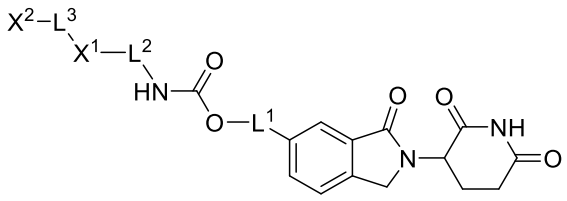
Summary of disclosure

In an aspect of the present disclosure, there is provided a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula I:



I

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);

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;

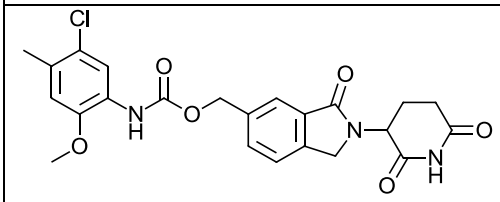
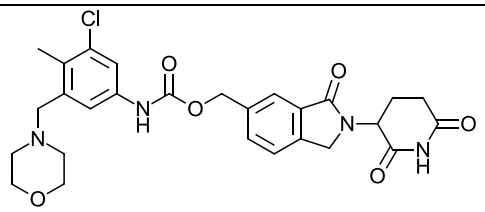
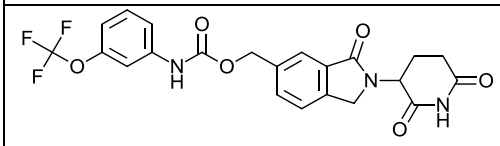
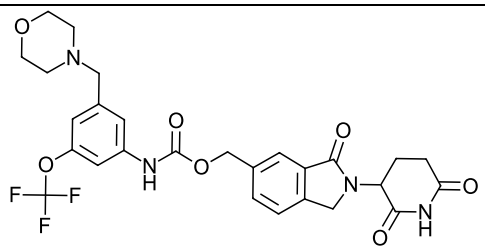
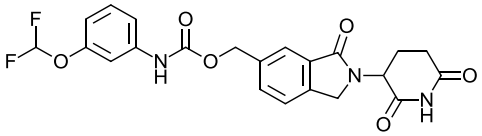
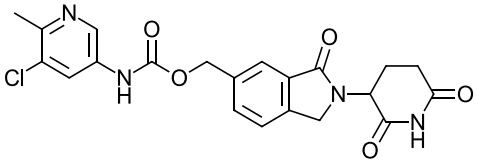
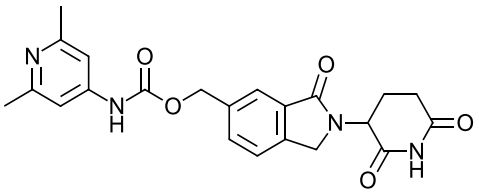
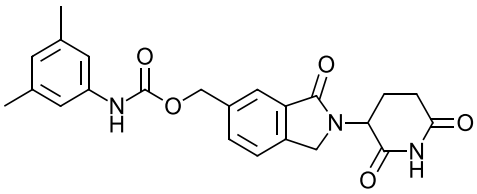
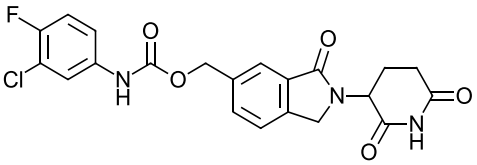
