.40 (s, 2H), 5.13 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.54 - 4.45 (m, 1H), 4.40 - 4.32 (m, 1H), 2.97 - 2.87 (m, 3H), 2.61 (br d, *J* = 17.1 Hz, 1H), 2.41 (br dd, *J* = 4.5, 13.0 Hz, 1H), 2.06 - 1.98 (m, 1H), 1.27 (t, *J* = 7.5 Hz, 3H). MS (ESI) *m/z* 423.2 [M+H]⁺

To a solution of 2-ethylpyridin-4-amine (0.500 g, 4.09 mmol, 1.00 eq) and pyridine (1.65 mL, 20.4 mmol, 5.00 eq) in dimethylformamide (50.0 mL) was added phenyl chloroformate (0.77 mL, 6.19 mmol, 1.51 eq) at 0°C. The reaction was stirred at 0°C for 12 h. The mixture was filtered and concentrated and the obtained residue was purified by standard methods to afford phenyl (2-ethylpyridin-4-yl)carbamate.

Compound 64: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (2-(piperidin-1-yl)pyrimidin-5-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 9.55 (br s, 1H), 8.39 (br s, 2H), 7.78 (s, 1H), 7.70 - 7.61 (m, 2H), 5.26 (s, 2H), 5.17 - 5.07 (m, 1H), 4.53 - 4.28 (m, 2H), 3.71 - 3.64 (m, 4H), 3.00 - 2.85 (m, 1H), 2.66 - 2.57 (m, 1H), 2.44 - 2.34 (m, 1H), 2.08 - 1.97 (m, 1H), 1.67 - 1.57 (m, 2H), 1.55 - 1.42 (m, 4H). MS (ESI) *m/z* 479.1 [M+H]⁺

Step 1: A solution of 2-chloro-5-nitro-pyrimidine (1.00 g, 6.27 mmol, 1.00 eq), piperidine (1.24 mL, 12.5 mmol, 2.00 eq) and potassium carbonate (2.60 g, 18.8 mmol, 3.00 eq) in dimethylformamide (5.00 mL) was stirred at 25°C for 12 h. The mixture was diluted with ethyl acetate (100 mL) and water (100 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 200 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 5-nitro-2-(piperidin-1-yl)pyrimidine.

Step 2: A mixture of 5-nitro-2-(1-piperidyl) pyrimidine (1.31 g, 6.27 mmol, 1.00 eq) and palladium on carbon (10% weight on C) (2.00 g, 6.27 mmol, 1.00 eq) in methanol (10.0 mL) was stirred at 25°C for 12 h under hydrogen (15 Psi). The mixture was filtered over Celite, and the filtrate was concentrated under reduced pressure to afford 2-(piperidin-1-yl)pyrimidin-5-amine.

Step 3: To a solution of 2-(piperidin-1-yl)pyrimidin-5-amine (300 mg, 1.68 mmol, 1.00 eq), and pyridine (0.41 mL, 5.05 mmol, 3.00 eq) in acetonitrile (10.0 mL) was added phenyl chloroformate (0.32 mL, 2.52 mmol, 1.50 eq). The reaction was stirred at 25°C for 12 h. The mixture was diluted with ethyl acetate (50.0 mL) and water (50.0 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 100 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated and the obtained residue was purified by standard methods to afford phenyl (2-(piperidin-1-yl)pyrimidin-5-yl)carbamate.

Compound 65: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)pyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 9.57 (br s, 1H), 8.28 (s, 1H), 8.17 (br s, 1H), 7.78 (s, 1H), 7.72 - 7.58 (m, 3H), 6.69 (d, *J* = 9.1 Hz, 1H), 5.25 (s, 2H), 5.13 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.50 - 4.32 (m, 4H), 3.71 (d, *J* = 11.6 Hz, 2H), 2.97 - 2.89 (m, 1H), 2.88 (d, *J* = 2.4 Hz, 1H), 2.85 (d, *J* = 2.4 Hz, 1H), 2.65 - 2.58 (m, 1H), 2.46 - 2.35 (m, 1H), 2.06 - 1.98 (m, 1H), 1.88 - 1.78 (m, 2H), 1.77 - 1.70 (m, 2H). MS (ESI) *m/z* 506.3 [M+H]⁺

Step 1: To a solution of 2-chloro-5-nitropyridine (1.00 g, 6.31 mmol, 1.00 eq) and 8-oxa-3-azabicyclo[3.2.1]octane hydrochloride (1.00 g, 6.68 mmol, 1.06 eq, hydrochloride) in dimethylformamide (10.0 mL) was added potassium carbonate (2.62 g, 18.9 mmol, 3.00 eq) in portions. The reaction was stirred at 25°C for 3 h. The mixture was diluted with water (100 mL) and extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-(5-nitro-2-pyridyl)-8-oxa-3-azabicyclo[3.2.1]octane.

Step 2: To a solution of 3-(5-nitropyridin-2-yl)-8-oxa-3-azabicyclo[3.2.1]octane (800 mg, 3.40 mmol, 1.00 eq) in methanol (10.0 mL) was added palladium on carbon (10% weight on C) (80.0 mg) in one portion under nitrogen. The reaction was stirred at 25°C for 1 h under hydrogen (15 Psi). The mixture was filtered, and the filtrate was concentrated under reduced pressure to afford 6-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)pyridin-3-amine.

Step 3: To a solution of 6-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)pyridin-3-amine (400 mg, 1.95 mmol, 1.00 eq) and pyridine (0.79 mL, 9.74 mmol, 5.00 eq) in acetonitrile (5.00 mL) was added phenyl chloroformate (0.32 mL, 2.53 mmol, 1.30 eq) at 0°C. The reaction was stirred at 25°C for 12 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (6-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)pyridin-3-yl)carbamate.

Compound 66: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (2,3-dihydrobenzofuran-5-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 9.56 (br s, 1H), 7.80 (s, 1H), 7.74 - 7.58 (m, 2H), 7.36 (br s, 1H), 7.14 (br d, *J* = 8.0 Hz, 1H), 6.68 (d, *J* = 8.6 Hz, 1H), 5.26 (s, 2H), 5.14 (dd, *J* = 5.0, 13.4 Hz, 1H), 4.54 - 4.44 (m, 3H), 4.42 - 4.30 (m, 1H), 3.18 - 3.10 (m, 2H), 2.98 -

2.86 (m, 1H), 2.62 (br d, $J = 16.8$ Hz, 1H), 2.48 - 2.32 (m, 1H), 2.10 - 1.98 (m, 1H). MS (ESI) m/z 436.2 $[M+H]^+$

To a mixture of 2,3-dihydrobenzofuran-5-amine (400 mg, 2.96 mmol, 1.00 eq) and phenyl chloroformate (0.41 mL, 3.26 mmol, 1.10 eq) in acetonitrile (3.00 mL) was added pyridine (0.72 mL, 8.88 mmol, 3.00 eq) in one portion. The reaction was stirred at 25°C for 2 h. The mixture was diluted with water (30.0 mL) and extracted with ethyl acetate (3×30.0 mL). The combined organic phases were separated, washed with brine (2×10.0 mL), dried over sodium sulfate, filtered, and concentrated and the obtained residue was purified by standard methods to afford phenyl (2,3-dihydrobenzofuran-5-yl)carbamate.

Compound 67: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl chroman-6-ylcarbamate. ^1H NMR (400 MHz, DMSO- d_6) δ = 11.00 (s, 1H), 9.52 (br s, 1H), 7.78 (s, 1H), 7.70 - 7.58 (m, 2H), 7.17 (br s, 1H), 7.10 (br d, $J = 8.8$ Hz, 1H), 6.64 (d, $J = 8.8$ Hz, 1H), 5.24 (s, 2H), 5.13 (dd, $J = 5.2, 13.2$ Hz, 1H), 4.51 - 4.42 (m, 1H), 4.39 - 4.30 (m, 1H), 4.11 - 4.03 (m, 2H), 2.97 - 2.86 (m, 1H), 2.69 (t, $J = 6.4$ Hz, 2H), 2.61 (br d, $J = 17.6$ Hz, 1H), 2.41 (dt, $J = 8.8, 13.2$ Hz, 1H), 2.06 - 1.98 (m, 1H), 1.93 - 1.84 (m, 2H). MS (ESI) m/z 450.3 $[M+H]^+$

Step 1: A solution of chromane (1.00 g, 7.45 mmol, 1.00 eq) in nitric acid (10.0 mL) was stirred at -10°C for 1 h. The reaction mixture was diluted with ice water (50.0 mL) and then quenched by addition of sodium hydroxide aqueous solution (1 N, 50.0 mL) at 0°C. The mixture was extracted with dichloromethane (3×20.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1 to 5/1) to afford 6-nitrochroman.

Step 2: To a solution of 6-nitrochromane (650 mg, 3.63 mmol, 1.00 eq) in ethyl acetate (6.00 mL) was added palladium on carbon (10% weight on C) (100 mg) under nitrogen atmosphere. The reaction mixture was stirred at 25°C for 2 h under hydrogen. The mixture was filtered and concentrated under reduced pressure to afford chroman-6-amine.

Step 3: To a solution of chroman-6-amine (120 mg, 804 μmol , 1.00 eq) and pyridine (0.20 mL, 2.41 mmol, 3.00 eq) in acetonitrile (2.00 mL) was added phenyl chloroformate (0.12 mL, 965 μmol , 1.20 eq) at 25°C. The reaction was stirred at 25°C for 12 h. The mixture was

concentrated and the obtained residue was purified by standard methods to afford phenyl chroman-6-ylcarbamate.

Compound 68: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-chloro-4-methyl-5-((1-methylpyrrolidin-3-yl)oxy)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.70 - 11.08 (m, 1H), 10.70 (br s, 1H), 9.70 (s, 1H), 7.80 (s, 1H), 7.70 - 7.66 (m, 1H), 7.66 - 7.62 (m, 1H), 7.26 (br s, 1H), 7.12 (s, 1H), 5.30 (s, 2H), 5.08 (br dd, *J* = 5.4, 13.0 Hz, 2H), 4.54 - 4.46 (m, 1H), 4.46 - 4.36 (m, 1H), 4.06 - 3.56 (m, 3H), 3.44 - 3.36 (m, 2H), 2.92 - 2.84 (m, 4H), 2.68 - 2.62 (m, 1H), 2.44 (dd, *J* = 4.6, 13.2 Hz, 1H), 2.20 (s, 4H), 2.12 - 2.04 (m, 1H). MS (ESI) *m/z* 541.3 [M+H]⁺

Step 1: A solution of *tert*-butyl 3-(3-chloro-2-methyl-5-nitrophenoxy)pyrrolidine-1-carboxylate (described in example **44**) (730 mg, 2.05 μ mol, 1.00 eq) and hydrochloric acid/ethyl acetate (10.0 mL) in ethyl acetate (20.0 mL) was stirred at 25°C for 4 h. The mixture was concentrated under reduced pressure to give a residue. The residue was diluted with saturated sodium bicarbonate (50.0 mL) and extracted with ethyl acetate (3 $\times$ 20.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-(3-chloro-2-methyl-5-nitrophenoxy)pyrrolidine.

Step 2: To a solution of 3-(3-chloro-2-methyl-5-nitrophenoxy)pyrrolidine (400 mg, 1.56 mmol, 1.00 eq) and formaldehyde 37% (12.0 mL, 161 mmol, 103 eq) in methanol (3.00 mL) was added acetic acid (0.09 mL, 1.56 mmol, 1.00 eq) at 25°C. The reaction was stirred at 25°C for 0.5 h. Then sodium cyanoborohydride (979 mg, 15.6 mmol, 10.0 eq) was added, and the reaction was stirred at 25°C for another 1.5 h. The mixture was concentrated under reduced pressure to give a residue. The residue was diluted with water (50.0 mL) and extracted with ethyl acetate (3 $\times$ 20.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC to afford 3-(3-chloro-2-methyl-5-nitrophenoxy)-1-methylpyrrolidine.

Step 3: To a mixture of 3-(3-chloro-2-methyl-5-nitrophenoxy)-1-methylpyrrolidine (250 mg, 923 μ mol, 1.00 eq), iron powder (258 mg, 4.62 mmol, 5.00 eq) and ammonium chloride (247 g, 4.62 mmol, 5.00 eq) in methanol (5.00 mL) was added water (5.00 mL) at 25°C. The reaction was stirred at 80°C for 2 h. The mixture was concentrated under reduced

pressure to give a residue. The residue was poured into saturated sodium bicarbonate (20.0 mL) and extracted with ethyl acetate (3 × 20.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-chloro-4-methyl-5-((1-methylpyrrolidin-3-yl)oxy)aniline.

Step 4: To a solution of 3-chloro-4-methyl-5-(1-methylpyrrolidin-3-yl)oxy-aniline (116 mg, 482 μmol, 1.00 eq) and phenyl chloroformate (0.66 mL, 530 μmol, 1.10 eq) in acetonitrile (5.00 mL) was added pyridine (0.12 mL, 1.45 mmol, 3.00 eq) in one portion at 25°C. The reaction was stirred at 25°C for 2 h. The mixture was diluted with water (30.0 mL) and exacted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with brine (2 × 10.0 mL), dried over sodium sulfate, filtered, and concentrated and the obtained residue was purified by standard methods to afford (3-chloro-4-methyl-5-((1-methylpyrrolidin-3-yl)oxy)phenyl)carbamate.

Compound 69: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-(3-methylpyrrolidin-1-yl)pyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 9.42 (br s, 1H), 8.15 (s, 1H), 8.10 (br s, 1H), 7.78 (s, 1H), 7.70 - 7.62 (m, 2H), 7.58 (br d, *J* = 7.7 Hz, 1H), 6.38 (d, *J* = 8.9 Hz, 1H), 5.24 (s, 2H), 5.13 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.52 - 4.43 (m, 1H), 4.39 - 4.31 (m, 1H), 3.54 (dd, *J* = 7.3, 9.9 Hz, 1H), 3.47 - 3.43 (m, 1H), 3.29 - 3.27 (m, 1H), 2.98 - 2.85 (m, 2H), 2.65 - 2.56 (m, 1H), 2.47 - 2.38 (m, 1H), 2.36 - 2.29 (m, 1H), 2.12 - 1.95 (m, 2H), 1.55 (qd, *J* = 8.3, 12.1 Hz, 1H), 1.07 (d, *J* = 6.6 Hz, 3H). MS (ESI) *m/z* 478.2 [M+H]⁺

Step 1: To a solution of 2-chloro-5-nitropyridine (2.00 g, 12.6 mmol, 1.00 eq) in dimethylformamide (20.0 mL) was added 3-methylpyrrolidine hydrochloride (2.30 g, 18.9 mmol, 1.50 eq) and potassium carbonate (5.23 g, 37.8 mmol, 3.00 eq). The reaction was stirred at 60°C for 1 h. The mixture was poured into water (500 mL) at 0°C. The resulting precipitate was collected by filtration and dried under vacuum to afford 2-(3-methylpyrrolidin-1-yl)-5-nitropyridine.

Step 2: To a solution of 2-(3-methylpyrrolidin-1-yl)-5-nitropyridine (2.60 g, 12.5 mmol, 1.00 eq) in methanol (30.0 mL) was added palladium on carbon (10% weight on C) (50.0 mg). The reaction was stirred at 25°C for 1 h under hydrogen (15 Psi). The mixture was filtered, and the filtrate was concentrated under reduced pressure to afford 6-(3-methylpyrrolidin-1-yl)pyridin-3-amine.

Step 3: To a solution of 6-(3-methylpyrrolidin-1-yl)pyridin-3-amine (1.60 g, 9.03 mmol, 1.00 eq) and pyridine (3.64 mL, 45.1 mmol, 5.00 eq) in acetonitrile (16.0 mL) was added phenyl chloroformate (1.47 mL, 11.7 mmol, 1.30 eq). The reaction was stirred at 25°C for 1 h. The mixture was concentrated and the residue was purified by a standard method to afford phenyl(6-(3-methylpyrrolidin-1-yl)pyridin-3-yl)carbamate.

Compound 70: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (3-chloro-4-methyl-5-((1-methylpyrrolidin-3-yl)methoxy)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 10.85 (br d, *J* = 3.7 Hz, 1H), 9.95 (s, 1H), 7.79 (s, 1H), 7.73 - 7.60 (m, 2H), 7.26 - 7.10 (m, 2H), 5.28 (s, 2H), 5.13 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.54 - 4.44 (m, 1H), 4.41 - 4.29 (m, 1H), 4.08 - 3.93 (m, 2H), 3.75 - 3.69 (m, 1H), 3.49 - 3.41 (m, 1H), 3.26 - 3.16 (m, 1H), 3.13 - 3.01 (m, 1H), 2.97 - 2.86 (m, 2H), 2.81 (t, *J* = 4.8 Hz, 3H), 2.61 (br d, *J* = 17.9 Hz, 1H), 2.56 - 2.52 (m, 1H), 2.41 (dq, *J* = 4.4, 13.2 Hz, 1H), 2.32 - 2.15 (m, 1H), 2.14 (s, 3H), 2.06 - 1.97 (m, 1H), 1.96 - 1.71 (m, 1H). MS (ESI) *m/z* 555.2 [M+H]⁺

Step 1: A mixture of *tert*-butyl 3-((3-chloro-2-methyl-5-nitrophenoxy)methyl)pyrrolidine-1-carboxylate (described in example **52**) (1.26 g, 3.40 mmol, 1.00 eq) in hydrochloric acid/ethyl acetate (4.0 M, 1.13 mL) was stirred at 25°C for 1 h. The mixture was concentrated under reduced pressure to afford 3-((3-chloro-2-methyl-5-nitrophenoxy)methyl)pyrrolidine.

Step 2: To a solution of 3-((3-chloro-2-methyl-5-nitrophenoxy)methyl)pyrrolidine (900 mg, 3.32 mmol, 1.00 eq) in 2,2,2-trifluoroethanol (10.0 mL) was added paraformaldehyde (0.46 mL, 16.6 mmol, 5.00 eq). The reaction was stirred at 60°C for 0.5 h. Then sodium borohydride (252 mg, 6.65 mmol, 2.00 eq) was added in portions, and the reaction was stirred at 60°C for 1 h. The mixture was diluted with water (100 mL) and extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with brine (20.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 3-((3-chloro-2-methyl-5-nitrophenoxy)methyl)-1-methylpyrrolidine.

Step 3: To a solution of 3-((3-chloro-2-methyl-5-nitrophenoxy)methyl)-1-methylpyrrolidine (850 mg, 2.99 mmol, 1.00 eq) and ammonium chloride (798 mg, 14.9 mmol, 5.00 eq) in methanol (5.00 mL) and water (5.00 mL) was added iron powder (500 mg, 8.96 mmol, 3.00 eq) in portions. The reaction was stirred at 80°C for 2 h. The mixture was concentrated

under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC to afford 3-chloro-4-methyl-5-((1-methylpyrrolidin-3-yl)methoxy)aniline.

Step 4: To a solution of 3-chloro-4-methyl-5-((1-methylpyrrolidin-3-yl)methoxy)aniline (300 mg, 1.18 mmol, 1.00 eq) and pyridine (0.29 mL, 3.53 mmol, 3.00 eq) in acetonitrile (5.00 mL) was added phenyl chloroformate (0.22 mL, 1.77 mmol, 1.50 eq) dropwise at 0°C. The reaction was stirred at 25°C for 12 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (3-chloro-4-methyl-5-((1-methylpyrrolidin-3-yl)methoxy)phenyl)carbamate.

Compound 71: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (2-ethyl-6-methylpyridin-4-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (br s, 1H), 10.11 (s, 1H), 8.27 (br s, 1H), 7.80 (s, 1H), 7.72 - 7.59 (m, 2H), 7.14 (d, *J* = 3.5 Hz, 2H), 5.30 (s, 2H), 5.13 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.51 - 4.31 (m, 2H), 2.98 - 2.87 (m, 1H), 2.61 (q, *J* = 7.5 Hz, 3H), 2.41 (br dd, *J* = 4.4, 13.1 Hz, 1H), 2.35 (s, 3H), 2.07 - 1.96 (m, 1H), 1.17 (t, *J* = 7.6 Hz, 3H). MS (ESI) *m/z* 437.1 [M+H]⁺

Step 1: To a mixture of 2-chloro-6-methyl-4-nitropyridine (2.00 g, 11.6 mmol, 1.00 eq), ethylboronic acid (2.57 g, 34.8 mmol, 3.00 eq) and potassium carbonate (4.81 g, 34.8 mmol, 3.00 eq) in dioxane (20.0 mL) was added tetrakis(triphenylphosphine)palladium(0) (1.34 g, 1.16 mmol, 0.100 eq) under nitrogen atmosphere. The reaction was stirred at 110°C for 12 h. The mixture was concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1) to afford 2-ethyl-6-methyl-4-nitropyridine.

Step 2: To a solution of 2-ethyl-6-methyl-4-nitropyridine (650 mg, 3.91 mmol, 1.00 eq) in methanol (50.0 mL) was added palladium on carbon (10% weight on C) (10.0 mg) in one portion. The reaction was stirred at 25°C for 2 h under hydrogen (15 Psi). The mixture was filtered, and the filtrate was concentrated under reduced pressure to afford 2-ethyl-6-methylpyridin-4-amine.

Step 3: To a solution of 2-ethyl-6-methylpyridin-4-amine (450 mg, 3.30 mmol, 1.00 eq) in dimethylformamide (5.00 mL) was added sodium hydride (60% dispersion in mineral oil) (396 mg, 9.91 mmol, 3.00 eq) in portions at 0°C. The reaction was stirred at 0°C for 0.5 h. Then phenyl chloroformate (0.50 mL, 3.96 mmol, 1.20 eq) was added dropwise at 0°C. The

reaction was stirred at 25°C for 12 h, then it was quenched with 1M hydrochloric acid and filtered. The filtrate was concentrated and the obtained residue was purified by standard methods to afford phenyl (2-ethyl-6-methylpyridin-4-yl)carbamate.

Compound 72: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (5-fluoro-6-(piperidin-1-yl)pyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 9.92 (br s, 1H), 8.07 (s, 1H), 7.79 (s, 1H), 7.72 - 7.59 (m, 3H), 5.28 (s, 2H), 5.13 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.52 - 4.43 (m, 1H), 4.38 - 4.31 (m, 1H), 3.23 (br d, *J* = 5.5 Hz, 4H), 2.97 - 2.87 (m, 1H), 2.65 - 2.57 (m, 1H), 2.46 - 2.35 (m, 1H), 2.07 - 1.97 (m, 1H), 1.66 - 1.54 (m, 6H). MS (ESI) *m/z* 496.2 [M+H]⁺

Step 1: To a solution of 2-chloro-3-fluoro-5-nitropyridine (0.500 g, 2.83 mmol, 1.00 eq) in dimethylformamide (5.00 mL) were added piperidine (250 mg, 2.94 mmol, 1.04 eq) and potassium carbonate (800 mg, 5.79 mmol, 2.04 eq). The reaction was stirred at 25°C for 2 h. The mixture was poured into water (100 mL). The resulting precipitate was collected by filtration and dried under vacuum to afford 3-fluoro-5-nitro-2-(piperidin-1-yl)pyridine.