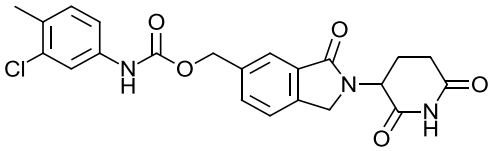
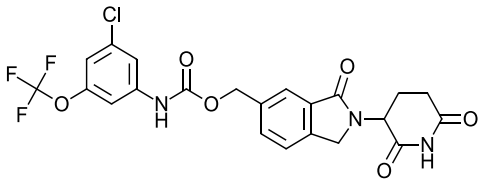
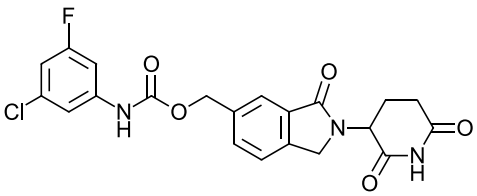
X^2 is H, C_{3-6} cycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, -C_{1-4} alkoxy, NH_2, NMe_2, halogen, CF_3, CHF_2, $CMeF_2$, -O-$(CH_2)_2$-OMe, OCF_3, $OCHF_2$, and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

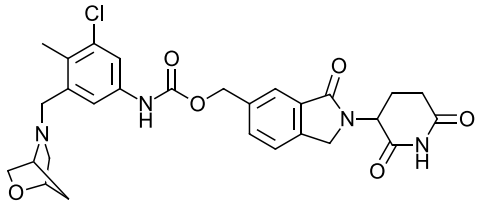
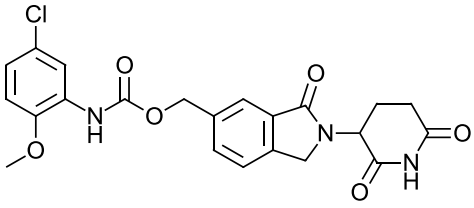
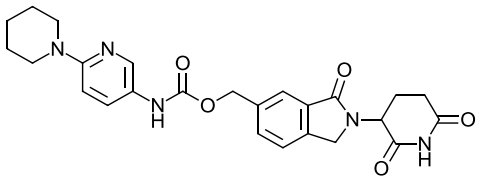
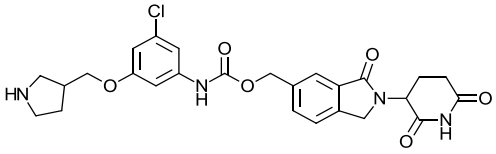
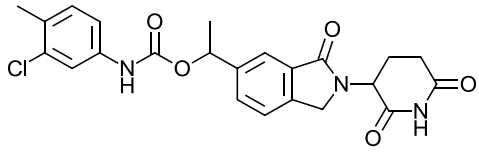
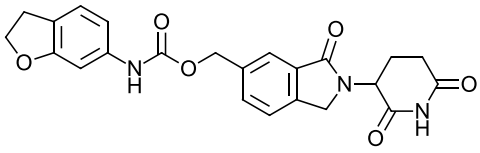
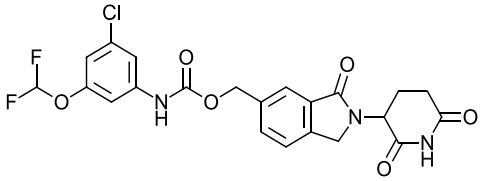
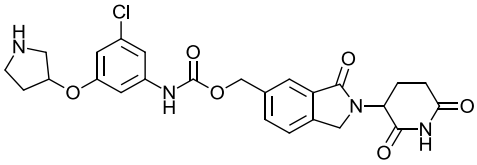