Step 2: To a solution of 3-fluoro-5-nitro-2-(piperidin-1-yl)pyridine (515 mg, 2.29 mmol, 1.00 eq) in methanol (10.0 mL) was added wet palladium on carbon (10% weight on C) (50.0 mg) under hydrogen. The mixture was stirred at 25°C for 2 h under hydrogen (15.0 Psi). The mixture was filtered, and the filtrate was concentrated under reduced pressure to afford 5-fluoro-6-(piperidin-1-yl)pyridin-3-amine.

Step 3: To a solution of 5-fluoro-6-(piperidin-1-yl)pyridin-3-amine (440 mg, 2.25 mmol, 1.00 eq) in acetonitrile (10.0 mL) were added pyridine (0.11 mL, 11.3 mmol, 5.00 eq) and phenyl chloroformate (0.34 mL, 2.70 mmol, 1.20 eq) at 0°C. The reaction was stirred at 0°C for 1 h. The pH was adjusted to pH = 5 with formic acid (1.00 mL) and the solution was filtered. The filtrate was concentrated and the obtained residue was purified by standard methods to afford phenyl (5-fluoro-6-(piperidin-1-yl)pyridin-3-yl)carbamate.

Compound 73: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-(3,3-difluoropiperidin-1-yl)pyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (br s, 1H), 9.61 (br s, 1H), 8.32 (br s, 1H), 8.18 (br s, 1H), 7.79 (s, 1H), 7.72 - 7.60 (m, 3H), 6.91 (d, *J* = 9.1 Hz, 1H), 5.26 (s, 2H), 5.13 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.52 - 4.44 (m, 1H), 4.39 - 4.30 (m, 1H), 3.80 (t, *J* = 12.1 Hz, 2H),

3.51 - 3.47 (m, 2H), 2.98 - 2.86 (m, 1H), 2.64 - 2.58 (m, 1H), 2.47 - 2.36 (m, 1H), 2.11 - 1.99 (m, 3H), 1.77 - 1.69 (m, 2H). MS (ESI) m/z 514.2 $[M+H]^+$

Step 1: To a solution of 2-chloro-5-nitropyridine (300 mg, 1.89 mmol, 1.00 eq) in dimethylformamide (6.00 mL) were added potassium carbonate (784 mg, 5.68 mmol, 3.00 eq) and 3,3-difluoropiperidine hydrochloride (447 mg, 2.84 mmol, 1.50 eq). The reaction was stirred at 50°C for 2 h. The mixture was poured slowly into ice-water (40.0 mL). The resulting precipitate was collected by filtration and dried under vacuum to afford 2-(3,3-difluoropiperidin-1-yl)-5-nitropyridine.

Step 2: To a solution of 2-(3,3-difluoropiperidin-1-yl)-5-nitropyridine (452 mg, 1.86 mmol, 1.00 eq) in methanol (10.0 mL) was added wet palladium on carbon (10% weight on C) (50.0 mg) under hydrogen. The reaction was stirred at 25°C for 3 h under hydrogen (15 Psi). The mixture was filtered, and the filtrate was concentrated under reduced pressure to afford 6-(3,3-difluoropiperidin-1-yl)pyridin-3-amine.

Step 3: To a solution of 6-(3,3-difluoropiperidin-1-yl)pyridin-3-amine (380 mg, 1.78 mmol, 1.00 eq) and pyridine (0.72 mL, 8.91 mmol, 5.00 eq) in acetonitrile (10.0 mL) was added phenyl chloroformate (0.34 mL, 2.67 mmol, 1.50 eq) at 0°C. The reaction was stirred at 0°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (6-(3,3-difluoropiperidin-1-yl)pyridin-3-yl)carbamate.

Compound 74: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-(2-methylpyrrolidin-1-yl)pyridin-3-yl)carbamate. ^1H NMR (400 MHz, DMSO- d_6) δ = 11.00 (s, 1H), 9.42 (br s, 1H), 8.14 (s, 1H), 8.10 (br s, 1H), 7.78 (s, 1H), 7.65 (q, J = 7.9 Hz, 2H), 7.57 (br d, J = 7.8 Hz, 1H), 6.41 (d, J = 9.1 Hz, 1H), 5.24 (s, 2H), 5.13 (dd, J = 5.1, 13.3 Hz, 1H), 4.53 - 4.43 (m, 1H), 4.39 - 4.29 (m, 1H), 4.11 - 4.00 (m, 1H), 3.43 (ddd, J = 2.4, 7.4, 9.8 Hz, 1H), 3.26 - 3.15 (m, 1H), 2.99 - 2.86 (m, 1H), 2.61 (br d, J = 18.5 Hz, 1H), 2.41 (br dd, J = 4.5, 13.1 Hz, 1H), 2.07 - 1.96 (m, 3H), 1.95 - 1.87 (m, 1H), 1.65 (br dd, J = 2.9, 4.6 Hz, 1H), 1.13 (d, J = 6.1 Hz, 3H). MS (ESI) m/z 478.3 $[M+H]^+$

Step 1: To a solution of 2-chloro-5-nitropyridine (400 mg, 2.52 mmol, 1.00 eq) in dimethylformamide (6.00 mL) were added potassium carbonate (1.05 g, 7.57 mmol, 3.00 eq) and 2-methylpyrrolidine hydrochloride (460 mg, 3.78 mmol, 1.50 eq). The reaction was stirred at 50°C for 1 h. The mixture was slowly poured into ice-water (40.0 mL). The resulting

precipitate was collected by filtration and dried under vacuum to afford 2-(2-methylpyrrolidin-1-yl)-5-nitropyridine.

Step 2: To a solution of 2-(2-methylpyrrolidin-1-yl)-5-nitropyridine (512 mg, 2.47 mmol, 1.00 eq) in methanol (10.0 mL) was added wet palladium on carbon (10% weight on C) (50.0 mg) under hydrogen. The reaction was stirred at 25°C for 3 h under hydrogen (15.0 psi). The mixture was filtered, and the filtrate was concentrated under reduced pressure to afford 6-(2-methylpyrrolidin-1-yl)pyridin-3-amine.

Step 3: To a solution of 6-(2-methylpyrrolidin-1-yl)pyridin-3-amine (371 mg, 2.09 mmol, 1.00 eq) and pyridine (0.85 mL, 10.5 mmol, 5.00 eq) in acetonitrile (10.0 mL) was added phenyl chloroformate (0.39 mL, 3.14 mmol, 1.50 eq) at 0°C. The reaction was stirred at 0°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (6-(2-methylpyrrolidin-1-yl)pyridine-3-yl)carbamate.

Compound 75: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-(piperidin-1-yl)pyridazin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.08 (s, 1H), 11.00 (s, 1H), 8.24 - 8.15 (m, 1H), 8.13 - 8.04 (m, 1H), 7.82 (s, 1H), 7.76 - 7.60 (m, 2H), 5.34 (s, 2H), 5.13 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.52 - 4.45 (m, 1H), 4.39 - 4.33 (m, 1H), 3.70 (br s, 4H), 3.01 - 2.84 (m, 1H), 2.61 (br d, *J* = 17.9 Hz, 1H), 2.45 - 2.36 (m, 1H), 2.07 - 1.97 (m, 1H), 1.65 (br s, 6H). MS (ESI) *m/z* 479.2 [M+H]⁺

Step 1: To a solution of 6-chloropyridazin-3-amine (500 mg, 3.86 mmol, 1.00 eq) and piperidine (0.76 mL, 7.72 mmol, 2.00 eq) in dimethylformamide (3.00 mL) was added *N,N*-diisopropylethylamine (1.34 mL, 7.72 mmol, 2.00 eq) dropwise. The reaction was stirred at 180°C for 2 h under microwave irradiation. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was purified by reversed phase preparative HPLC to afford 6-(piperidin-1-yl)pyridazin-3-amine.

Step 2: To a solution of 6-(piperidin-1-yl)pyridazin-3-amine (180 mg, 1.01 mmol, 1.00 eq) and pyridine (0.25 mL, 3.03 mmol, 3.00 eq) in dimethylformamide (0.50 mL) and acetonitrile (3.00 mL) was added phenyl chloroformate (0.16 mL, 1.31 mmol, 1.30 eq) dropwise at 0°C. The reaction was stirred at 25°C for 12 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (6-(piperidin-1-yl)pyridazin-3-yl)carbamate.

Compound 76: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-morpholinopyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (br s, 1H), 9.61 (br s, 1H), 8.20 (br s, 1H), 7.78 (s, 1H), 7.70 - 7.61 (m, 3H), 6.81 (d, *J* = 9.0 Hz, 1H), 5.25 (s, 2H), 5.12 (dd, *J* = 5.1, 13.4 Hz, 1H), 4.51 - 4.43 (m, 1H), 4.37 - 4.30 (m, 1H), 3.70 - 3.66 (m, 4H), 3.35 (br s, 4H), 2.97 - 2.86 (m, 1H), 2.63 - 2.57 (m, 1H), 2.40 (br dd, *J* = 4.6, 13.2 Hz, 1H), 2.05 - 1.97 (m, 1H). MS (ESI) *m/z* 480.2 [M+H]⁺

To a solution of 6-morpholinopyridin-3-amine (300 mg, 1.67 mmol, 1.00 eq) and pyridine (0.41 mL, 5.02 mmol, 3.00 eq) in acetonitrile (8.00 mL) was added phenyl chloroformate (0.25 mL, 2.01 mmol, 1.20 eq) in portions at 0°C. The reaction was stirred at 25°C for 1 h. The mixture was concentrated under reduced pressure to give a residue which was diluted with ethyl acetate (6.00 mL) and water (4.00 mL). The resulting precipitate was collected by filtration and dried by standard methods to afford phenyl (6-morpholinopyridin-3-yl)carbamate.

Compound 77: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-(2-methylpiperidin-1-yl)pyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.07 - 10.89 (m, 1H), 9.50 (br s, 1H), 8.14 (br s, 1H), 7.78 (s, 1H), 7.72 - 7.51 (m, 3H), 6.72 (d, *J* = 9.3 Hz, 1H), 5.25 (s, 2H), 5.13 (dd, *J* = 5.0, 13.3 Hz, 1H), 4.59 - 4.51 (m, 1H), 4.51 - 4.43 (m, 1H), 4.40 - 4.29 (m, 1H), 3.97 (br d, *J* = 13.0 Hz, 1H), 2.99 - 2.86 (m, 1H), 2.79 (dt, *J* = 2.8, 12.8 Hz, 1H), 2.65 - 2.57 (m, 1H), 2.48 - 2.38 (m, 1H), 2.07 - 1.96 (m, 1H), 1.73 - 1.54 (m, 5H), 1.47 - 1.31 (m, 1H), 1.02 (d, *J* = 6.7 Hz, 3H). MS (ESI) *m/z* 492.2 [M+H]⁺

Step 1: To a solution of 2-chloro-5-nitropyridine (2.00 g, 12.6 mmol, 1.00 eq) in dimethylformamide (10.0 mL) were added 2-methylpiperidine (2.24 mL, 18.9 mmol, 1.50 eq) and potassium carbonate (5.23 g, 37.8 mmol, 3.00 eq). The reaction was stirred at 60°C for 1 h. The mixture was poured into water (200 mL) and extracted with ethyl acetate (2 × 100 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 2-(2-methylpiperidin-1-yl)-5-nitropyridine.

Step 2: To a solution of 2-(2-methylpiperidin-1-yl)-5-nitropyridine (2.70 g, 12.2 mmol, 1.00 eq) in methanol (30.0 mL) was added palladium on carbon (50.0 mg, 10% weight on C). The reaction was stirred at 25°C for 1 h under hydrogen (15 Psi). The mixture was filtered,

and the filtrate was concentrated under reduced pressure to afford 6-(2-methylpiperidin-1-yl)pyridin-3-amine.

Step 3: To a solution of 6-(2-methylpiperidin-1-yl)pyridin-3-amine (2.20 g, 11.5 mmol, 1.00 eq) and pyridine (4.64 mL, 57.5 mmol, 5.00 eq) in acetonitrile (30.0 mL) was added phenyl chloroformate (1.73 mL, 13.8 mmol, 1.20 eq). The reaction was stirred at 25°C for 1 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (6-(2-methylpiperidin-1-yl)pyridin-3-yl)carbamate.

Compound 78: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-(4,4-difluoropiperidin-1-yl)pyridin-3-yl) carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (s, 1H), 9.63 (br s, 1H), 8.30 - 8.11 (m, 1H), 7.79 (s, 1H), 7.75 - 7.60 (m, 3H), 6.95 (d, *J* = 9.2 Hz, 1H), 5.26 (s, 2H), 5.13 (dd, *J* = 5.1, 13.3 Hz, 1H), 4.52 - 4.43 (m, 1H), 4.40 - 4.30 (m, 1H), 3.67 - 3.58 (m, 4H), 2.99 - 2.85 (m, 1H), 2.65 - 2.57 (m, 1H), 2.46 - 2.36 (m, 1H), 2.05 - 1.91 (m, 5H). MS (ESI) *m/z* 514.2 [M+H]⁺

Step 1: To a solution of 2-chloro-5-nitropyridine (2.00 g, 12.6 mmol, 1.00 eq) in dimethylformamide (10.0 mL) was added 4,4-difluoropiperidine hydrochloride (2.00 g, 12.6 mmol, 1.01 eq, HCl) and potassium carbonate (4.00 g, 28.9 mmol, 2.29 eq). The reaction was stirred at 60°C for 2 h. The mixture was poured into water (100 mL). The resulting yellow precipitate was collected by filtration and dried under vacuum to afford 2-(4,4-difluoropiperidin-1-yl)-5-nitropyridine.

Step 2: To a solution of 2-(4,4-difluoropiperidin-1-yl)-5-nitropyridine (2.70 g, 11.1 mmol, 1.00 eq) in methanol (30.0 mL) was added palladium on carbon (50.0 mg, 10% weight on C). The reaction was stirred at 25°C for 1 h under hydrogen (15 Psi). The mixture was filtered, and the filtrate was concentrated under reduced pressure to afford 6-(4,4-difluoropiperidin-1-yl)pyridin-3-amine.

Step 3: To a solution of 6-(4,4-difluoropiperidin-1-yl)pyridin-3-amine (2.30 g, 10.7 mmol, 1.00 eq) and pyridine (4.35 mL, 53.9 mmol, 5.00 eq) in acetonitrile (30.0 mL) was added phenyl chloroformate (1.62 mL, 12.9 mmol, 1.20 eq). The reaction was stirred at 25°C for 1 h. The mixture was concentrated under reduced pressure to give a residue. Water (30.0 mL) was added, and the mixture was extracted with ethyl acetate (3 × 30.0 mL). The combined

organic layers were dried, filtered, and concentrated by standard methods to afford phenyl(6-(4,4-difluoropiperidin-1-yl)pyridin-3-yl)carbamate.

Compound 79: General procedure A with variant i) was used for the preparation from compound **VIII** employing (2,2-difluorobenzo[d][1,3]dioxol-5-yl)carbamate. ¹H NMR (400MHz, DMSO-*d*₆) δ = 10.99 (br s, 1H), 10.06 (br s, 1H), 7.80 (s, 1H), 7.71 - 7.67 (m, 1H), 7.67 - 7.62 (m, 1H), 7.58 (d, *J* = 1.6 Hz, 1H), 7.33 (d, *J* = 8.8 Hz, 1H), 7.18 (dd, *J* = 2.0, 8.8 Hz, 1H), 5.29 (s, 2H), 5.13 (dd, *J* = 5.2, 13.2 Hz, 1H), 4.54 - 4.43 (m, 1H), 4.41 - 4.29 (m, 1H), 2.98 - 2.86 (m, 1H), 2.64 - 2.57 (m, 1H), 2.46 - 2.35 (m, 1H), 2.06 - 1.97 (m, 1H). MS (ESI) *m/z* 474.2 [M+H]⁺

To a solution of 2,2-difluorobenzo[d][1,3]dioxol-5-amine (500 mg, 2.57 mmol, 1.00 eq) and pyridine (0.70 mL, 8.66 mmol, 3.00 eq) in acetonitrile (5.00 mL) was added phenyl chloroformate (0.43 mL, 3.47 mmol, 1.20 eq) at 25°C. The reaction was stirred at 25°C for 2 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (2,2-difluorobenzo[d][1,3]dioxol-5-yl)carbamate.

Compound 80: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-cyclopropylpyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (br s, 1H), 9.87 (br s, 1H), 8.44 (d, *J* = 2.2 Hz, 1H), 8.30 (s, 1H), 7.79 (s, 1H), 7.74 (br d, *J* = 7.6 Hz, 1H), 7.70 - 7.66 (m, 1H), 7.65 - 7.61 (m, 1H), 7.20 (d, *J* = 8.6 Hz, 1H), 5.27 (s, 2H), 5.18 - 5.05 (m, 1H), 4.51 - 4.43 (m, 1H), 4.38 - 4.30 (m, 1H), 2.98 - 2.84 (m, 1H), 2.65 - 2.56 (m, 1H), 2.47 - 2.34 (m, 1H), 2.08 - 1.95 (m, 2H), 0.92 - 0.85 (m, 2H), 0.85 - 0.80 (m, 2H). MS (ESI) *m/z* 435.1 [M+H]⁺

To a solution of 6-cyclopropylpyridin-3-amine (0.500 g, 3.73 mmol, 1.00 eq) and pyridine (0.90 mL, 11.2 mmol, 3.00 eq) in acetonitrile (5.00 mL) was added phenyl chloroformate (0.56 mL, 4.47 mmol, 1.20 eq). The reaction was stirred at 25°C for 12 h. The mixture was diluted with ethyl acetate (50.0 mL) and water (50.0 mL). The organic layer was separated, and the aqueous phase was extracted with ethyl acetate (3 × 100 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated and the obtained residue was purified by standard methods to afford phenyl (6-cyclopropylpyridin-3-yl)carbamate.

Compound 81: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl(4-(oxetan-3-yl)phenyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.00 (br s, 1H), 9.82 (br s, 1H), 7.80 (s, 1H), 7.72 - 7.66 (m, 1H), 7.66 -

7.62 (m, 1H), 7.47 (br d, $J = 8.4$ Hz, 2H), 7.32 (d, $J = 8.6$ Hz, 2H), 5.28 (s, 2H), 5.20 - 5.07 (m, 1H), 4.97 - 4.85 (m, 2H), 4.58 (t, $J = 6.4$ Hz, 2H), 4.51 - 4.44 (m, 1H), 4.39 - 4.30 (m, 1H), 4.24 - 4.14 (m, 1H), 2.97 - 2.87 (m, 1H), 2.65 - 2.57 (m, 1H), 2.48 - 2.34 (m, 1H), 2.06 - 1.96 (m, 1H). MS (ESI) m/z 450.2 $[M+H]^+$

- 5 To a solution of 4-(oxetan-3-yl)aniline (200 mg, 1.34 mmol, 1.00 eq) and pyridine (0.32 mL, 4.02 mmol, 3.00 eq) in acetonitrile (10.0 mL) was added phenyl chloroformate (0.20 mL, 1.61 mmol, 1.20 eq). The reaction was stirred at 25°C for 12 h. The mixture was diluted with ethyl acetate (50.0 mL) and water (50.0 mL). The organic layer was separated, and the aqueous phase was extracted with ethyl acetate (3×100 mL). The combined organic layers
10 were dried over sodium sulfate, filtered, and concentrated and the obtained residue was purified by standard methods to afford phenyl(4-(oxetan-3-yl)phenyl)carbamate.

Compound 82: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-(4-methylpiperazin-1-yl)pyridin-3-yl)carbamate. ^1H NMR (400 MHz, DMSO- d_6) $\delta = 10.99$ (s, 1H), 9.57 (br s, 1H), 8.18 (s, 2H), 7.78 (s, 1H),
15 7.65 (q, $J = 7.8$ Hz, 3H), 6.81 (d, $J = 9.2$ Hz, 1H), 5.24 (s, 2H), 5.12 (dd, $J = 5.1, 13.3$ Hz, 1H), 4.51 - 4.44 (m, 1H), 4.37 - 4.30 (m, 1H), 3.42 - 3.37 (m, 4H), 2.91 (ddd, $J = 5.3, 13.5, 17.5$ Hz, 1H), 2.60 (br dd, $J = 2.0, 15.6$ Hz, 1H), 2.46 - 2.42 (m, 4H), 2.38 (br d, $J = 4.4$ Hz, 1H), 2.24 (s, 3H), 2.05 - 1.98 (m, 1H). MS (ESI) m/z 493.3 $[M+H]^+$

To a solution of 6-(4-methylpiperazin-1-yl)pyridin-3-amine (500 mg, 2.60 mmol, 1.00 eq)
20 and pyridine (1.05 mL, 13.0 mmol, 5.00 eq) in acetonitrile (5.00 mL) was added phenyl chloroformate (0.39 mL, 3.12 mmol, 1.20 eq) at 0°C. The reaction was stirred at 25°C for 12 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (6-(4-methylpiperazin-1-yl)pyridin-3-yl)carbamate.

Compound 83: General procedure A with variant i) was used for the preparation from
25 compound **VIII** employing phenyl (3,3-dimethyl-2,3-dihydrobenzofuran-6-yl)carbamate. ^1H NMR (400 MHz, DMSO- d_6) $\delta = 11.00$ (s, 1H), 9.74 (br s, 1H), 7.80 (s, 1H), 7.74 - 7.60 (m, 2H), 7.08 (d, $J = 8.0$ Hz, 1H), 6.98 (s, 1H), 6.96 - 6.84 (m, 1H), 5.26 (s, 2H), 5.14 (dd, $J = 5.0, 13.4$ Hz, 1H), 4.48 (d, $J = 17.4$ Hz, 1H), 4.36 (d, $J = 17.4$ Hz, 1H), 4.20 (s, 2H), 3.00 - 2.85 (m, 1H), 2.70 - 2.56 (m, 1H), 2.47 - 2.33 (m, 1H), 2.12 - 1.98 (m, 1H),
30 1.25 (s, 6H). MS (ESI) m/z 464.2 $[M+H]^+$

Step 1: To a solution of 2-bromo-5-nitrophenol (1.00 g, 4.59 mmol, 1.00 eq) and 3-bromo-2-methylprop-1-ene (0.60 mL, 5.96 mmol, 1.30 eq) in acetone (5.00 mL) was added potassium carbonate (1.27 g, 9.17 mmol, 2.00 eq) in one portion at 25°C. The reaction was stirred for 12 h at 25°C. The mixture was diluted with water (30.0 mL) and extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with brine (2 × 10.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1 to 2/1) to afford 1-bromo-2-((2-methylallyl)oxy)-4-nitrobenzene.

Step 2: To a solution of 1-bromo-2-((2-methylallyl)oxy)-4-nitrobenzene (900 mg, 3.31 mmol, 1.00 eq) in dimethylformamide (5.00 mL) were added sodium acetate (678 mg, 8.27 mmol, 2.50 eq), palladium acetate (149 mg, 662 µmol, 0.20 eq), tetraethylammonium iodide (936 mg, 3.64 mmol, 1.10 eq) and sodium formate (0.18 mL, 3.31 mmol, 1.00 eq) in one portion under nitrogen. The reaction was stirred for 12 h at 100°C. The mixture was diluted with water (30.0 mL) and extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with brine (2 × 10.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1 to 2/1) to afford 3,3-dimethyl-6-nitro-2H-benzofuran.

Step 3: To a solution of 3,3-dimethyl-6-nitro-2,3-dihydrobenzofuran (300 mg, 1.55 mmol, 1.00 eq) in water (3.00 mL) and methanol (6.00 mL) were added ammonium chloride (415 mg, 7.76 mmol, 5.00 eq) and iron powder (434 mg, 7.76 mmol, 5.00 eq). The reaction was stirred at 80°C for 2 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was diluted with water (30.0 mL) and extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with brine (2 × 10.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 3,3-dimethyl-2,3-dihydrobenzofuran-6-amine.

Step 4: To a solution of 3,3-dimethyl-2,3-dihydrobenzofuran-6-amine (162 mg, 993 µmol, 1.00 eq) and pyridine (0.24 mL, 2.98 mmol, 3.00 eq) in acetonitrile (5.00 mL) was added phenyl chloroformate (0.14 mL, 1.09 mmol, 1.10 eq) in one portion at 25°C. The reaction was stirred at 25°C for 12 h. The mixture was diluted with water (30.0 mL) and extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with brine (2 × 10.0 mL), dried over sodium sulfate, filtered, and concentrated and the obtained residue was

purified by standard methods to afford phenyl (3,3-dimethyl-2,3-dihydrobenzofuran -6-yl)carbamate.

Compound 84: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-(2-fluorophenyl)pyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.02 (s, 1H), 10.23 (br s, 1H), 8.78 (d, *J* = 2.3 Hz, 1H), 8.07 - 8.00 (m, 1H), 7.92 (dt, *J* = 1.8, 7.9 Hz, 1H), 7.83 (s, 1H), 7.80 - 7.74 (m, 1H), 7.74 - 7.69 (m, 1H), 7.68 - 7.63 (m, 1H), 7.45 (ddt, *J* = 1.8, 5.3, 7.6 Hz, 1H), 7.36 - 7.23 (m, 2H), 5.33 (s, 2H), 5.14 (dd, *J* = 5.1, 13.4 Hz, 1H), 4.53 - 4.44 (m, 1H), 4.39 - 4.32 (m, 1H), 2.99 - 2.86 (m, 1H), 2.65 - 2.56 (m, 1H), 2.46 - 2.37 (m, 1H), 2.06 - 1.97 (m, 1H). MS (ESI) *m/z* 489.2 [M+H]⁺

Step 1: To a solution of 2-chloro-5-nitropyridine (2.00 g, 12.6 mmol, 1.00 eq) in dimethylformamide (20.0 mL) were added potassium carbonate (5.23 g, 37.8 mmol, 3.00 eq), (2-fluorophenyl)boronic acid (1.77 g, 12.6 mmol, 1.00 eq) and tetrakis(triphenylphosphine)palladium (728 mg, 630 μ mol, 0.05 eq) under nitrogen. The reaction was stirred at 110°C for 12 h. The mixture was diluted with water (200 mL) and extracted with ethyl acetate (2 $\times$ 100 mL). The combined organic layers were washed with brine (2 $\times$ 30.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by column chromatography (petroleum ether/ethyl acetate=10/1 to 5/1) to afford 2-(2-fluorophenyl)-5-nitropyridine.

Step 2: To a solution of 2-(2-fluorophenyl)-5-nitropyridine (2.00 g, 9.17 mmol, 1.00 eq) in methanol (15.0 mL) and water (5.00 mL) were added iron powder (2.56 g, 45.8 mmol, 5.00 eq) and ammonium chloride (3.92 g, 73.3 mmol, 8.00 eq). The reaction was stirred at 80°C for 1 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was diluted with water (30.0 mL) and extracted with ethyl acetate (3 $\times$ 30.0 mL). The combined organic layers were washed with brine (2 $\times$ 10.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 6-(2-fluorophenyl)pyridin-3-amine.

Step 3: To a solution of 6-(2-fluorophenyl)pyridin-3-amine (1.70 g, 9.03 mmol, 1.00 eq) and pyridine (3.65 mL, 45.1 mmol, 5.00 eq) in acetonitrile (20.0 mL) was added phenyl chloroformate (1.60 mL, 12.8 mmol, 1.41 eq). The reaction was stirred at 25°C for 1 h. The mixture was concentrated under reduced pressure to give a residue. The residue was triturated with water (100 mL) and the resulting solid was collected by filtration. The filter

cake was washed with water (5 ml) and dried by standard methods to afford phenyl (6-(2-fluorophenyl)pyridin-3-yl)carbamate.

Compound 85: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (5-fluoro-6-phenylpyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.08 - 10.94 (m, 1H), 10.57 - 10.27 (m, 1H), 8.59 (d, *J* = 1.6 Hz, 1H), 8.00 - 7.92 (m, 1H), 7.91 - 7.85 (m, 2H), 7.83 (s, 1H), 7.75 - 7.70 (m, 1H), 7.68 - 7.64 (m, 1H), 7.53 - 7.47 (m, 2H), 7.46 - 7.40 (m, 1H), 5.35 (s, 2H), 5.14 (dd, *J* = 5.2, 13.2 Hz, 1H), 4.57 - 4.44 (m, 1H), 4.43 - 4.30 (m, 1H), 2.98 - 2.83 (m, 1H), 2.61 (br d, *J* = 17.2 Hz, 1H), 2.46 - 2.36 (m, 1H), 2.05 - 1.97 (m, 1H). MS (ESI) *m/z* 489.3[M+H]⁺

Step 1: To a solution of 2-chloro-3-fluoro-5-nitropyridine (2.00 g, 11.3 mmol, 1.00 eq), phenylboronic acid (2.76 g, 22.6 mmol, 2.00 eq) and potassium carbonate (4.70 g, 34.0 mmol, 3.00 eq) in dioxane (20.0 mL) was added tetrakis(triphenylphosphine)palladium(0) (1.31 g, 1.13 mmol, 0.10 eq) at 25°C. The reaction was stirred at 110°C for 12 h under nitrogen. The mixture was poured into water (120 mL) and stirred for 10 min. The aqueous phase was extracted with ethyl acetate (3 × 60.0 mL). The combined organic layers were washed with brine (50.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 50/1) to afford 3-fluoro-5-nitro-2-phenylpyridine.

Step 2: To a solution of 3-fluoro-5-nitro-2-phenylpyridine (300 mg, 1.37 mmol, 1.00 eq), in methanol (4.00 mL) and water (2.00 mL) were added ammonium chloride (367 mg, 6.87 mmol, 5.00 eq) and iron powder (230 mg, 4.12 mmol, 3.00 eq). The reaction was stirred at 80°C for 1 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. Water (80.0 mL) was added, and the solution was stirred for 10 min. The aqueous layer was extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with brine (50.0 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 5-fluoro-6-phenylpyridin-3-amine.

Step 3: To a solution of 5-fluoro-6-phenylpyridin-3-amine (250 mg, 1.33 mmol, 1.00 eq) and pyridine (0.54 mL, 6.64 mmol, 5.00 eq) in acetonitrile (5.00 mL) was added phenyl chloroformate (0.25 mL, 1.99 mmol, 1.50 eq). The reaction was stirred at 25°C for 1 h. The

mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (5-fluoro-6-phenylpyridin-3-yl)carbamate.

Compound 86: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-(*o*-tolyl)pyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.02 (s, 1H), 10.69 - 10.33 (m, 1H), 8.95 - 8.73 (m, 1H), 8.35 - 8.00 (m, 1H), 7.86 - 7.63 (m, 4H), 7.47 - 7.29 (m, 4H), 5.36 (br s, 2H), 5.14 (dd, *J* = 5.0, 13.4 Hz, 1H), 4.52 - 4.45 (m, 1H), 4.39 - 4.32 (m, 1H), 2.96 - 2.88 (m, 1H), 2.64 - 2.58 (m, 1H), 2.45 - 2.37 (m, 1H), 2.32 (s, 3H), 2.06 - 1.98 (m, 1H). MS (ESI) *m/z* 485.2 [M+H]⁺

Step 1: To a solution of 2-chloro-5-nitropyridine (3.00 g, 18.9 mmol, 1.00 eq) in dimethylformamide (30.0 mL) were added *O*-tolylboronic acid (2.57 g, 18.9 mmol, 1.00 eq), potassium carbonate (7.85 g, 56.7 mmol, 3.00 eq) and tetrakis(triphenylphosphine)palladium (1.09 g, 946 μ mol, 0.05 eq) under nitrogen. The reaction was stirred at 110°C for 12 h. The mixture was diluted with water (300 mL) and extracted with ethyl acetate (3 $\times$ 300 mL). The combined organic layers were washed with brine (2 $\times$ 100 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate=10/1) to afford 5-nitro-2-(*o*-tolyl)pyridine.

Step 2: To a solution of 5-nitro-2-(*o*-tolyl)pyridine (3.00 g, 14.0 mmol, 1.00 eq) in methanol (30.0 mL) and water (10.0 mL) were added iron powder (3.91 g, 70.0 mmol, 5.00 eq) and ammonium chloride (5.99 g, 112 mmol, 8.00 eq). The reaction was stirred at 80°C for 1 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was diluted with water (50.0 mL) and extracted with ethyl acetate (3 $\times$ 30.0 mL). The combined organic layers were washed with brine (2 $\times$ 10.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 6-(*o*-tolyl)pyridin-3-amine.

Step 3: To a solution of 6-(*o*-tolyl)pyridin-3-amine (2.50 g, 13.5 mmol, 1.00 eq) in acetonitrile (25.0 mL) were added pyridine (5.48 mL, 67.8 mmol, 5.00 eq) and phenyl chloroformate (2.21 mL, 17.6 mmol, 1.30 eq). The reaction was stirred at 25°C for 1 h. The mixture was concentrated under reduced pressure to give a residue. The residue was triturated with water (100 mL) and the resulting solid was collected by filtration. The filter cake was washed with water (5.00 mL) and dried under standard methods to afford phenyl (6-(*o*-tolyl)pyridin-3-yl)carbamate.

Compound 87: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-(2-methoxyphenyl)pyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.02 (s, 1H), 10.75 (br s, 1H), 8.91 (br d, *J* = 1.6 Hz, 1H), 8.32 (br d, *J* = 8.7 Hz, 1H), 8.11 (d, *J* = 8.9 Hz, 1H), 7.84 (s, 1H), 7.76 - 7.62 (m, 3H), 7.58 - 7.50 (m, 1H), 7.25 (d, *J* = 8.3 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 5.37 (s, 2H), 5.13 (dd, *J* = 5.0, 13.3 Hz, 1H), 4.53 - 4.46 (m, 1H), 4.38 - 4.31 (m, 1H), 3.87 (s, 3H), 2.97 - 2.88 (m, 1H), 2.61 (br d, *J* = 17.1 Hz, 1H), 2.45 - 2.35 (m, 1H), 2.07 - 1.97 (m, 1H). MS (ESI) *m/z* 501.2 [M+H]⁺

Step 1: To a solution of 2-chloro-5-nitropyridine (2.00 g, 12.6 mmol, 1.00 eq) in dimethylformamide (5 mL) were added potassium carbonate (5.23 g, 37.8 mmol, 3.00 eq), (2-fluorophenyl)boronic acid (1.92 g, 12.6 mmol, 1.00 eq) and tetrakis(triphenylphosphine)palladium (1.46 g, 1.26 mmol, 0.10 eq) under nitrogen. The reaction was stirred at 100°C for 12 h. The mixture was diluted with water (300 mL) and extracted with ethyl acetate (3 × 300 mL). The combined organic layers were washed with brine (2 × 100 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1) to afford 2-(2-methoxyphenyl)-5-nitropyridine.

Step 2: To a solution of 2-(2-methoxyphenyl)-5-nitropyridine (2.90 g, 12.6 mmol, 1.00 eq) in methanol (30.0 mL) and water (10.0 mL) were added iron powder (3.52 g, 62.9 mmol, 5.00 eq) and ammonium chloride (5.39 g, 100 mmol, 8.00 eq). The reaction was stirred at 80°C for 1 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was diluted with water (50.0 mL) and extracted with ethyl acetate (3 × 50.0 mL). The combined organic layers were washed with brine (2 × 10.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 6-(2-methoxyphenyl)pyridin-3-amine.

Step 3: To a solution of 6-(2-methoxyphenyl)pyridin-3-amine (2.50 g, 12.4 mmol, 1.00 eq) in acetonitrile (25.0 mL) were added pyridine (3.02 mL, 37.4 mmol, 3.00 eq) and phenyl chloroformate (2.03 mL, 16.2 mmol, 1.30 eq). The reaction was stirred at 25°C for 1 h. The mixture was concentrated under reduced pressure to give a residue. The residue was triturated with water (100 mL) and the resulting solid was collected by filtration. The filter cake was washed with water (5.00 mL) and dried by standard methods to afford phenyl (6-(2-methoxyphenyl)pyridin-3-yl)carbamate.

Compound 88: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (5-methyl-6-phenylpyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.02 (s, 1H), 10.76 (br s, 1H), 8.80 - 8.76 (m, 1H), 8.26 (s, 1H), 7.84 (s, 1H), 7.76 - 7.72 (m, 1H), 7.68 - 7.66 (m, 1H), 7.64 - 7.62 (m, 2H), 7.60 (br s, 3H), 5.38 (s, 2H), 5.22 - 5.04 (m, 1H), 4.50 (d, *J* = 17.6 Hz, 1H), 4.36 (d, *J* = 17.6 Hz, 1H), 2.98 - 2.86 (m, 1H), 2.68 - 2.58 (m, 1H), 2.46 - 2.34 (m, 4H), 2.10 - 1.98 (m, 1H). MS (ESI) *m/z* 485.4 [M+H]⁺

Step 1: To a solution of 2-chloro-3-methyl-5-nitropyridine (5.00 g, 29.0 mmol, 1.00 eq) and phenylboronic acid (4.24 g, 34.8 mmol, 1.20 eq) in dioxane (50.0 mL) were added tetrakis[triphenylphosphine]palladium(0) (6.70 g, 5.79 mmol, 0.20 eq) and potassium carbonate (6.01 g, 43.5 mmol, 1.50 eq) in one portion at 25°C under nitrogen. The reaction was stirred at 100°C for 12 h. The mixture was diluted with water (30.0 mL) and extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with brine (2 × 10.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1 to 2/1) to afford 3-methyl-5-nitro-2-phenyl-pyridine.

Step 2: To a solution of 3-methyl-5-nitro-2-phenylpyridine (1.00 g, 4.67 mmol, 1.00 eq) in methanol (6.00 mL) and water (3.00 mL) were added iron powder (1.30 g, 23.3 mmol, 5.00 eq) and ammonium chloride (1.25 g, 23.3 mmol, 5.00 eq) in one portion at 25°C. The reaction was stirred at 80°C for 2 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue. The residue was diluted with water (30.0 mL) and extracted with ethyl acetate (3 × 30.0 mL). The combined organic layers were washed with brine (2 × 10.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 5-methyl-6-phenylpyridin-3-amine.

Step 3: To a solution of 5-methyl-6-phenylpyridin-3-amine (843 mg, 4.58 mmol, 1.00 eq) and pyridine (1.11 mL, 13.7 mmol, 3.00 eq) in acetonitrile (2.00 mL) was added phenyl chloroformate (0.63 mL, 5.03 mmol, 1.10 eq) at 25°C. The reaction was stirred at 25°C for 12 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (5-methyl-6-phenylpyridin-3-yl)carbamate.

Compound 89: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (6-(3-(dimethylamino)azetidin-1-yl)pyridin-3-yl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.99 (s, 1H), 9.52 (br s, 1H), 8.17 (s,

1H), 8.12 (br s, 1H), 7.77 (s, 1H), 7.69 - 7.56 (m, 3H), 6.37 (d, $J = 8.9$ Hz, 1H), 5.24 (s, 2H), 5.12 (dd, $J = 5.1, 13.3$ Hz, 1H), 4.51 - 4.43 (m, 1H), 4.38 - 4.30 (m, 1H), 3.92 (t, $J = 7.4$ Hz, 2H), 3.63 (dd, $J = 5.6, 8.1$ Hz, 2H), 3.15 (quin, $J = 6.1$ Hz, 1H), 2.97 - 2.86 (m, 1H), 2.64 - 2.56 (m, 1H), 2.45 - 2.38 (m, 1H), 2.10 (s, 6H), 2.04 - 1.98 (m, 1H). MS (ESI) m/z 493.2 $[M+H]^+$

Step 1: To a solution of 2-fluoro-5-nitropyridine (2.00 g, 14.1 mmol, 1.00 eq) and N,N-dimethylazetidin-3-amine dihydrochloride (3.65 g, 21.1 mmol, 1.50 eq, 2 HCl) in dimethylformamide (20.0 mL) was added potassium carbonate (9.73 g, 70.4 mmol, 5.00 eq) in one portion. The reaction was stirred at 60°C for 12 h. The mixture was diluted with water (150 mL) and extracted with ethyl acetate (3×80.0 mL). The combined organic layers were washed with brine (60.0 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford N,N-dimethyl-1-(5-nitropyridin-2-yl)azetidin-3-amine.

Step 2: To a solution of N,N-dimethyl-1-(5-nitropyridin-2-yl)azetidin-3-amine (2.00 g, 9.00 mmol, 1.00 eq) in methanol (40.0 mL) was added palladium on carbon (200 mg, 10% weight on C) in one portion under hydrogen (15 Psi). The reaction was stirred at 25°C for 2 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure to afford 6-(3-(dimethylamino)azetidin-1-yl)pyridin-3-amine.

Step 3: To a solution of 6-(3-(dimethylamino)azetidin-1-yl)pyridin-3-amine (500 mg, 2.60 mmol, 1.00 eq) and pyridine (1.05 mL, 13.0 mmol, 5.00 eq) in acetonitrile (5.00 mL) was added phenyl chloroformate (0.39 mL, 3.12 mmol, 1.20 eq) dropwise at 0°C. The reaction was stirred at 20°C for 12 h. The mixture was concentrated and the obtained residue was purified by standard methods to afford phenyl (6-(3-(dimethylamino)azetidin-1-yl)pyridin-3-yl)carbamate.

Compound 90: General procedure A with variant i) was used for the preparation from compound **VIII** employing phenyl (5-methoxy-6-phenylpyridin-3-yl)carbamate. ^1H NMR (400 MHz, DMSO- d_6) $\delta = 11.02$ (s, 1H), 10.80 - 10.36 (m, 1H), 8.60 - 8.38 (m, 1H), 8.12 - 7.92 (m, 1H), 7.88 - 7.78 (m, 3H), 7.76 - 7.64 (m, 2H), 7.50 (br d, $J = 7.2$ Hz, 3H), 5.36 (s, 2H), 5.14 (dd, $J = 5.2, 13.2$ Hz, 1H), 4.50 (d, $J = 17.6$ Hz, 1H), 4.36 (d, $J = 17.6$ Hz, 1H), 3.90 (s, 3H), 2.99 - 2.86 (m, 1H), 2.62 (br d, $J = 17.2$ Hz, 1H), 2.50 - 2.34 (m, 1H), 2.10 - 1.94 (m, 1H). MS (ESI) m/z 501.2 $[M+H]^+$

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 2
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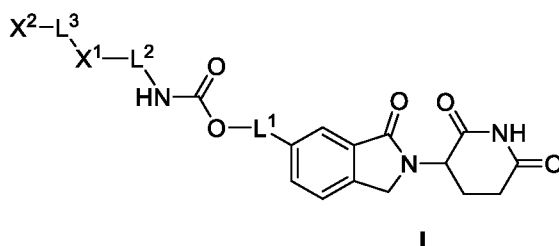
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CLAIMS

1. A compound or pharmaceutically acceptable salts or stereoisomers thereof of formula I:



5 wherein

X^1 is linear or branched C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched C_{1-6} alkyl, linear or branched C_{1-6} heteroalkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-CHF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , C_{1-6} alkylamino, $-CN$, $-N(H)C(O)-C_{1-6}$ alkyl, $-OC(O)-C_{1-6}$ alkyl, $-OC(O)-C_{1-4}$ alkylamino, $-C(O)O-C_{1-6}$ alkyl, $-COOH$, $-C_{1-6}$ alkyl $C(O)OH$, $-C_{1-6}$ alkyl $C(O)O-C_{1-6}$ alkyl, NH_2 , C_{1-4} alkoxy, C_{1-4} alkylhydroxy, $-CH_2F$, $-N(H)C(O)-O-C_{1-6}$ alkyl, and $C(OH)(CF_3)$;

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or X^1 together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-6}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, $-N(H)C(O)-C_{1-6}$ alkyl, $-OC(O)-C_{1-6}$ alkyl, $-C(O)O-C_{1-6}$ alkyl, $-COOH$, $-C_{1-6}$ alkyl $C(O)OH$, $-C_{1-6}$ alkyl $C(O)O-C_{1-6}$ alkyl, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy;

15

X^2 is H, C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and C_{1-4} alkylhydroxy;

20

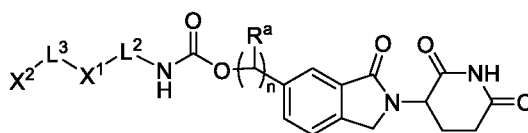
L^1 is a covalent bond, linear or branched C_{1-6} alkyl;

L^2 is a covalent bond, linear or branched C_{1-6} alkyl; and

L^3 is a covalent bond, linear or branched C_{1-6} alkyl, $-O-$, or $-C_{1-4}$ alkoxy, wherein linear or branched C_{1-6} alkyl is unsubstituted or substituted with one or more of halogen.