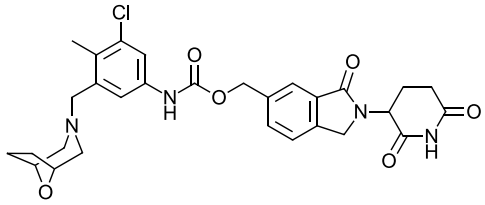
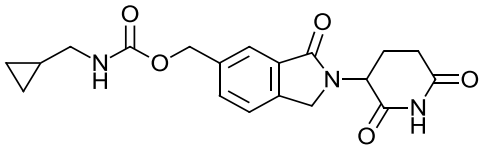
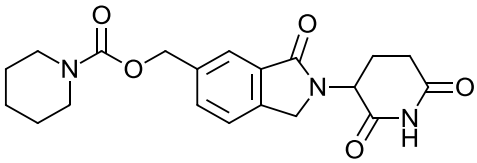
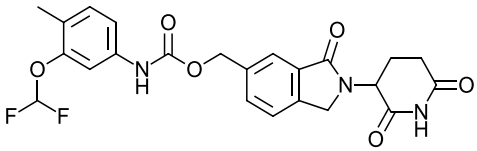
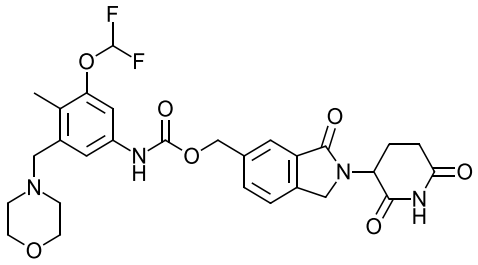
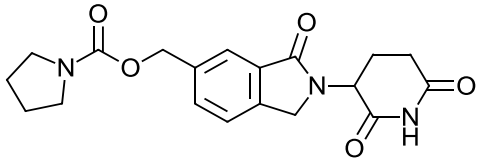
L^1 is a covalent bond, linear or branched C_{1-6} alkyl;

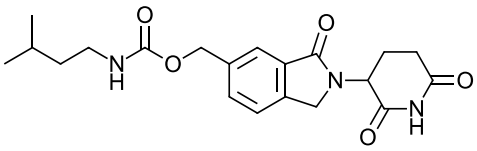
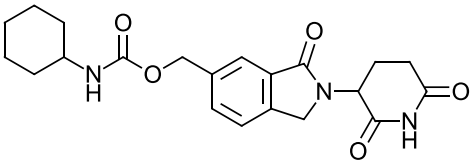
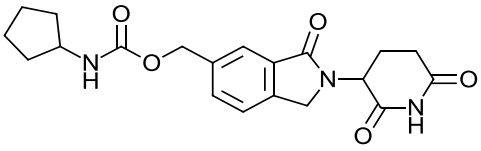
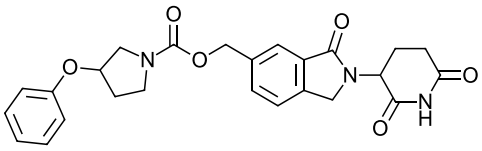
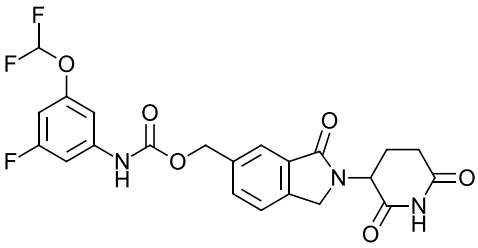
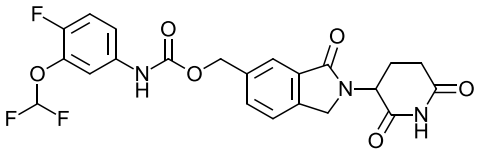
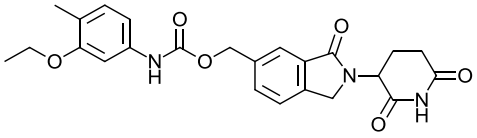
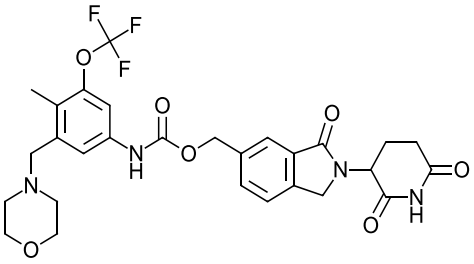
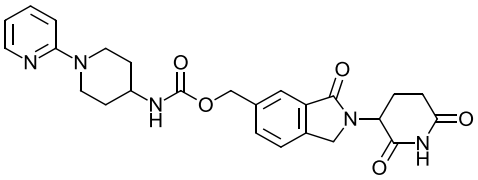