25

2. The compound of claim 1 or pharmaceutically acceptable salts or stereoisomers thereof, wherein X^1 is linear or branched $-C_{1-6}$ alkyl, $-C_{3-6}$ cycloalkyl, $-C_{6-10}$ aryl, 5-10 membered heteroaryl, 5-6 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy; or X^1 together with the N atom of the carbamate forms a 5-6 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched $-C_{1-4}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy.
3. The compound of claim 1, wherein X^2 is H, C_{3-6} cycloalkyl, C_6 aryl, 5-6 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-4} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and $-C_{1-4}$ alkylhydroxy.
4. The compound of claim 1, wherein L^1 is $-CH_2-$ or $-CH(CH_3)-$ and/or L^2 is a covalent bond, $-CH_2-$ or $-CH(CH_3)-$ and/or L^3 is a $-CH_2-$, $-O-$, $-CH_2-O-$, $-CH_2-CH_2-O-$.
5. The compound of claim 1 or pharmaceutically acceptable salts or stereoisomers thereof of formula II:



II

wherein

X^1 is linear or branched C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^1 is unsubstituted or substituted with one or more of halogen, linear or branched C_{1-6} alkyl, linear or branched C_{1-6} heteroalkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-CHF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , C_{1-6} alkylamino, $-CN$, $-N(H)C(O)-C_{1-6}$ alkyl, $-OC(O)-C_{1-6}$ alkyl, $-OC(O)-C_{1-4}$ alkylamino, $-C(O)O-C_{1-6}$ alkyl, $-COOH$, $-C_{1-6}$ alkyl $C(O)OH$, $-C_{1-6}$ alkyl $C(O)O-C_{1-6}$ alkyl, NH_2 , C_{1-4} alkoxy and C_{1-4} alkylhydroxy;

or X^1 together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen,

linear or branched $-C_{1-6}$ alkyl, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, C_{1-6} alkylamino, $-CN$, $-N(H)C(O)-C_{1-6}alkyl$, $-OC(O)-C_{1-6}alkyl$, $-C(O)O-C_{1-6}alkyl$, $-COOH$, $-C_{1-6}alkylC(O)OH$, $-C_{1-6}alkylC(O)O-C_{1-6}alkyl$, NH_2 , C_{1-4} alkylhydroxy, and C_{1-4} alkoxy;

X^2 is H, C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$ alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, and C_{1-4} alkylhydroxy;

L^2 is a covalent bond, linear or branched C_{1-6} alkyl;

L^3 is a covalent bond, linear or branched C_{1-6} alkyl, $-O-$, $-C_{1-4}$ alkoxy;

R^a is H or linear or branched C_{1-4} alkyl, such as methyl or ethyl,

n is 1 or 2.

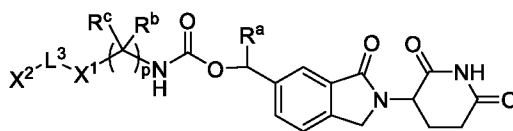
6. The compound of claim 5 or pharmaceutically acceptable salts or stereoisomers thereof, wherein n is 1 and R^a is H or methyl.

7. The compound of claim 5 or pharmaceutically acceptable salts or stereoisomers thereof, wherein p is 0.

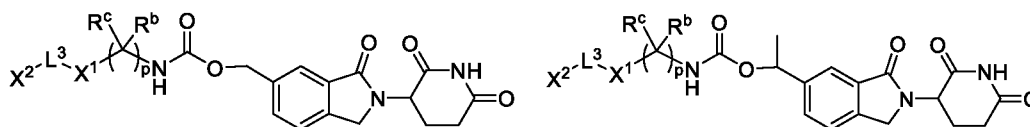
8. The compound of claim 5 or pharmaceutically acceptable salts or stereoisomers thereof, wherein p is 1 and R^b , R^c are H or wherein p is 1, R^b is methyl and R^c is H.

9. The compound of claim 5, wherein L^2 is a covalent bond, $-CH_2-$ or $-CH(CH_3)-$ and/or L^3 is a $-CH_2-$, $-O-$, $-CH_2-O-$, $-CH_2-CH_2-O-$.

10. The compound of claim 1 or pharmaceutically acceptable salts or stereoisomers thereof, of formula III, such as IVa or IVb:



III



IVa

IVb

wherein

X¹ is linear or branched C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X¹ is unsubstituted or substituted with one or more of halogen, linear or branched C₁₋₆ alkyl, linear or branched C₁₋₆ heteroalkyl, CF₃, CHF₂, CMeF₂, -O-CHF₂, -O-(CH₂)₂-OMe, OCF₃, C₁₋₆ alkylamino, -CN, -N(H)C(O)-C₁₋₆alkyl, -OC(O)-C₁₋₆alkyl, -OC(O)-C₁₋₄alkylamino, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, C₁₋₄ alkoxy and C₁₋₄ alkylhydroxy;

or X¹ together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with one or more of halogen, linear or branched -C₁₋₆ alkyl, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, C₁₋₆ alkylamino, -CN, -N(H)C(O)-C₁₋₆alkyl, -OC(O)-C₁₋₆alkyl, -C(O)O-C₁₋₆alkyl, -COOH, -C₁₋₆alkylC(O)OH, -C₁₋₆alkylC(O)O-C₁₋₆alkyl, NH₂, C₁₋₄ alkylhydroxy, and C₁₋₄ alkoxy;

X² is H, C₃₋₆ cycloalkyl, C₆₋₁₀ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X² is unsubstituted or substituted with one or more of linear or branched C₁₋₆ alkyl, -C₁₋₄ alkoxy, NH₂, NMe₂, halogen, CF₃, CHF₂, CMeF₂, -O-(CH₂)₂-OMe, OCF₃, OCHF₂, and C₁₋₄ alkylhydroxy;

L³ is a covalent bond, linear or branched C₁₋₆ alkyl, -O-, -C₁₋₄ alkoxy;

R^a, R^b, R^c are independently of each other H, linear or branched C₁₋₄ alkyl, such as methyl;

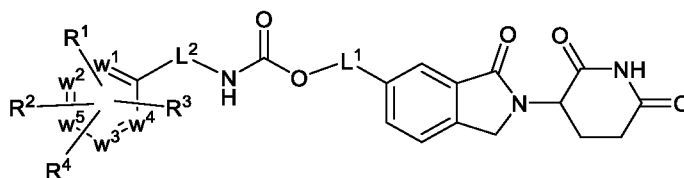
p is 0 or 1.

11. The compound of claim 10 or pharmaceutically acceptable salts or stereoisomers thereof, wherein p is 0.

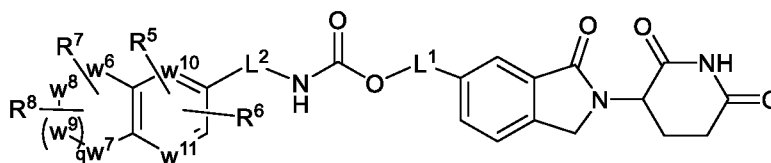
12. The compound of claim 10 or pharmaceutically acceptable salts or stereoisomers thereof, wherein p is 1 and R^b, R^c are H or wherein p is 1, R^b is methyl and R^c is H.

13. The compound of claim 1 or pharmaceutically acceptable salts or stereoisomers thereof, of formula V, VI or VII:

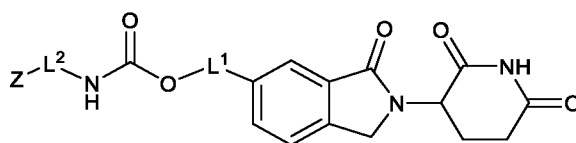
526



V



VI



VII

wherein

one or two of w^1 , w^2 , w^3 , w^4 , w^5 are independently of each other selected from C, N, S, and O, and the remaining of w^1 , w^2 , w^3 , w^4 , w^5 are C;

one or two of w^6 , w^7 , w^8 , w^9 are selected from C and O and the remaining of w^6 , w^7 , w^8 , w^9 are C;

w^{10} , w^{11} are independently of each other selected from C and N;

L^1 is a covalent bond, linear or branched C_{1-6} alkyl;

L^2 is a covalent bond, linear or branched C_{1-6} alkyl;

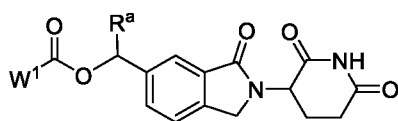
R^1 , R^2 , R^3 , R^4 are independently of each other selected from H, linear or branched $-C_{1-6}$ alkyl, linear or branched C_{1-6} heteroalkyl, $-C_{1-4}$ alkoxy, CF_3 , CHF_2 , $CMeF_2$, $-O-(CH_2)_2-OMe$, OCF_3 , $OCHF_2$, $-C_{1-6}$ alkylamino, $-CN$, $-OC(O)-C_{1-6}$ alkyl, $-N(H)C(O)-C_{1-6}$ alkyl, $-C(O)O-C_{1-6}$ alkyl, $-COOH$, $-C_{1-6}$ alkyl $C(O)OH$, $-C_{1-6}$ alkyl $C(O)O-C_{1-6}$ alkyl, NH_2 , $-C_{1-4}$ alkylhydroxy, and halogen, such as F, Cl or Br, e.g. F or Cl, or a group of formula $-L^3-X^2$, wherein L^3 is a covalent bond, linear or branched C_{1-6} alkyl, $-O-$, $-C_{1-4}$ alkoxy and X^2 is C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, $-C_{1-4}$

alkoxy, NH_2 , NMe_2 , halogen, CF_3 , CHF_2 , CMeF_2 , $-\text{O}-(\text{CH}_2)_2-\text{OMe}$, OCF_3 , OCHF_2 , and $-\text{C}_{1-4}$ alkylhydroxy;

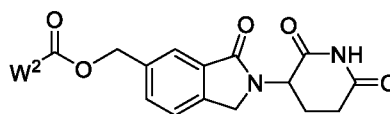
R^5 , R^6 , R^7 , R^8 are independently of each other selected from H, linear or branched C_{1-4} alkyl, such as methyl, and halogen, such as F or Cl, e.g. F;

- 5 Z is linear or branched $-\text{C}_{1-6}$ alkyl, $-\text{C}_{3-6}$ cycloalkyl, 4-8 membered heterocycloalkyl, wherein Z is unsubstituted or substituted with C_{1-4} alkyl, C_6 aryl, C_6 aryloxy, 6 membered heteroaryl or CF_3 ; or Z together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is unsubstituted or substituted with C_{1-4} alkyl, C_6 aryl, C_6 aryloxy, 6 membered heteroaryl or CF_3 ;
- 10 q is 0, 1.

14. The compound of claim 1 or pharmaceutically acceptable salts or stereoisomers thereof, of formula VIII or VIIIa

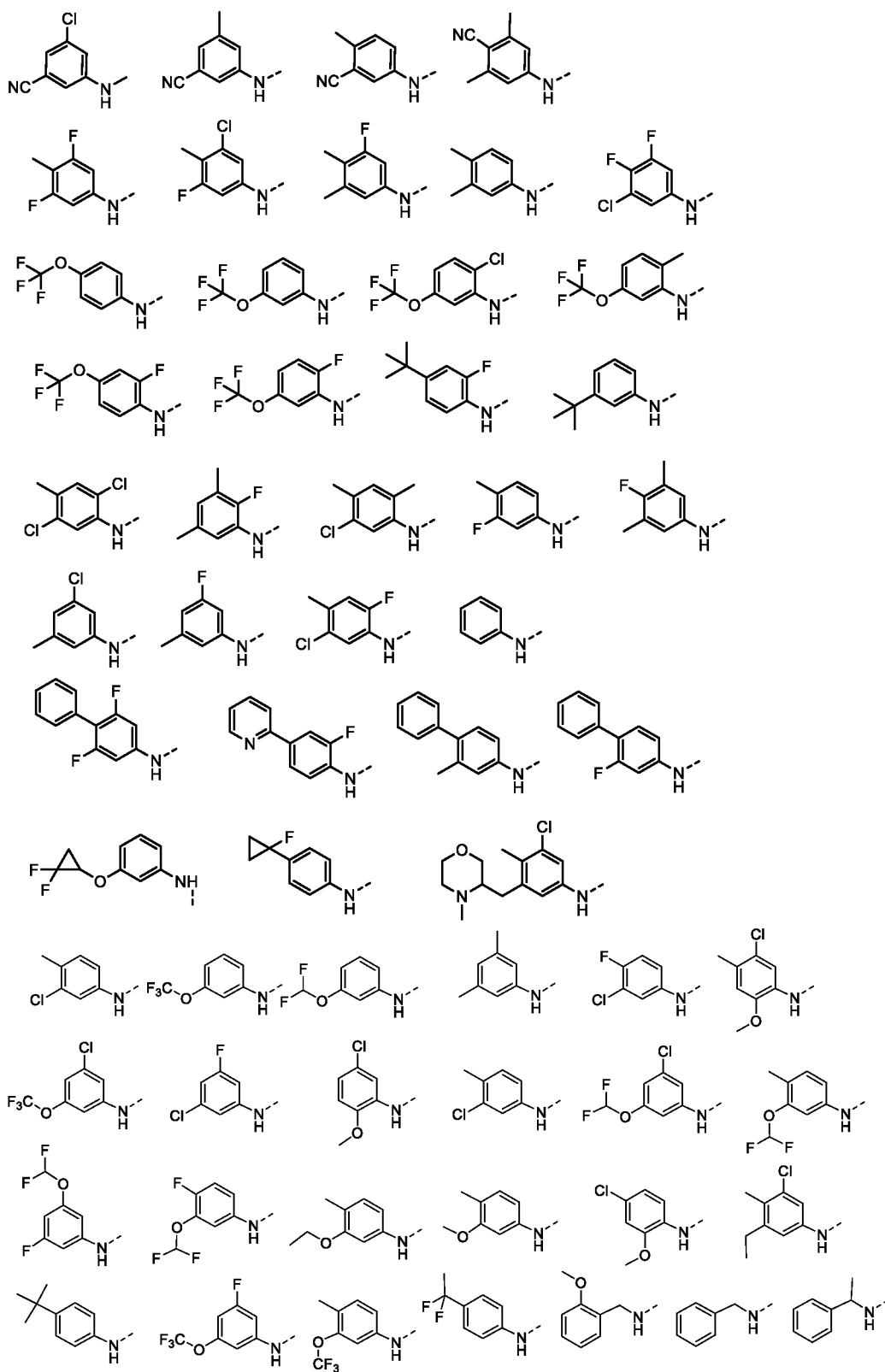


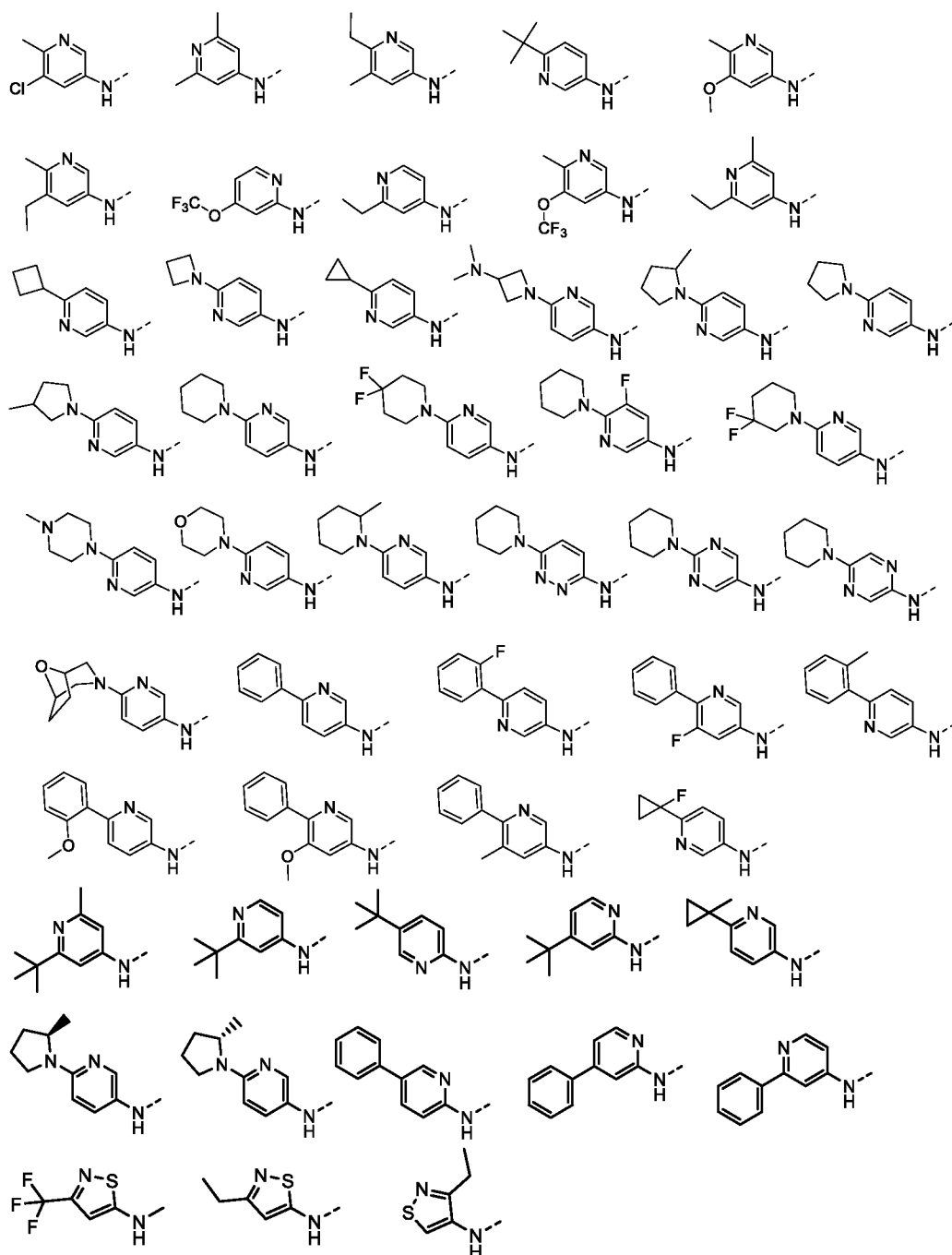
VIII



VIIIa

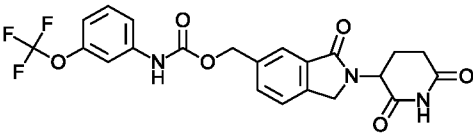
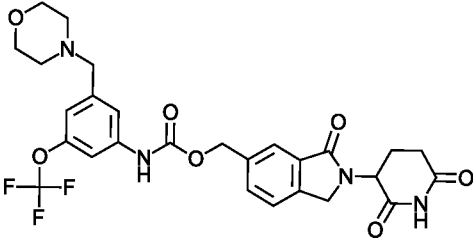
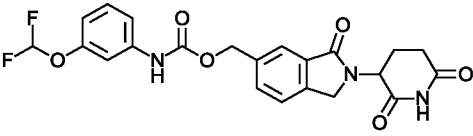
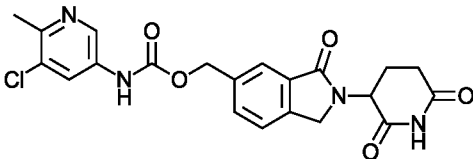
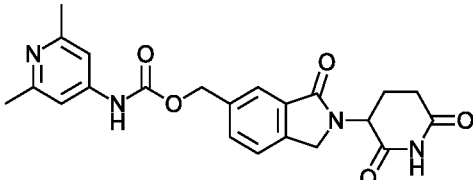
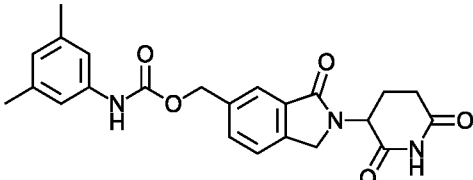
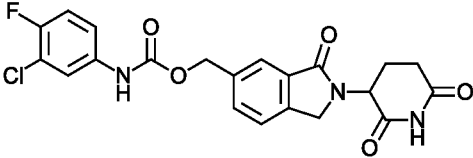
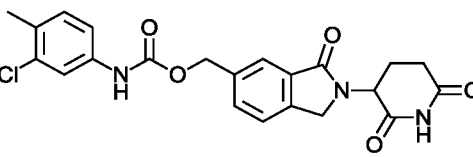
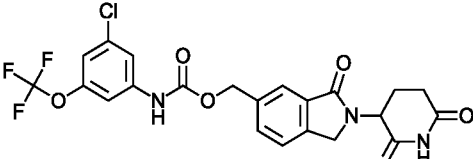
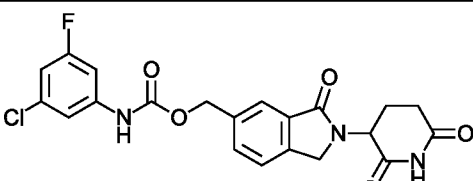
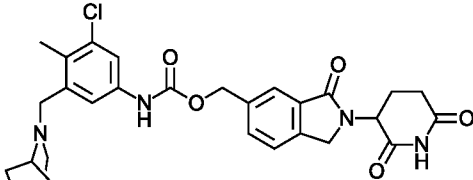
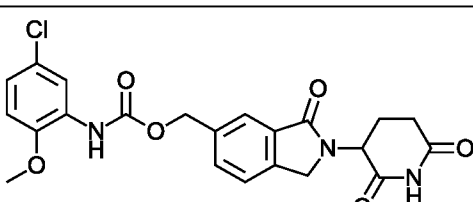
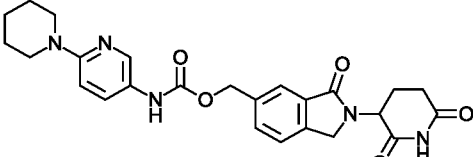
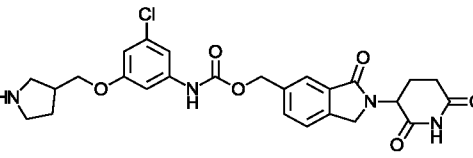
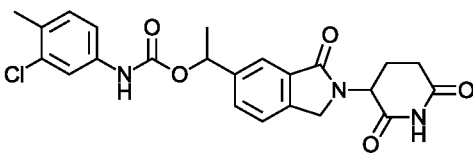
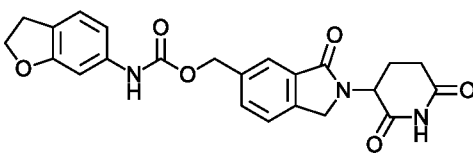
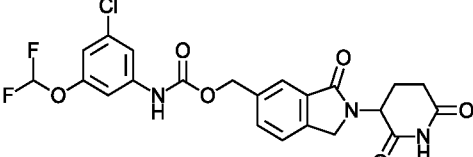
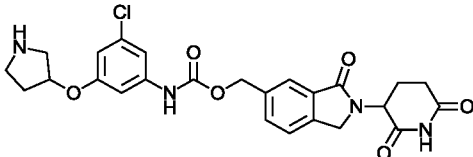
wherein R^a is H or methyl and W^1 and W^2 are selected from