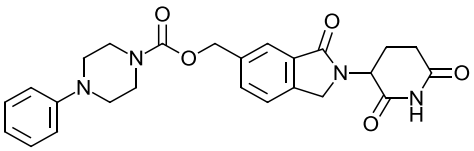
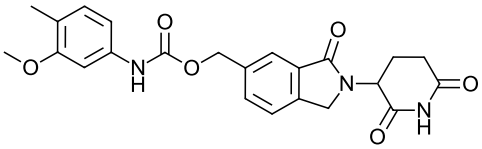
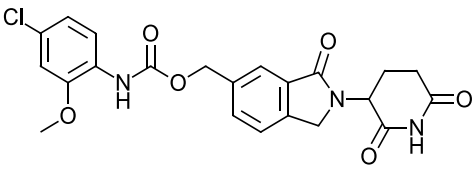
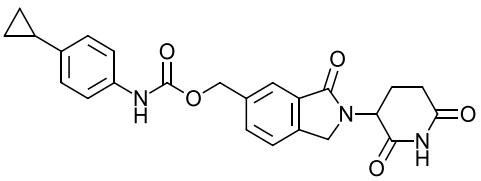
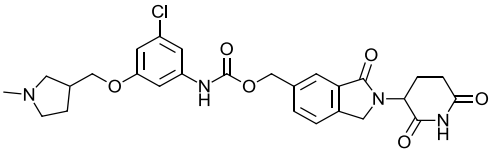
L^2 is a covalent bond, linear or branched C_{1-6} alkyl; and

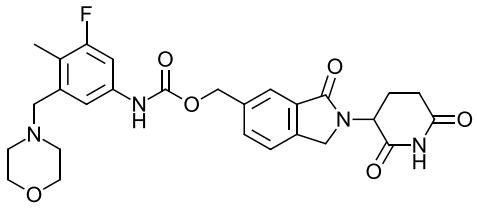
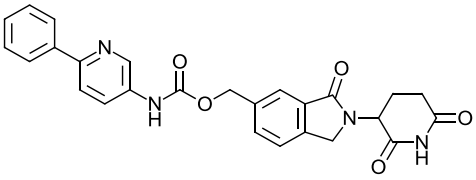
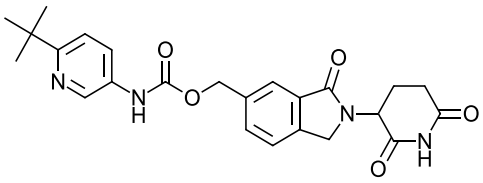
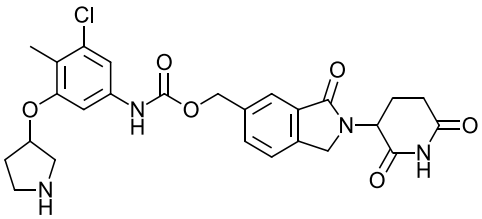
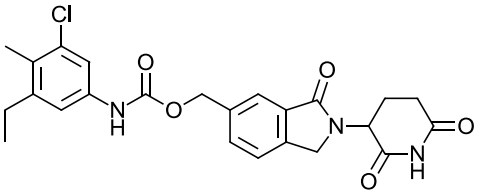
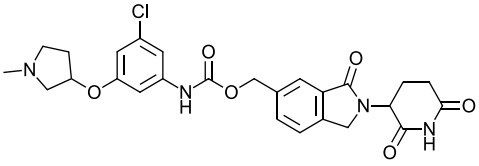
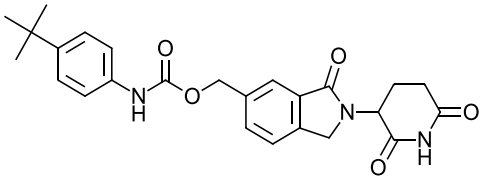
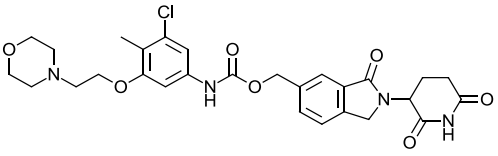
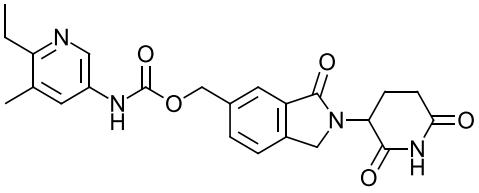
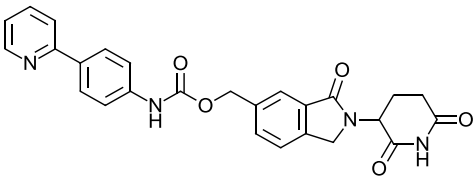
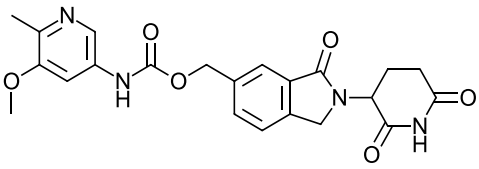
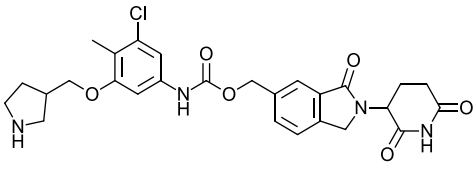
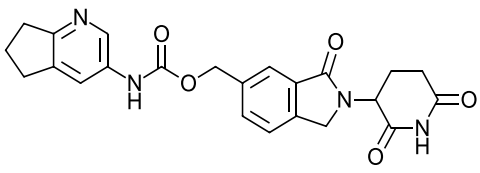
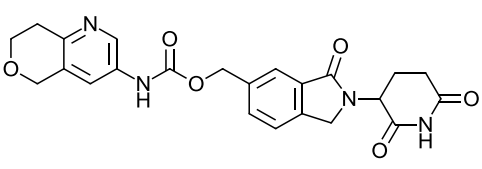
L^3 is a covalent bond, linear or branched C_{1-6} alkyl, -O-, or -C_{1-4} alkoxy, wherein linear or branched C_{1-6} alkyl is unsubstituted or substituted with one or more of halogen.

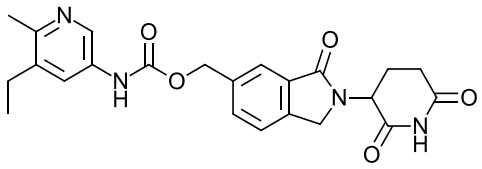
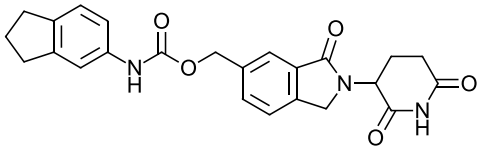
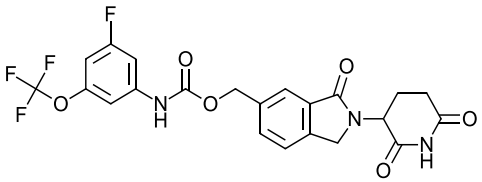
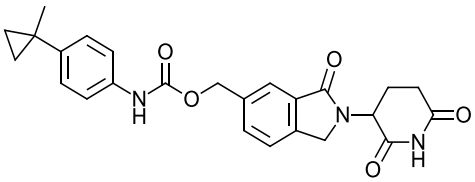
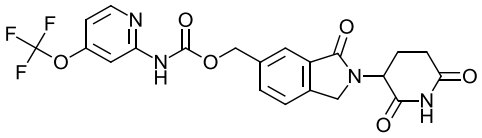
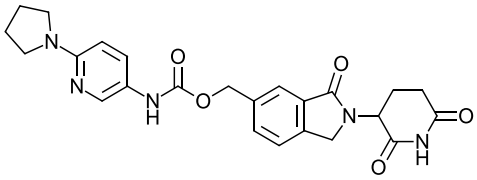
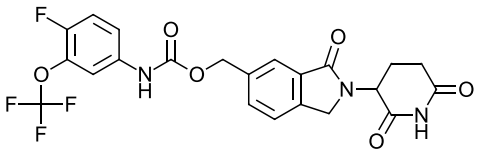
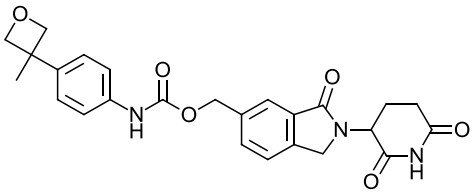