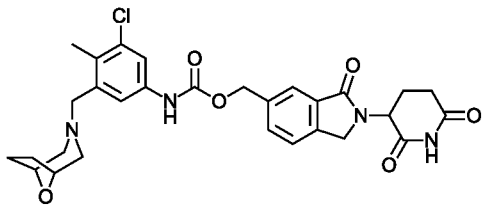
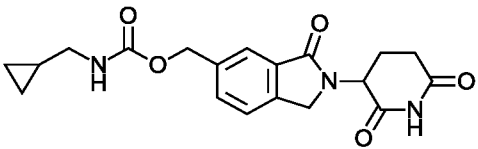
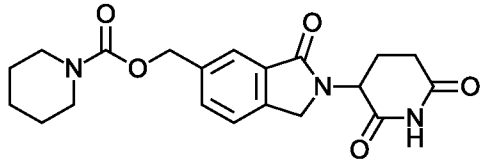
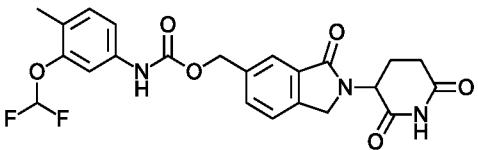
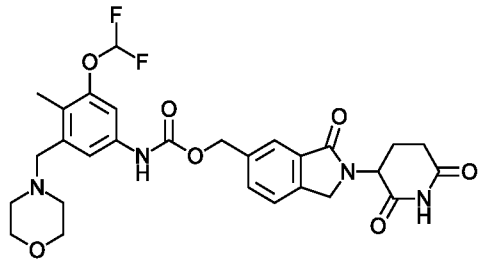
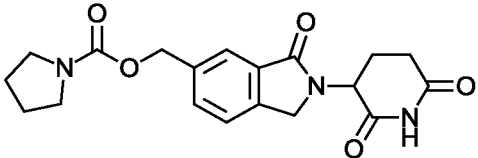
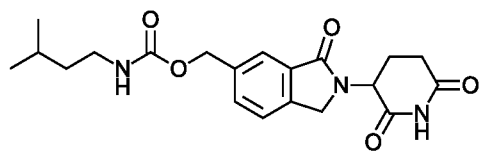
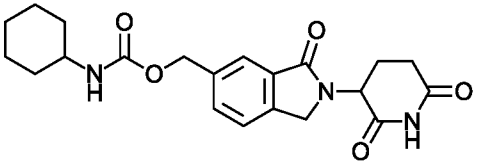
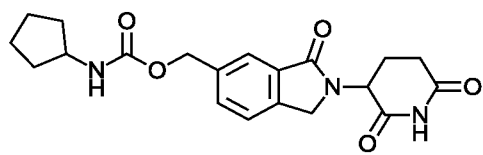
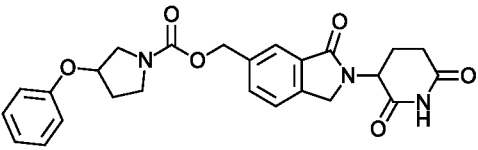
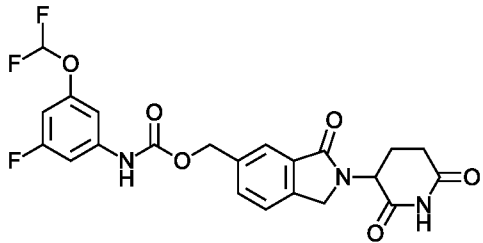
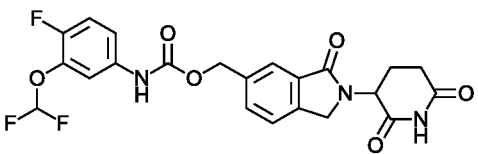
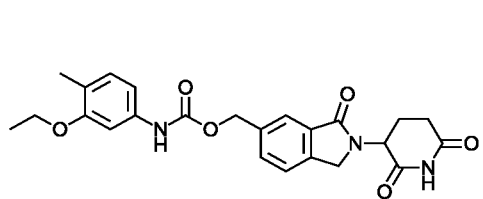
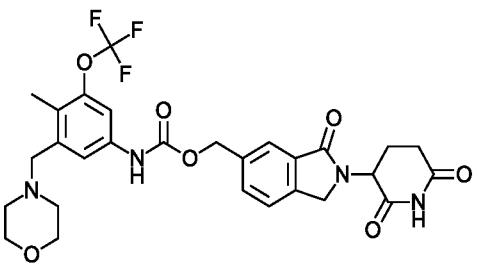
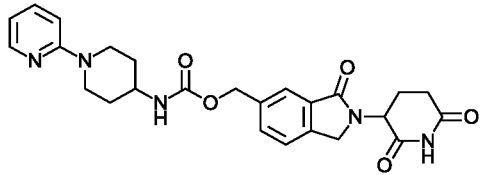
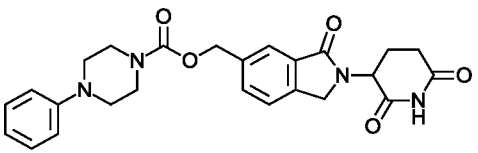


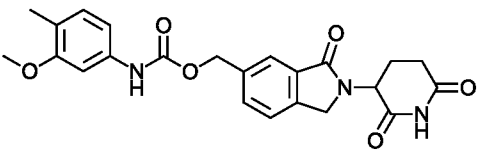
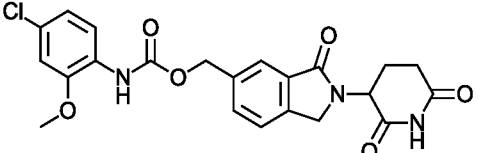
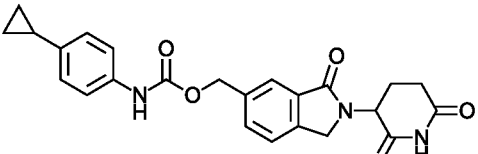
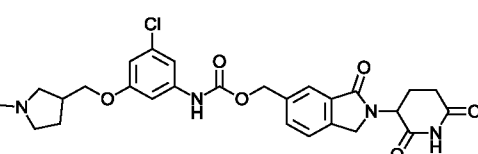
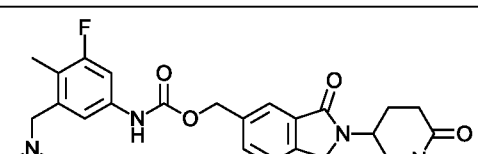
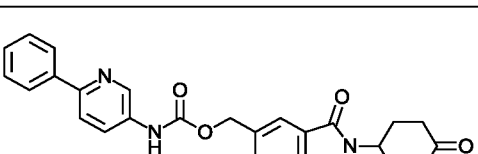
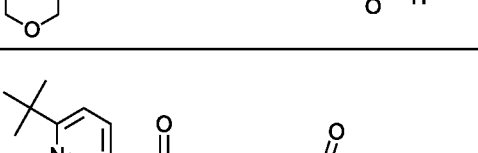
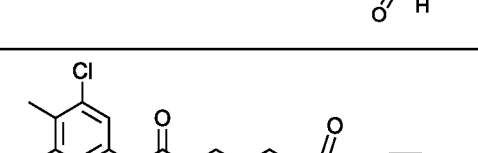
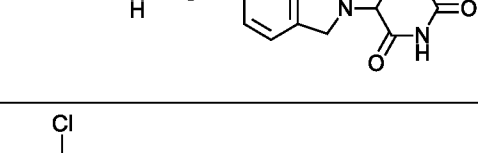
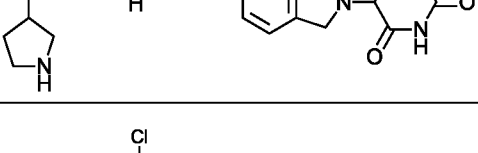
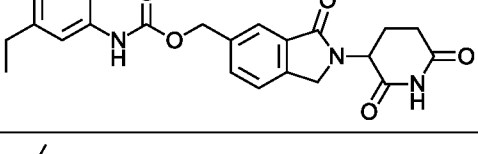
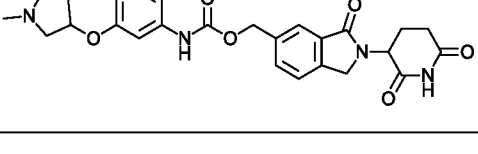
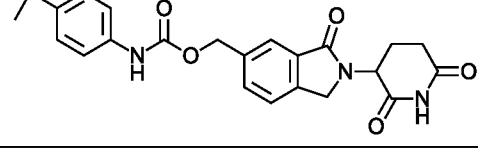
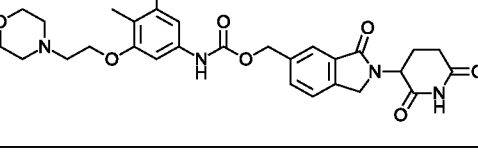
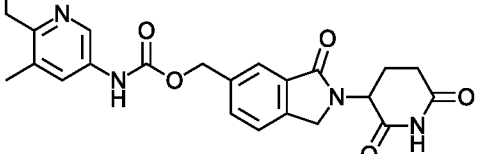
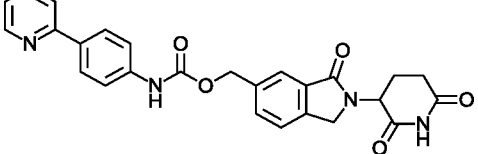
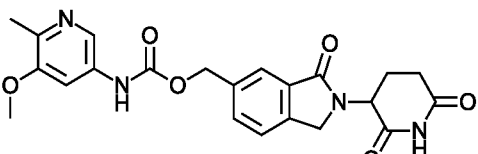
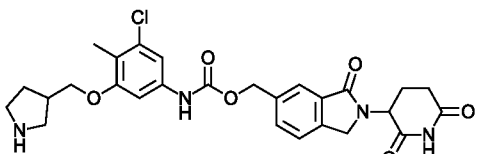


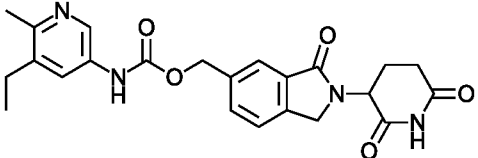
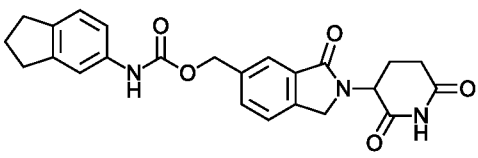
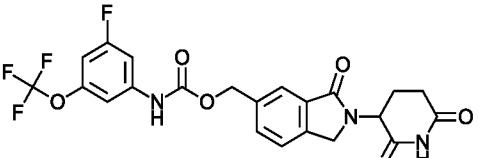
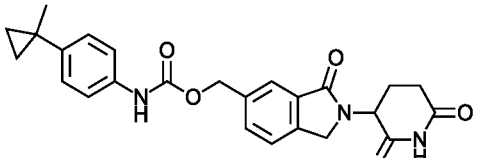
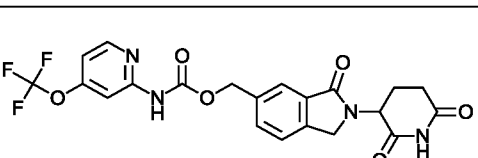
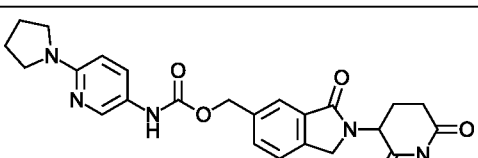
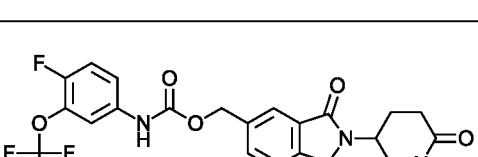
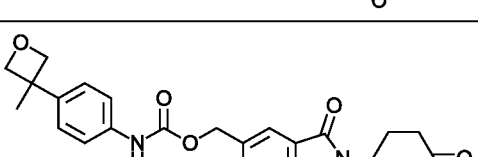
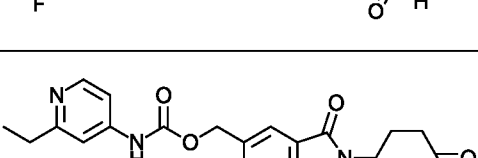
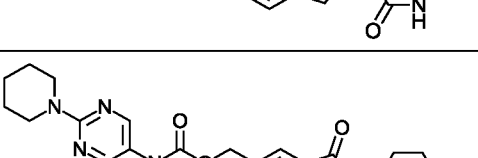
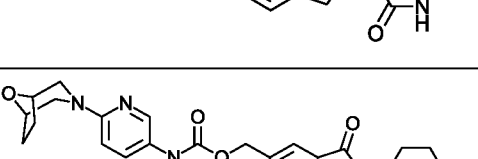
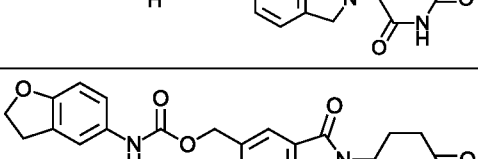
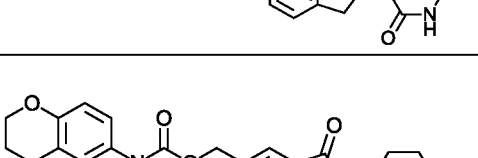
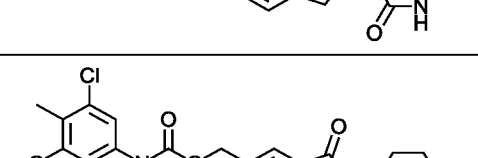
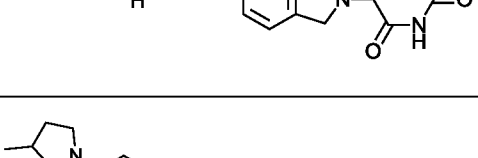
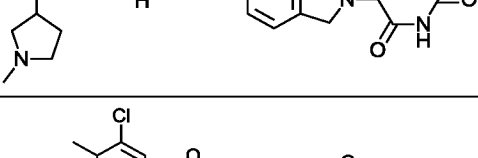
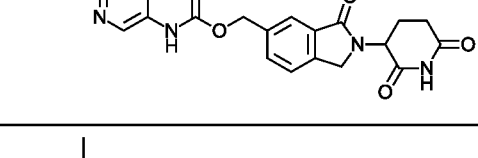
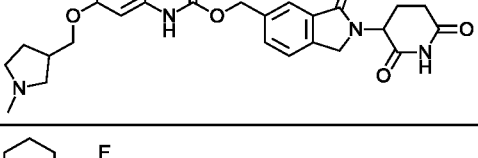
5 15. A compound selected from the group consisting of:

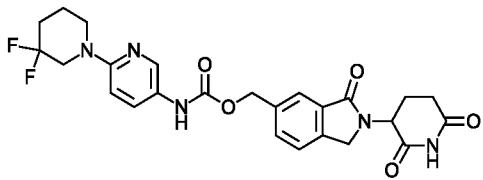
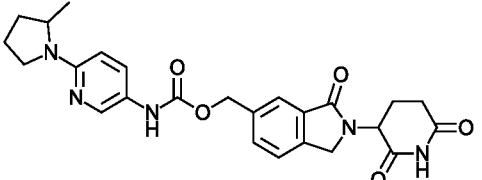
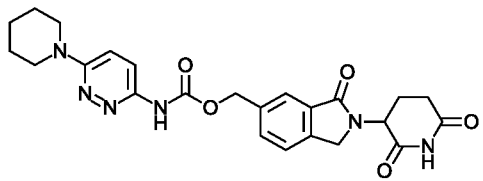
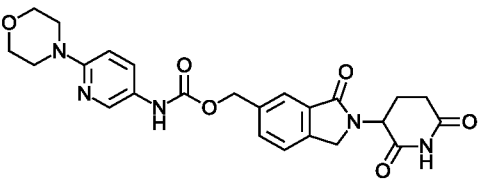
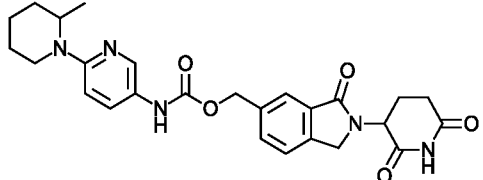
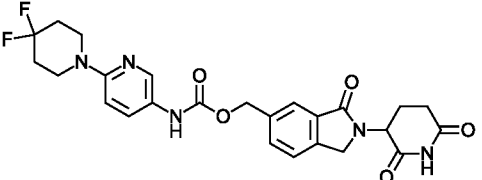
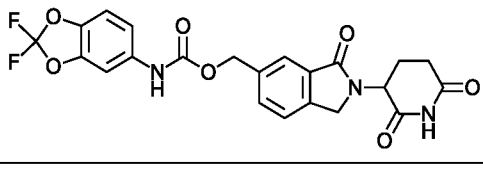
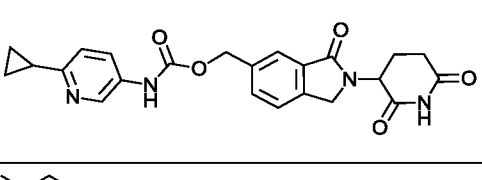
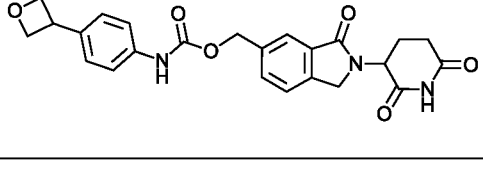
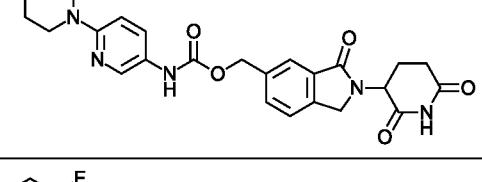
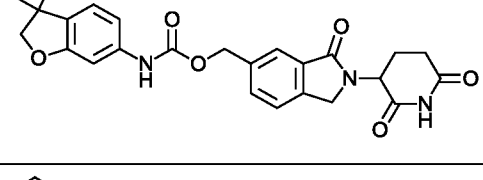
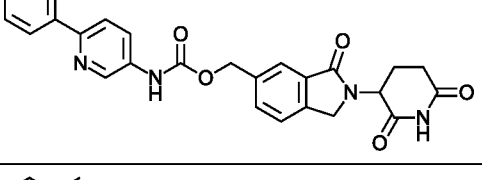
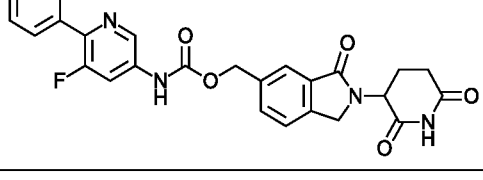
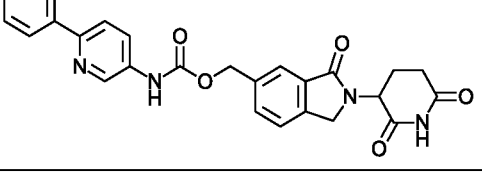
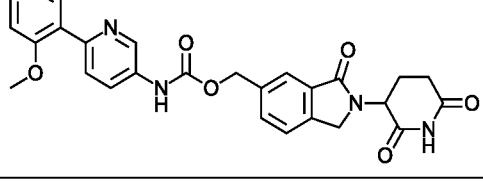
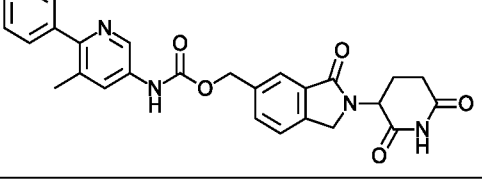
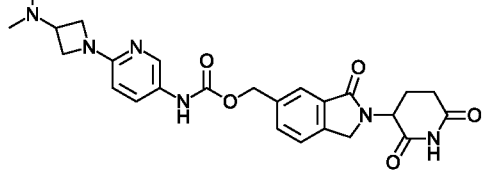
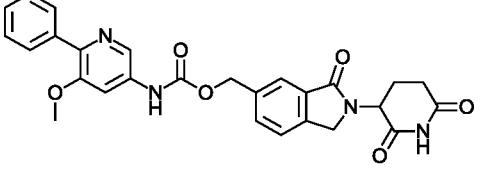
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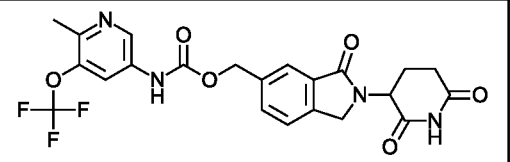
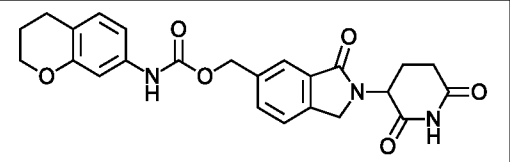
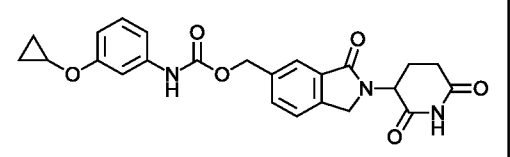
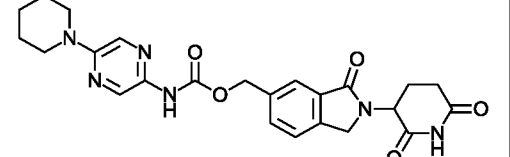
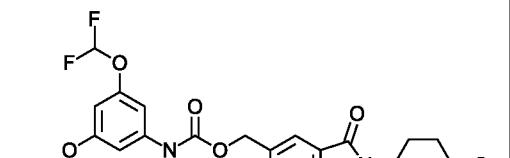
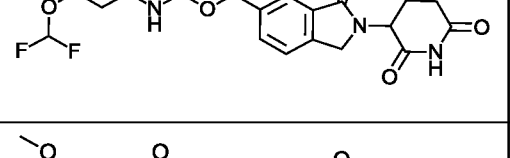
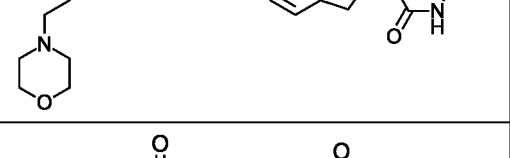
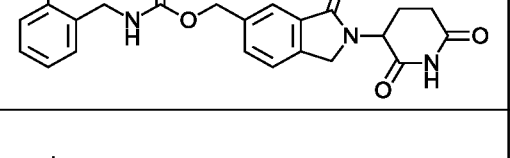
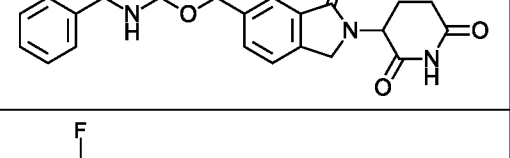
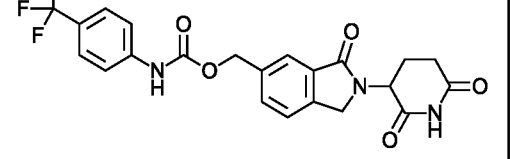
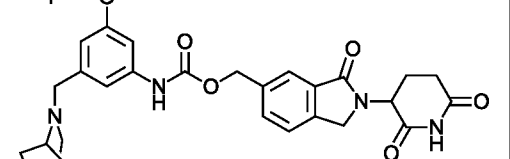
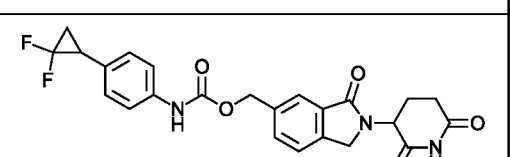
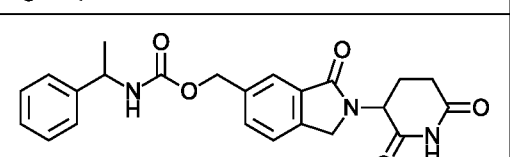
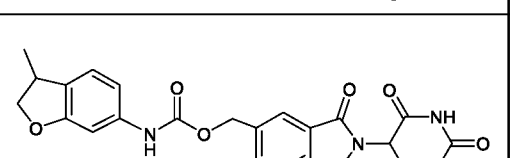
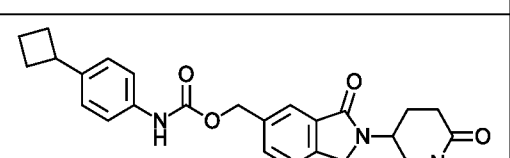
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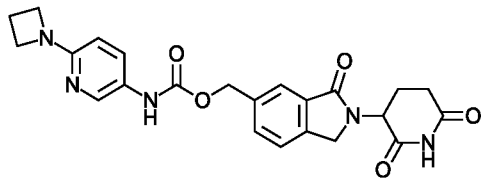
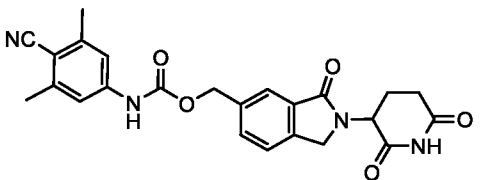
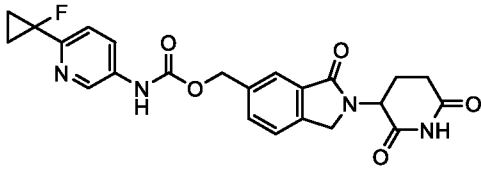
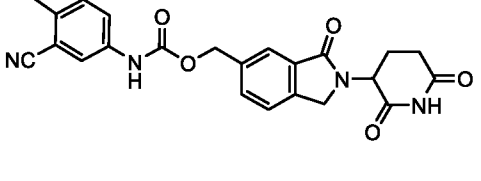
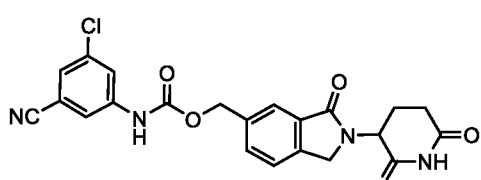
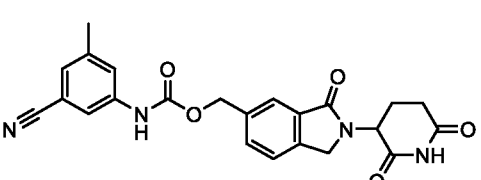
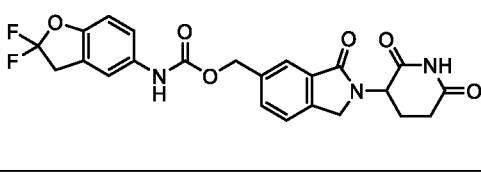
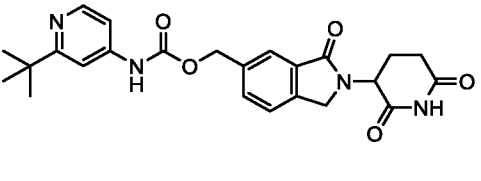
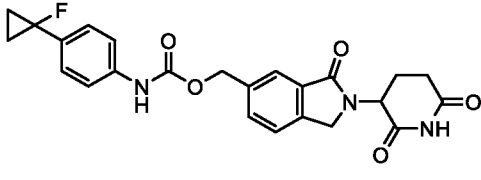
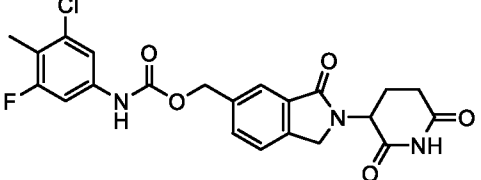
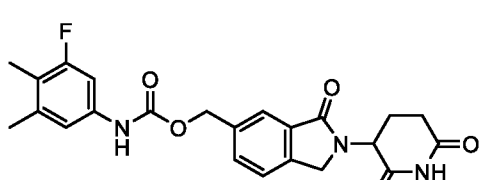
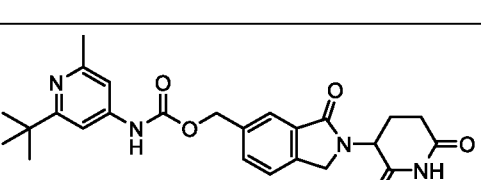
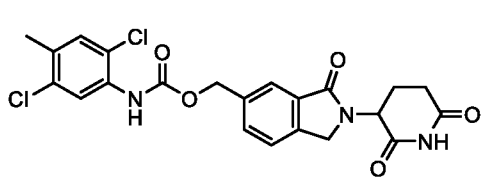
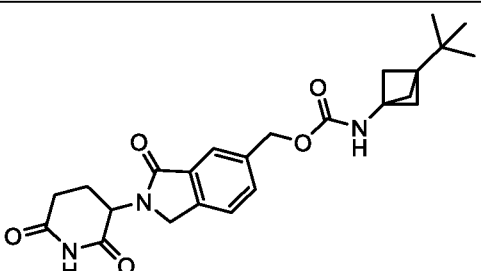
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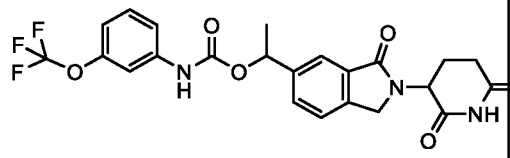
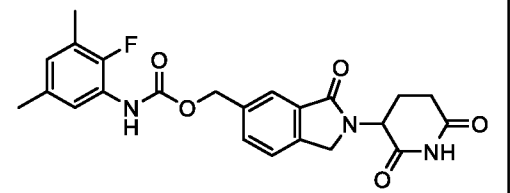
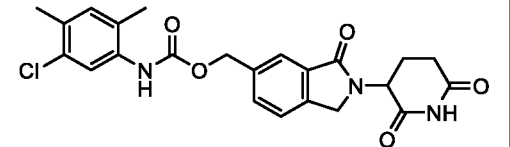
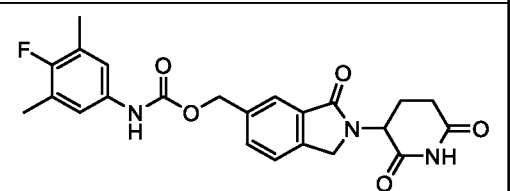
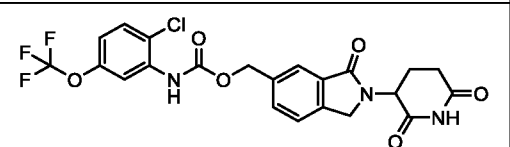
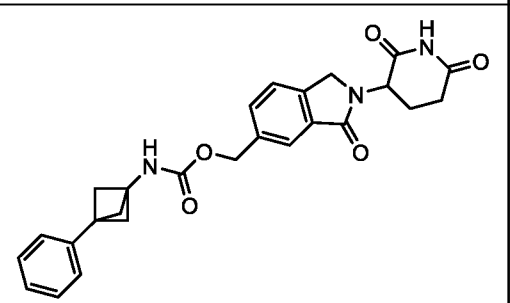
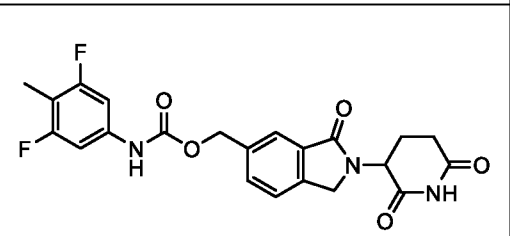
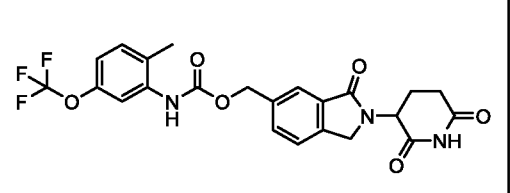
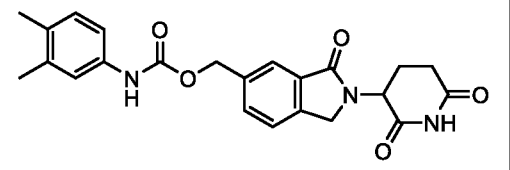
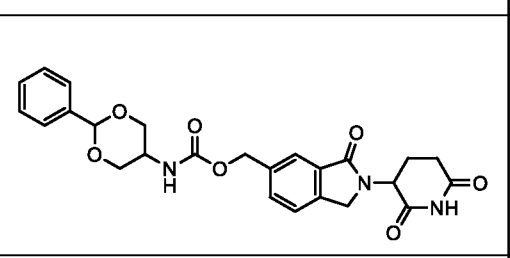
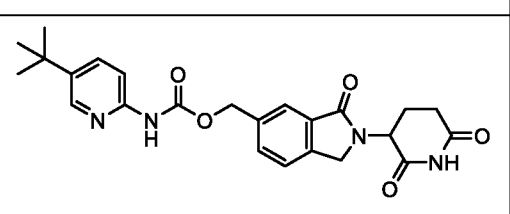
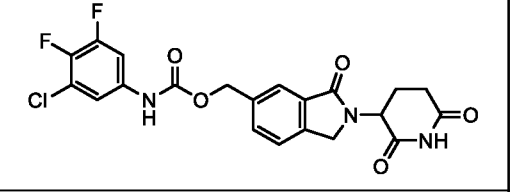
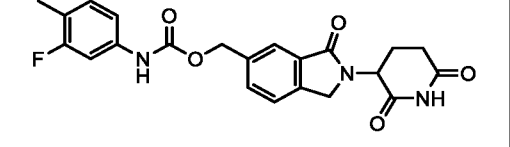
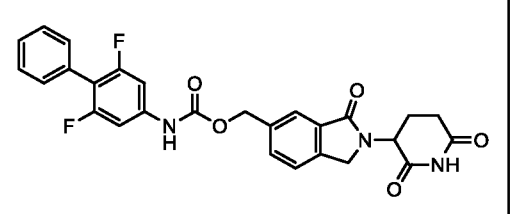
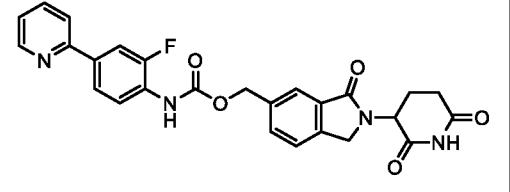
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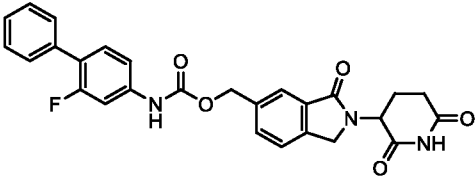
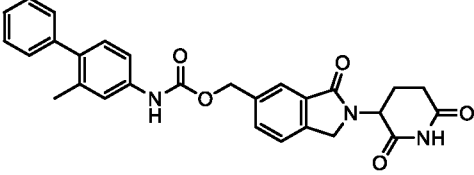
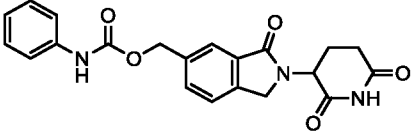
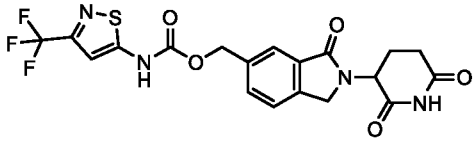
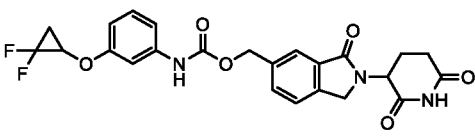
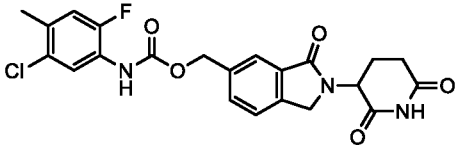
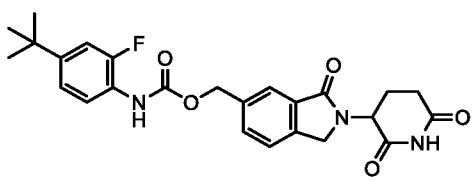
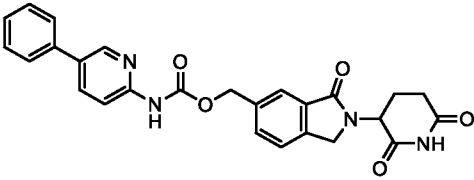
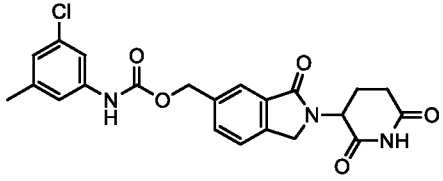
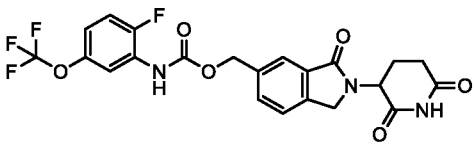
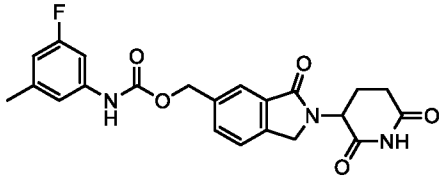
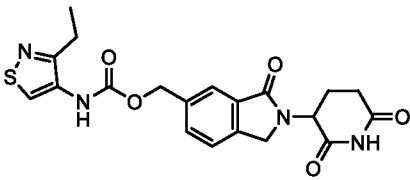
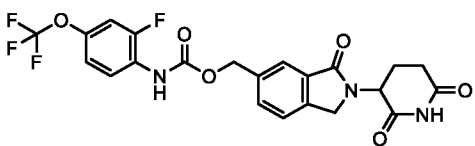
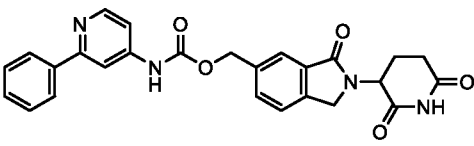
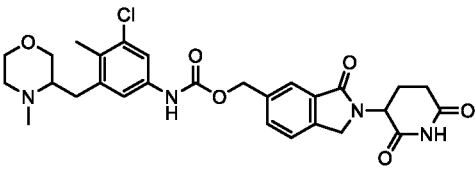
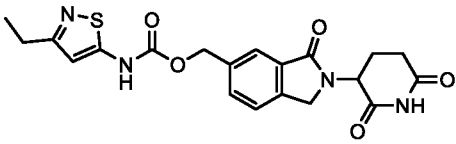
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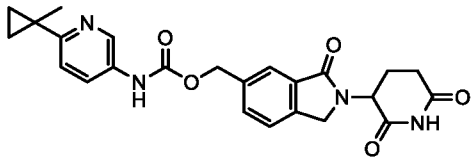
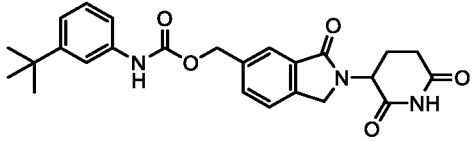
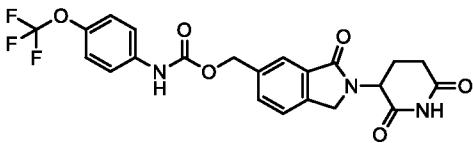
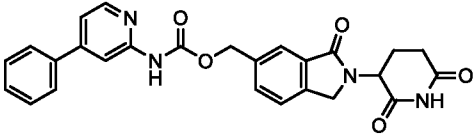
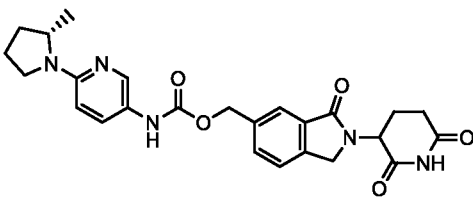
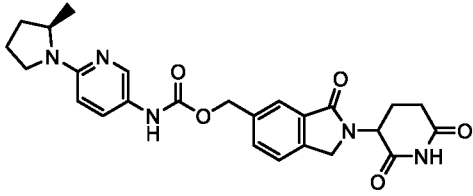
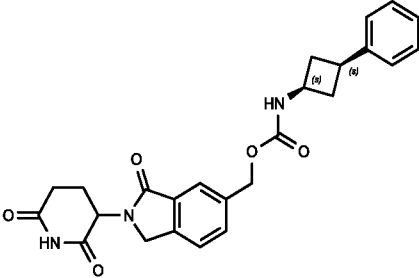
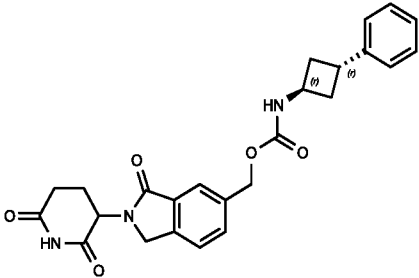
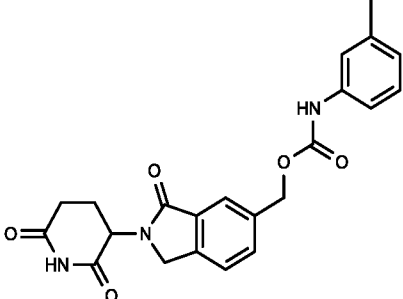
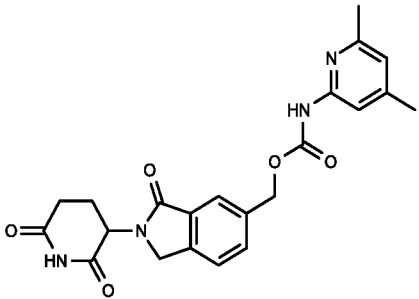
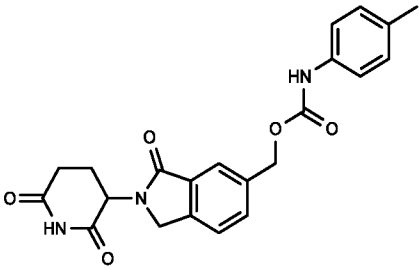
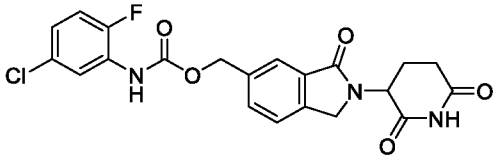
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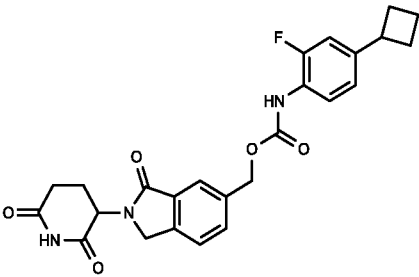
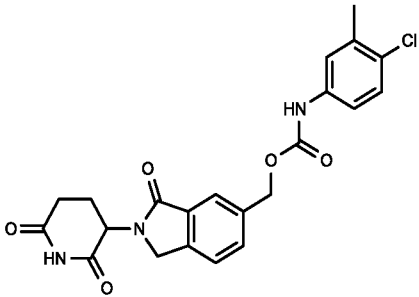
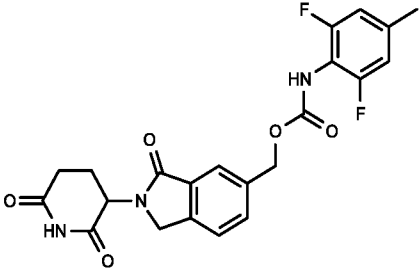
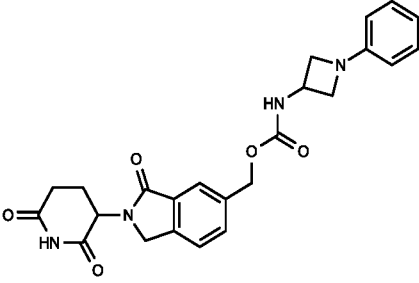
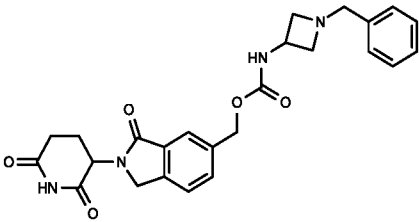
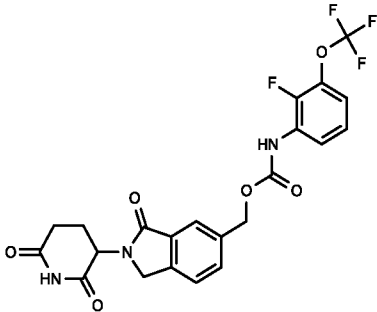
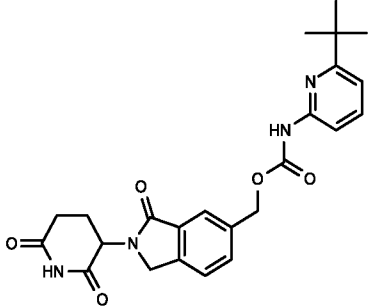
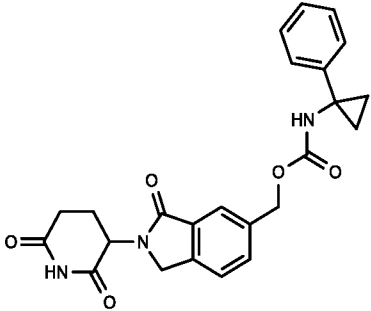
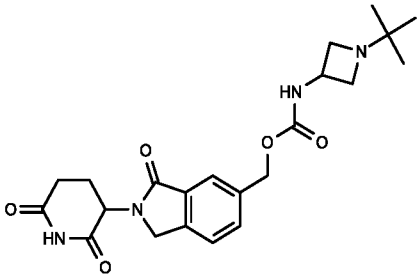
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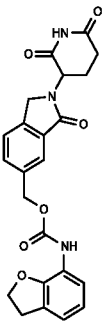
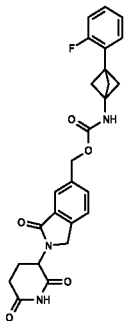
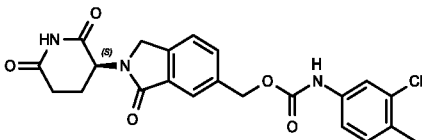
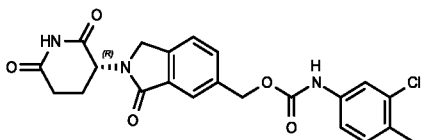
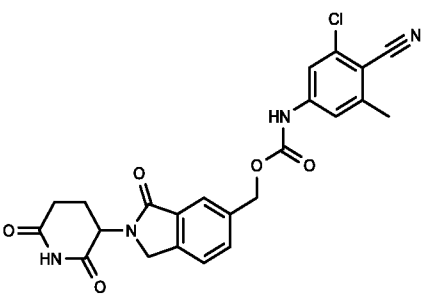
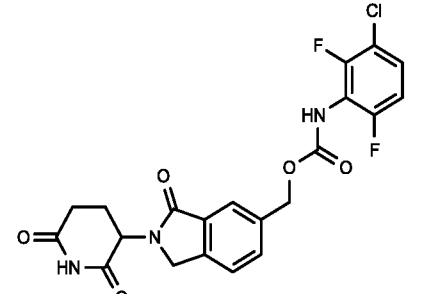
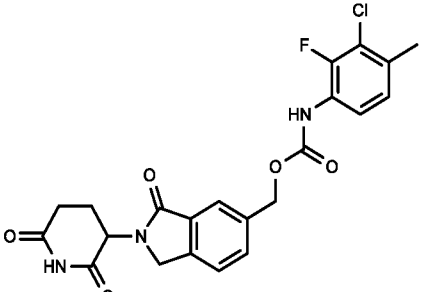
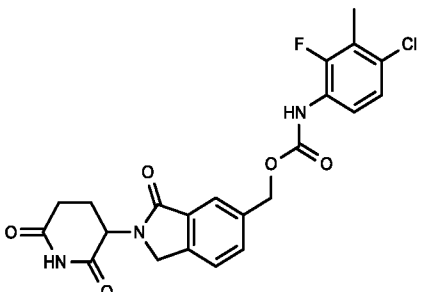
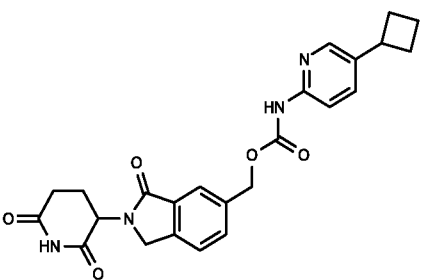
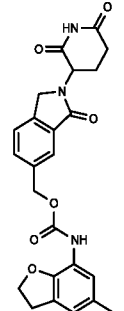
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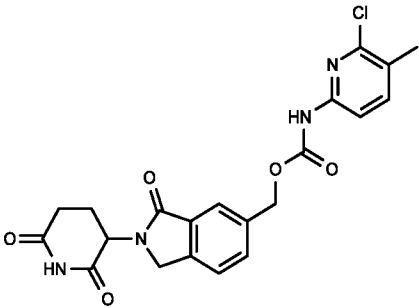
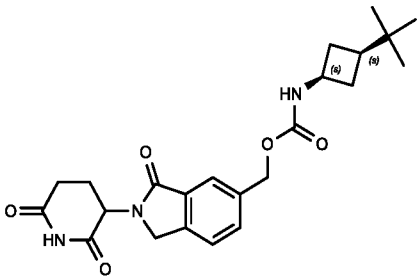
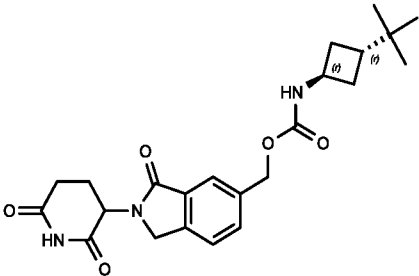
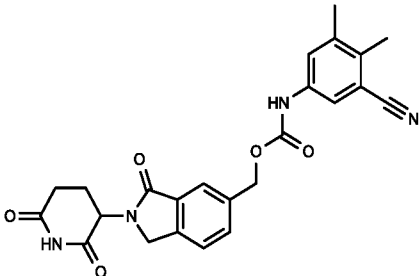
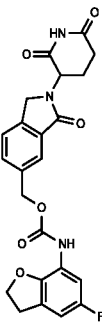
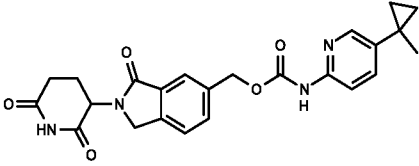
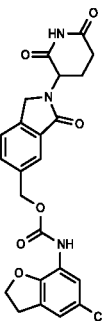
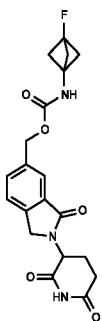
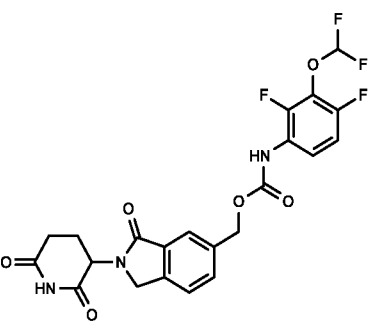
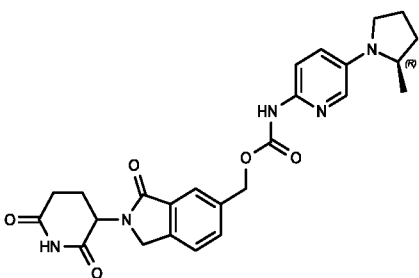
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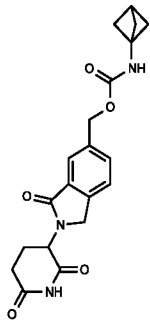
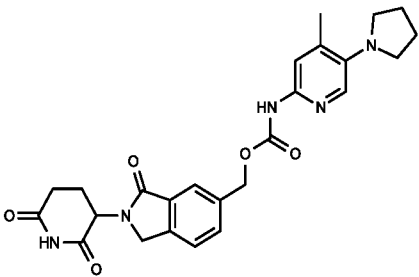
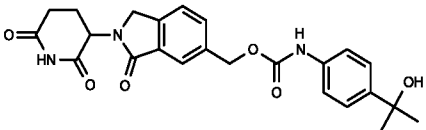
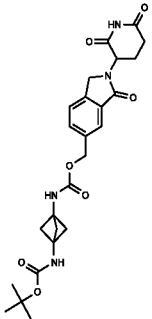
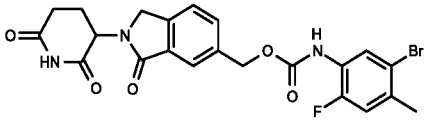
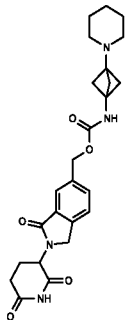
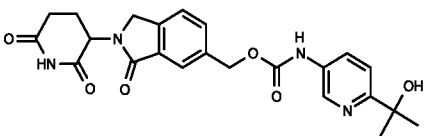
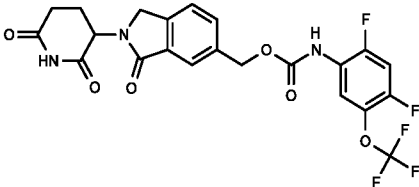
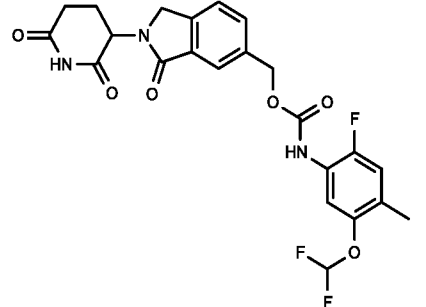
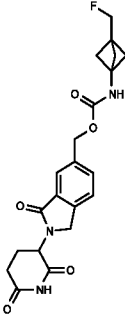
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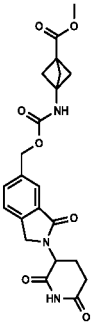
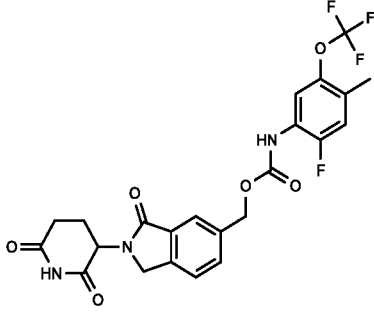
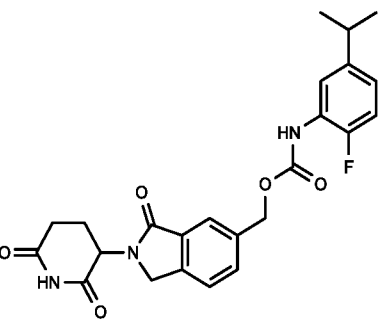
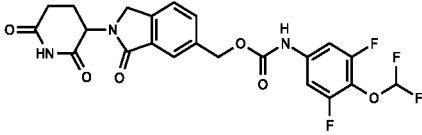
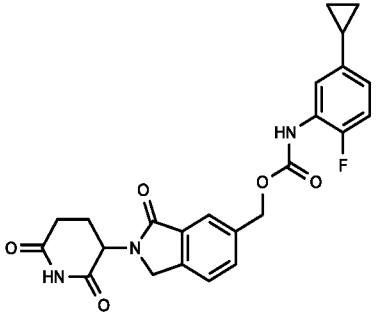
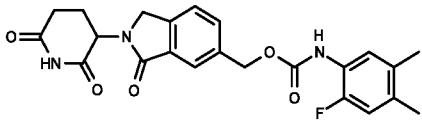
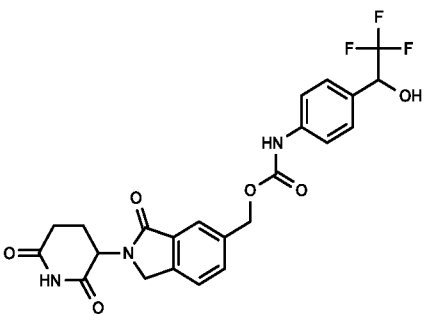
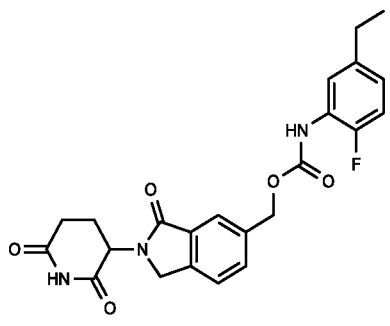
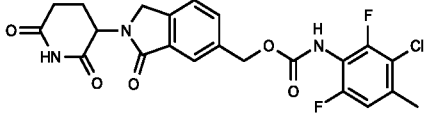
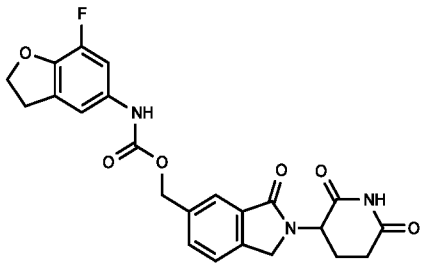
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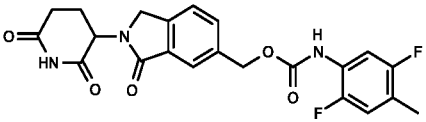
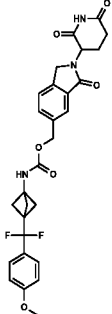
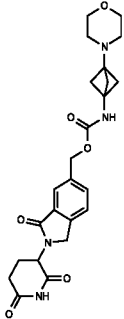
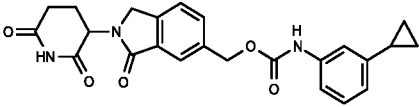
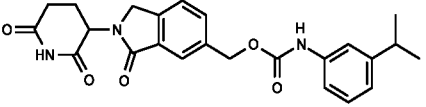
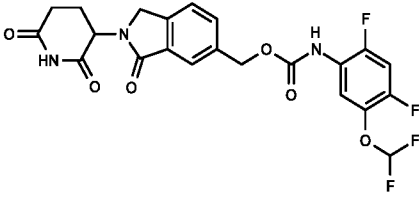
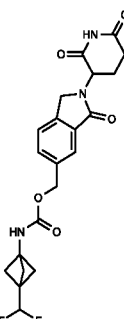
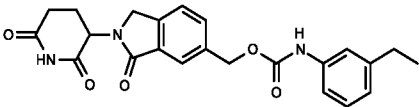
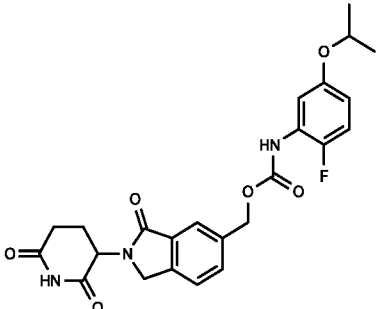
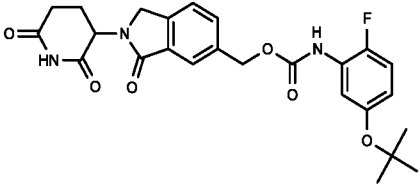
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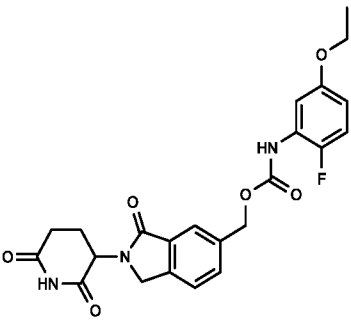
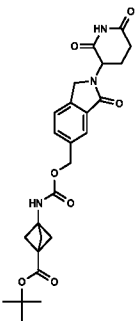
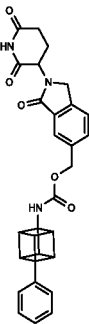
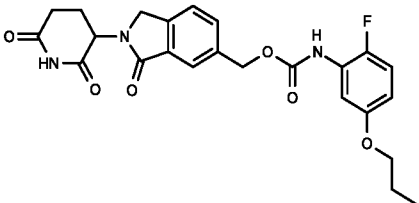
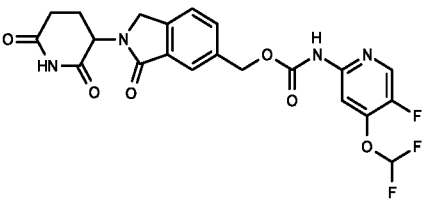
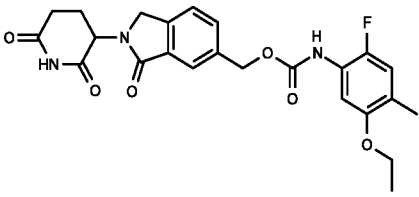
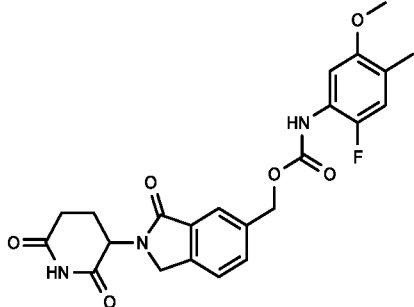
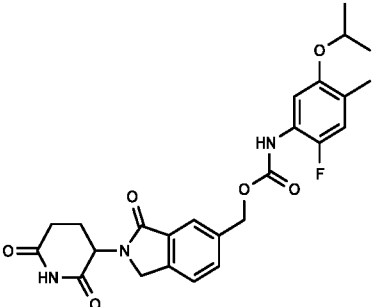
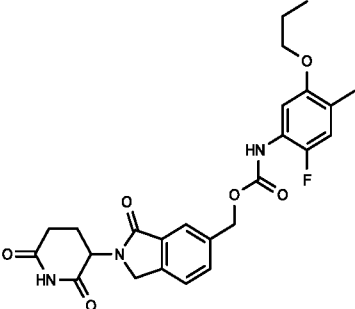
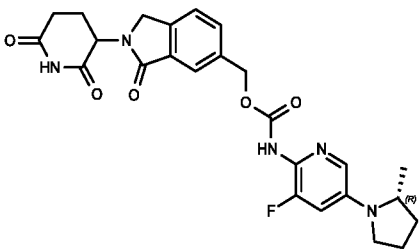
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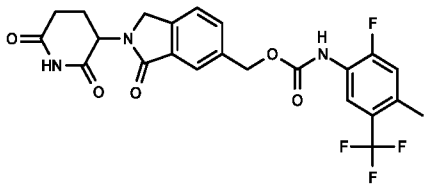
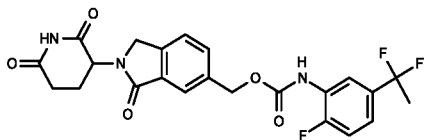
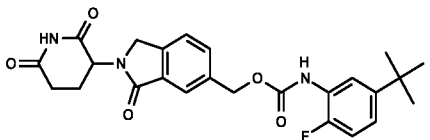
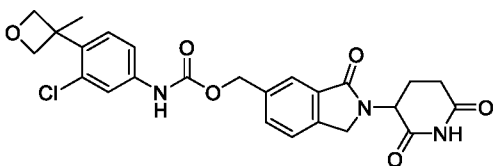
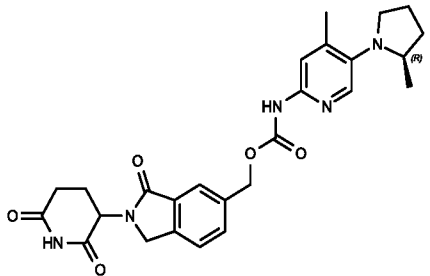
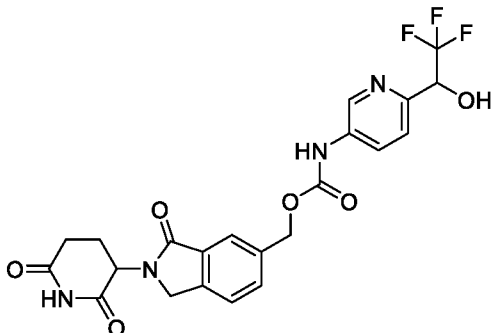
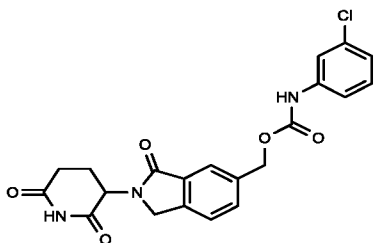
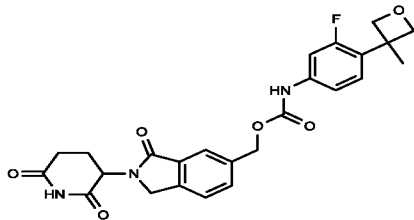
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and pharmaceutically acceptable salts and stereoisomers thereof.