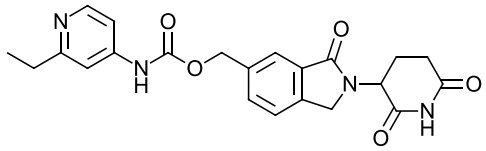
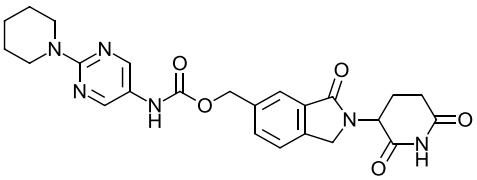
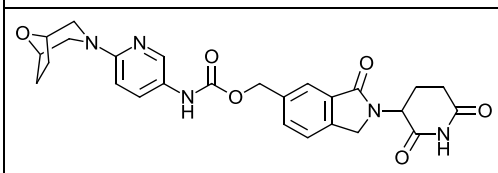
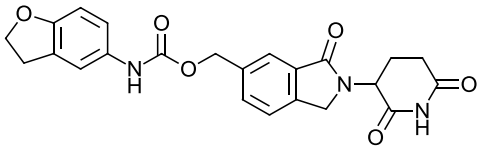
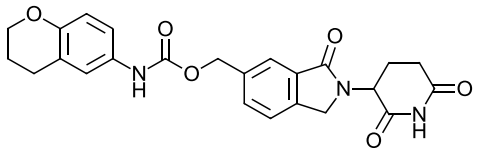
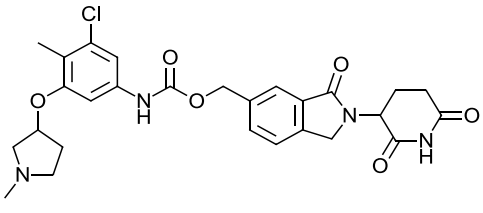
In another aspect of the present disclosure, there is provided a compound selected from the group consisting of:

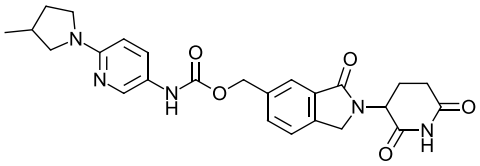
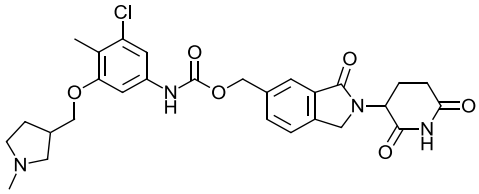
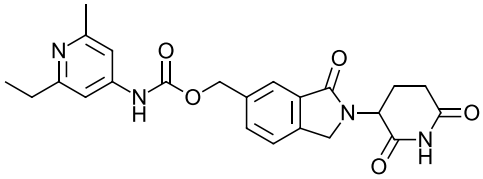
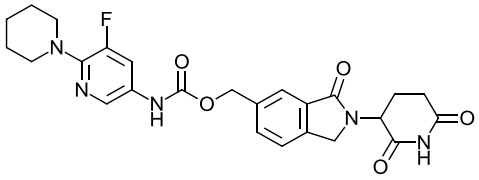
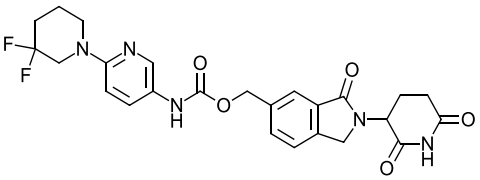
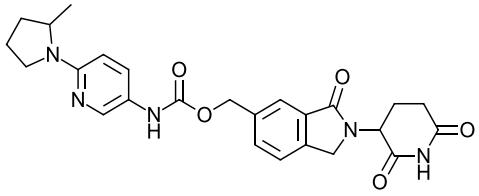
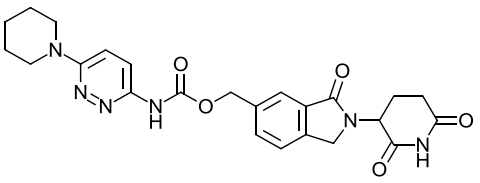