16. A composition comprising the compound according to claim 1 or pharmaceutically acceptable salts or stereoisomers thereof.
17. The composition of claim 16, further comprising a pharmaceutically acceptable carrier and/or a second therapeutically active agent.
18. A method of treating cancer, in particular lung cancer, breast cancer and neuroendocrine cancer in a subject, comprising administering to a subject a therapeutically effective amount of the compound of claim 1.

18. A method of treating cancer, in particular lung cancer, breast cancer and neuroendocrine cancer in a subject, comprising administering to a subject a therapeutically effective amount of the compound of claim 1.
19. A method of treating a Myc-driven cancer in a subject in need thereof, comprising
5 administering to the subject a therapeutically effective amount of the compound of claim 1.
20. The method of claim 19, wherein the Myc-driven cancer is a Myc-driven lung cancer.
21. The method of claim 19, wherein the Myc-driven cancer is a Myc-driven small cell lung cancer.
- 10 22. The method of claim 21, wherein the Myc-driven small cell lung cancer is a high L-Myc small cell lung cancer.
23. The method of claim 19, wherein the Myc-driven cancer is a Myc-driven non-small cell lung cancer.
24. The method of claim 23, wherein the Myc-driven non-small cell lung cancer is a high N-
15 Myc non-small cell lung cancer.
25. The method of claim 19, wherein the compound is administered to the subject via oral administration.
26. A method of degrading GSPT1 in a subject suffering from cancer, comprising
20 administering to the subject a therapeutically effective amount of the compound of claim 1.
27. The method of claim 26, wherein the cancer is a Myc-driven cancer.
28. The method of claim 27, wherein the Myc-driven cancer is a Myc-driven lung cancer.
29. The method of claim 27, wherein the Myc-driven cancer is a Myc-driven small cell lung cancer.
- 25 30. The method of claim 29, wherein the Myc-driven small cell lung cancer is a high L-Myc small cell lung cancer.

31. The method of claim 26, wherein the Myc-driven cancer is a Myc-driven non-small cell lung cancer.
32. The method of claim 31, wherein the Myc-driven non-small cell lung cancer is a high N-Myc non-small cell lung cancer.
- 5 33. The method of claim 26, wherein the compound is administered to the subject via oral administration.
34. A method of reducing the level of GSPT1 in a subject suffering from cancer, comprising administering to the subject a therapeutically effective amount of the compound of claim 1.
- 10 35. The method of claim 34, wherein the cancer is a Myc-driven cancer.
36. The method of claim 35, wherein the Myc-driven cancer is a Myc-driven lung cancer.
37. The method of claim 35, wherein the Myc-driven cancer is a Myc-driven small cell lung cancer.
38. The method of claim 37, wherein the Myc-driven small cell lung cancer is a high L-Myc
15 small cell lung cancer.
39. The method of claim 35, wherein the Myc-driven cancer is a Myc-driven non-small cell lung cancer.
40. The method of claim 39, wherein the Myc-driven non-small cell lung cancer is a high N-Myc non-small cell lung cancer.
- 20 41. The method of claim 34, wherein the compound is administered to the subject via oral administration.

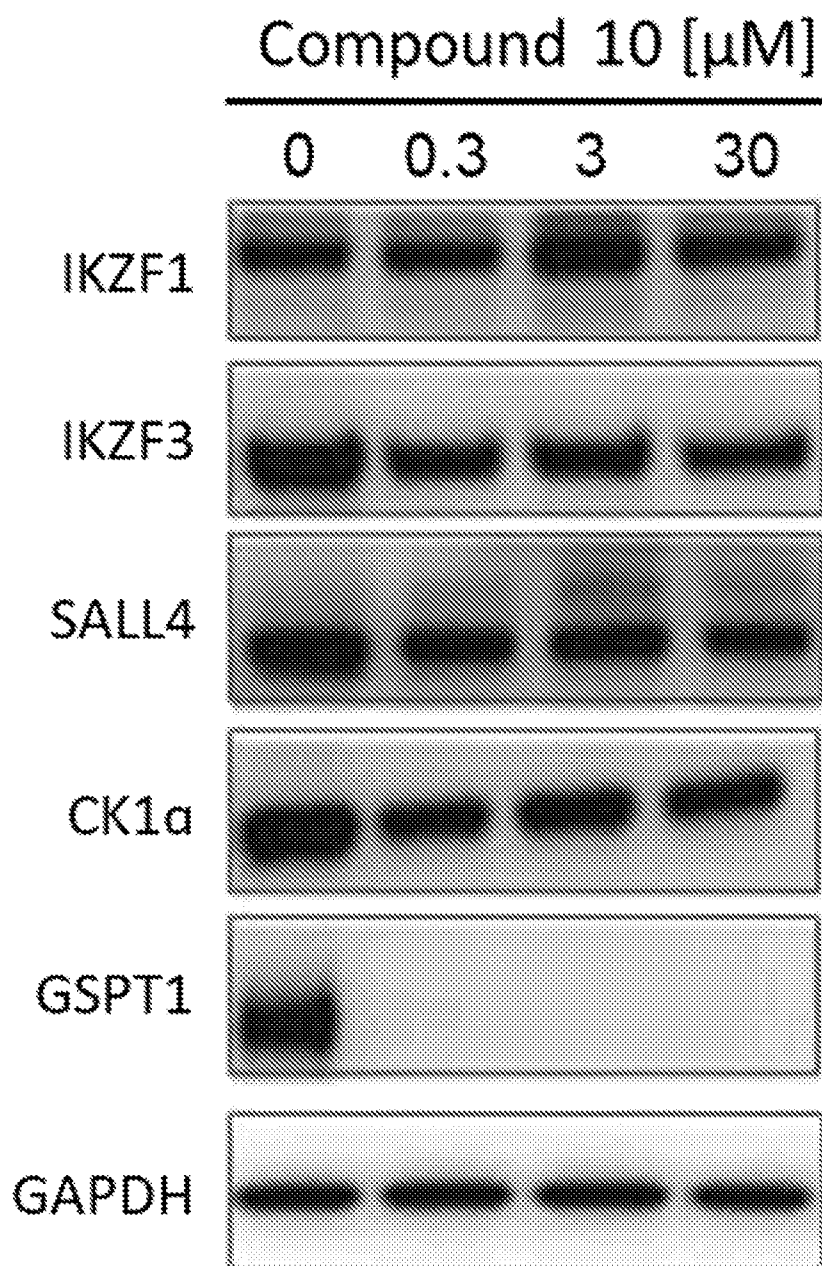
Figure 1A

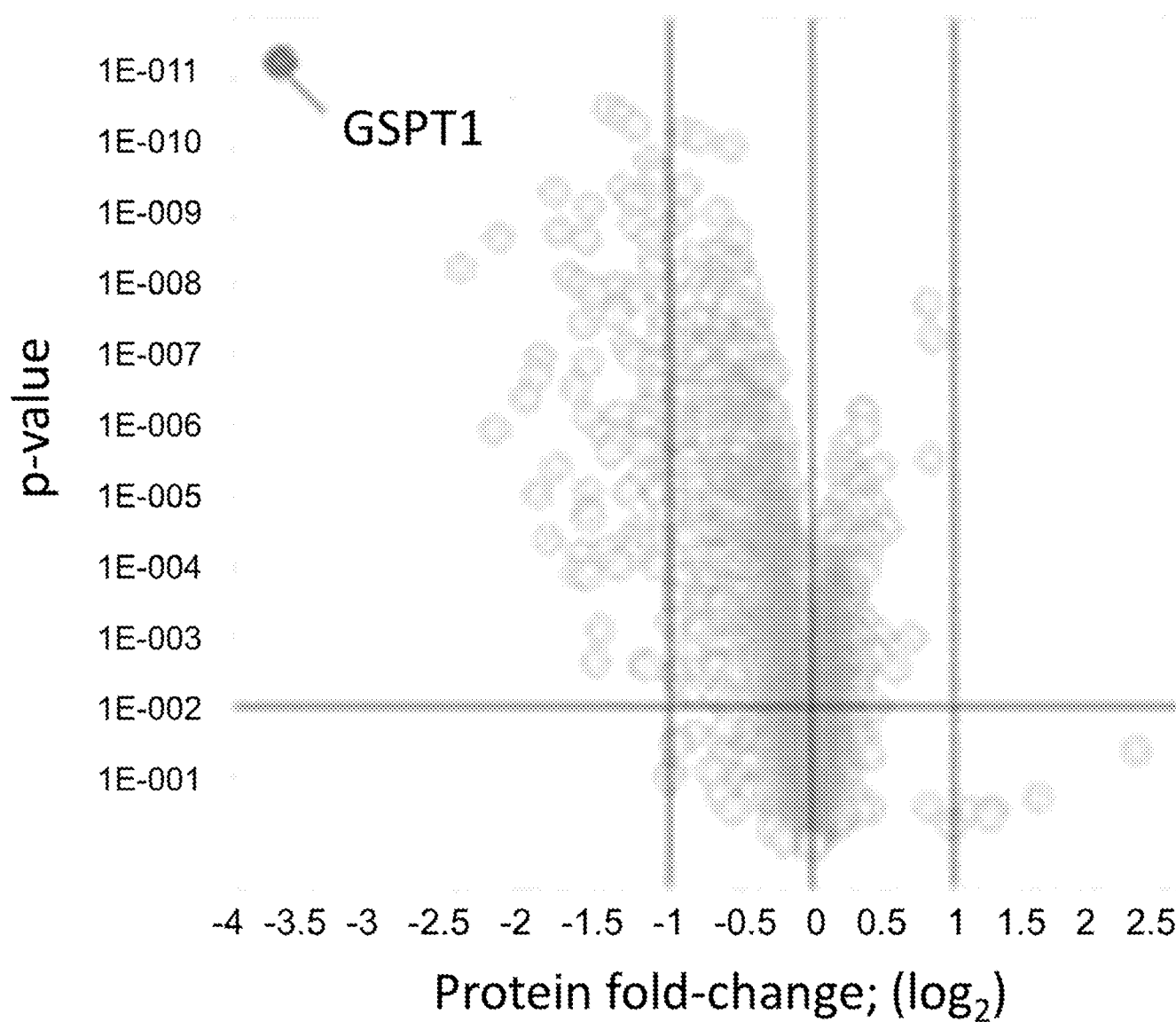
Figure 1B

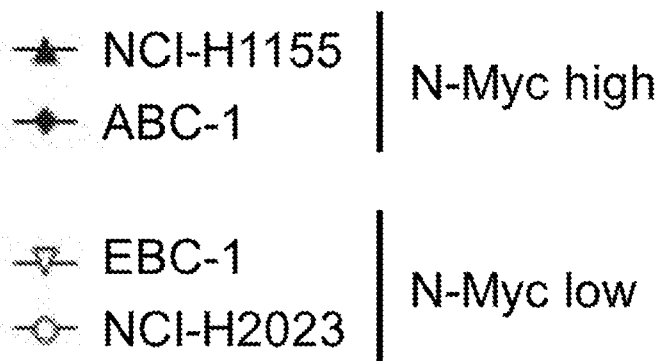
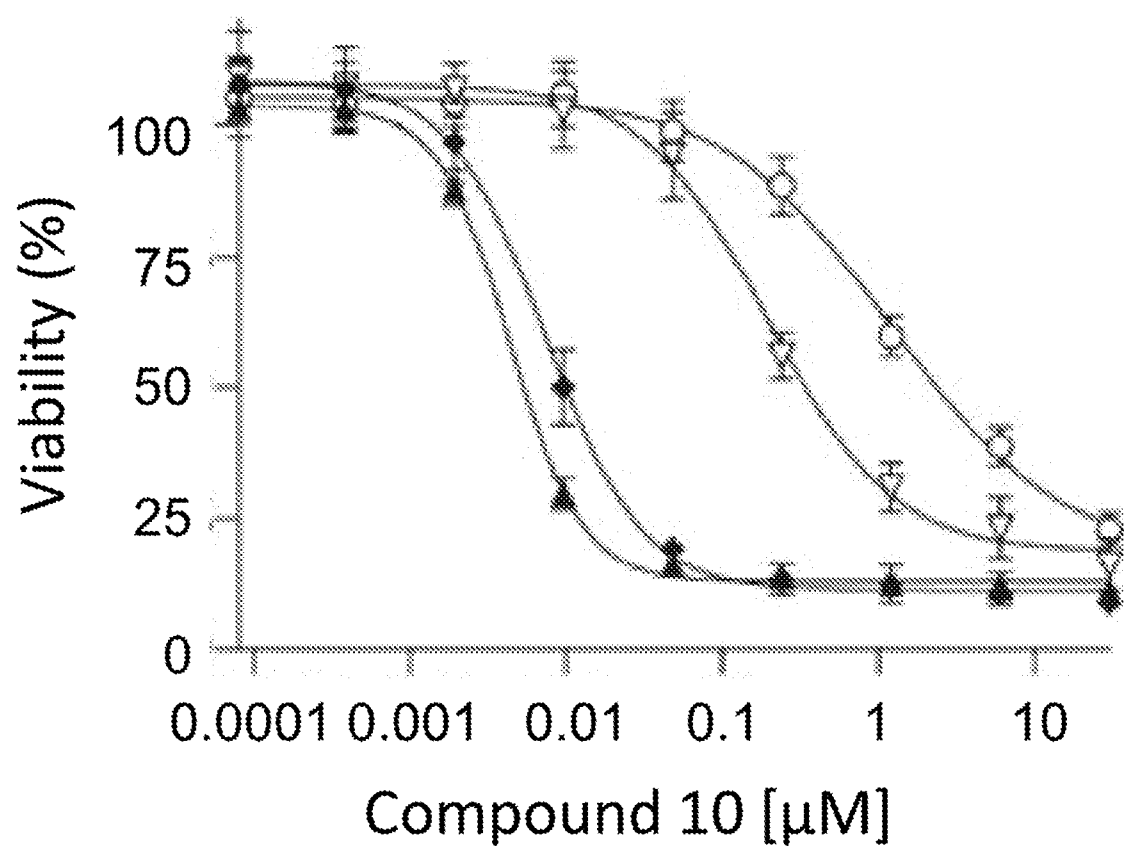
Figure 2A

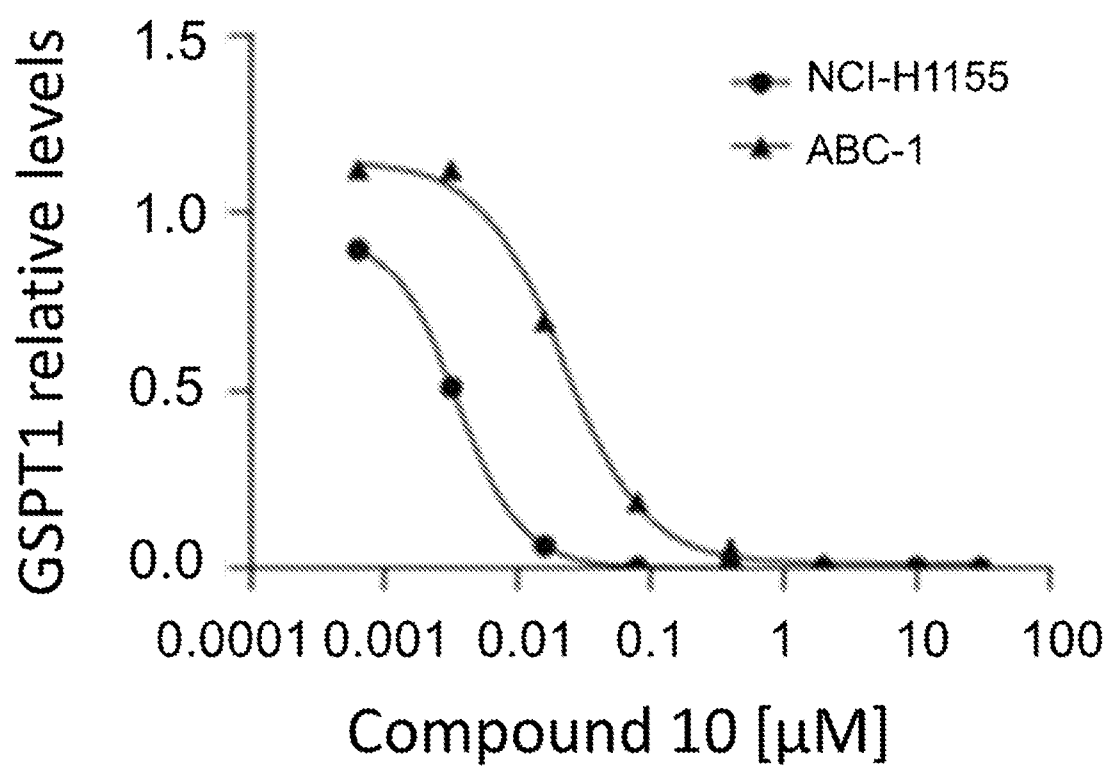
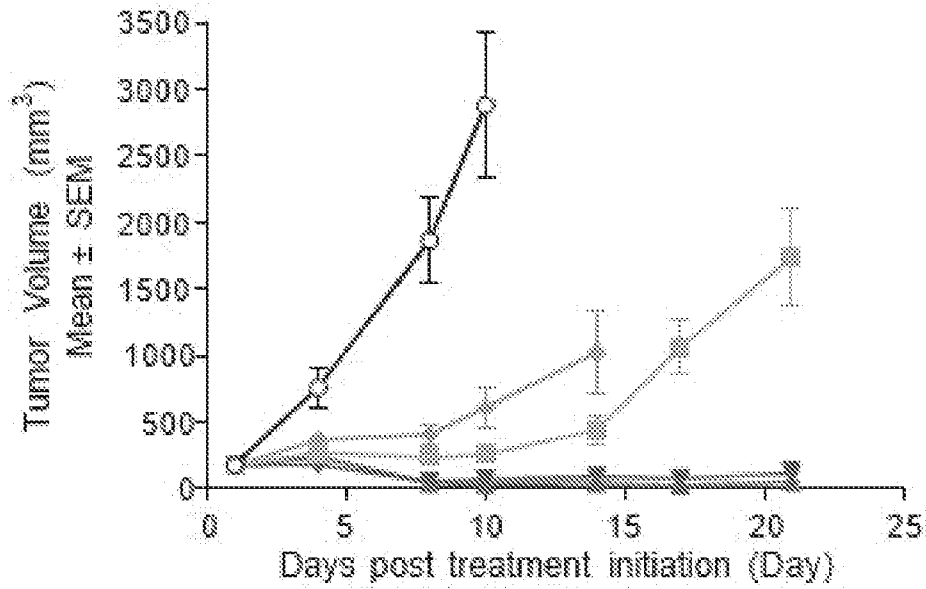
Figure 2B

Figure 3A



- O Vehicle, PO, QD
- Compound 10, 1 mg/kg PO, QD
- ▲ Compound 10, 3 mg/kg PO, QD
- ▼ Compound 10, 6 mg/kg PO, 5 ON – 9 OFF
- ◆ Gemcitabine, 40 mg/kg IP, Q4Dx5

Figure 3B

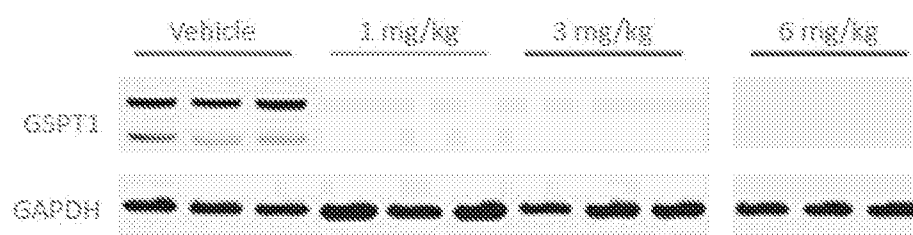
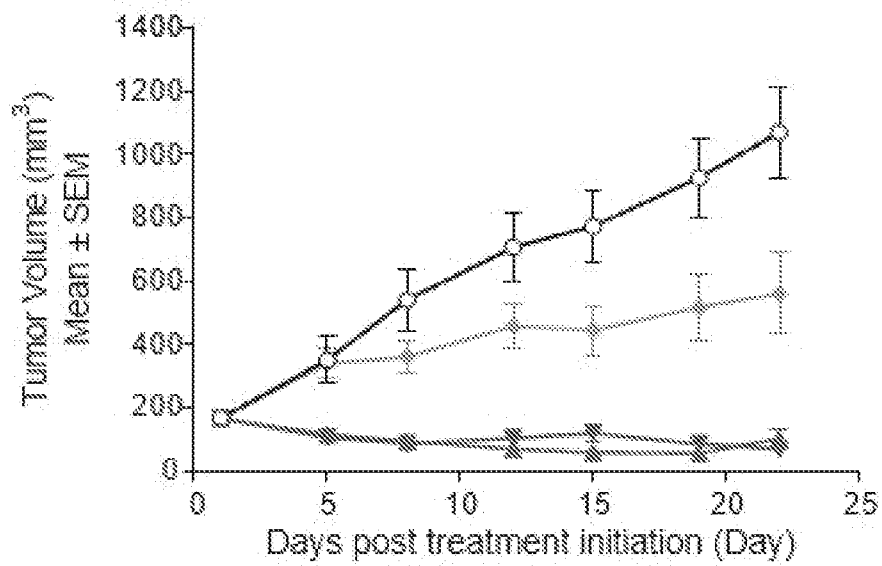
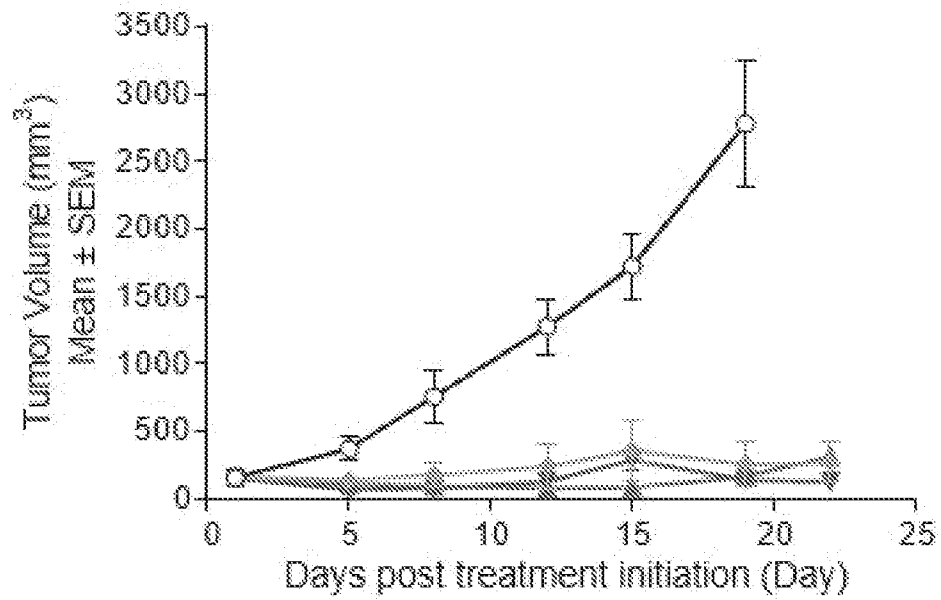


Figure 3C



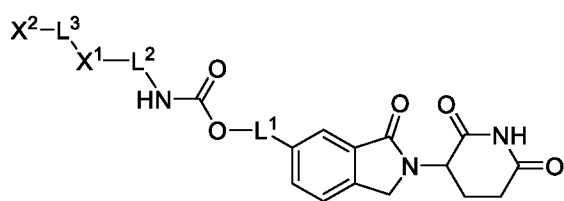
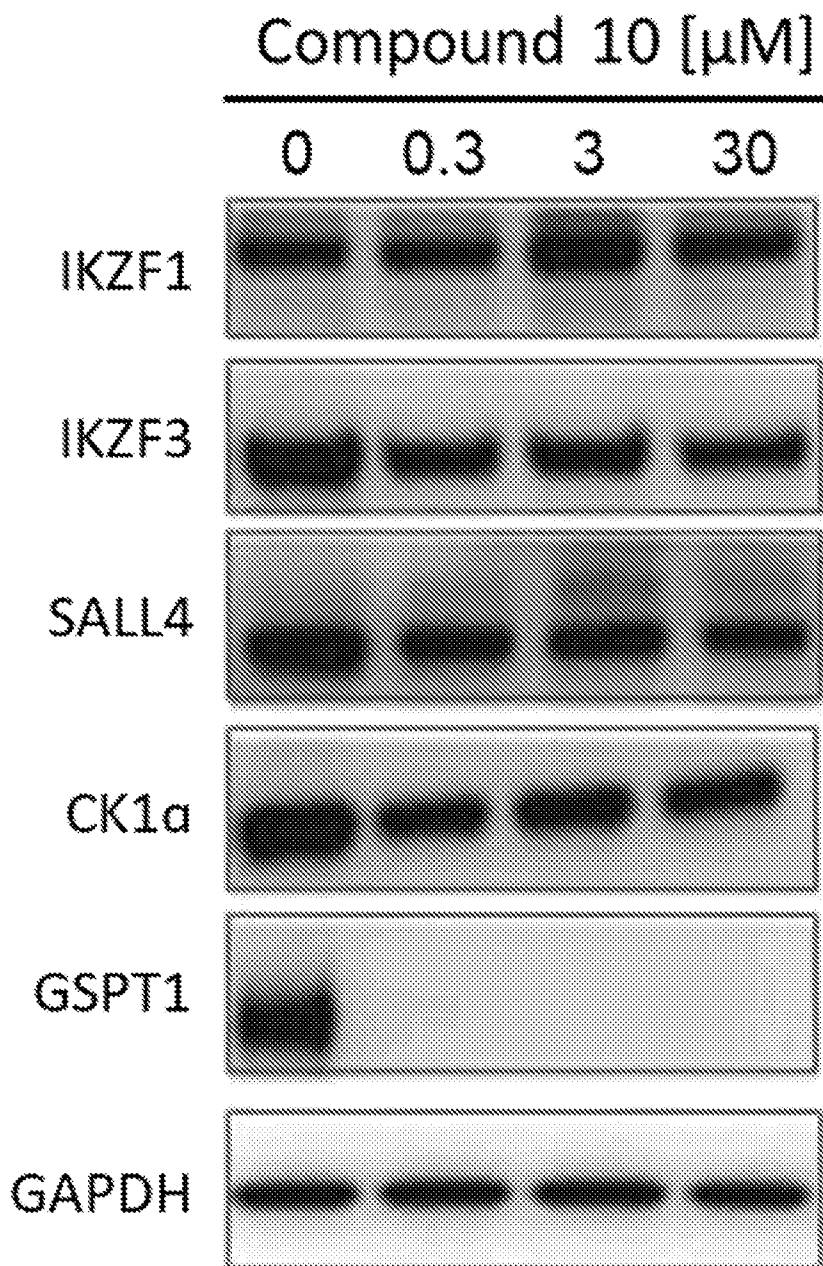
- Vehicle, PO, QD
- ▲ Compound 10, 3 mg/kg PO, QD
- ▼ Compound 10, 6 mg/kg PO, 5 ON – 9 OFF
- ◆ Cisplatin, 6 mg/kg IP, QWx3

Figure 3D



- O Vehicle, PO, QD
- ▲ Compound 10, 3 mg/kg PO, QD
- ▼ Compound 10, 6 mg/kg PO, 5 ON – 9 OFF
- ◆ Cisplatin, 6 mg/kg IP, QWx3

Figure 1A



(I)