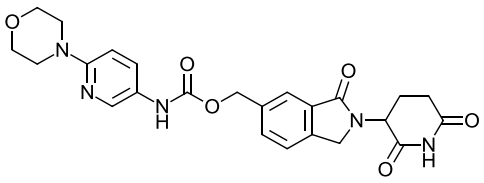
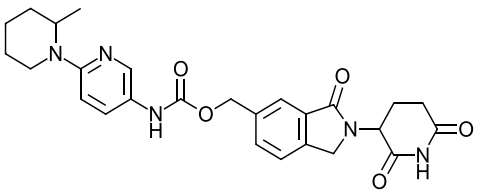
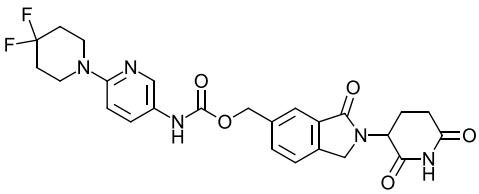
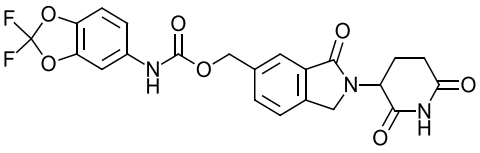
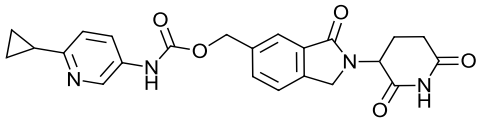
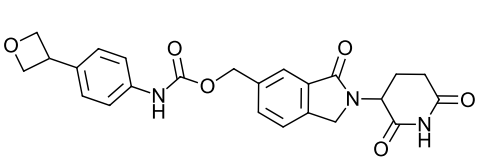
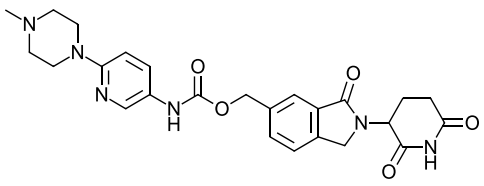
Compound	No.	Compound	No.
	1		2
	3		4
	5		6
	7		8
	9		10
	11		12

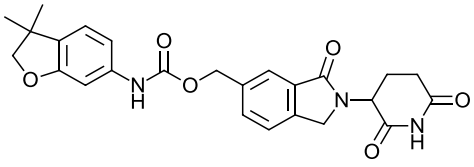
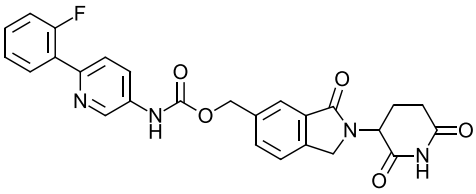
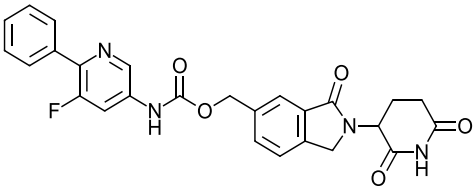
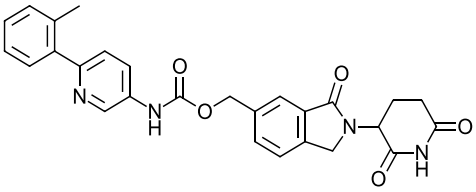
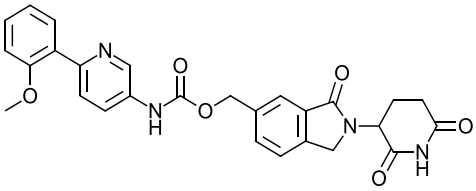
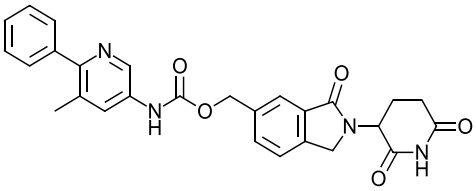
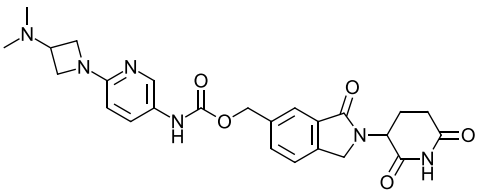
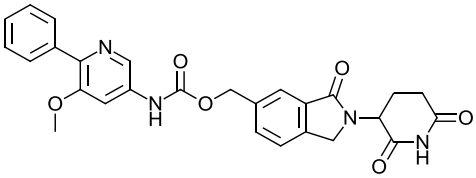
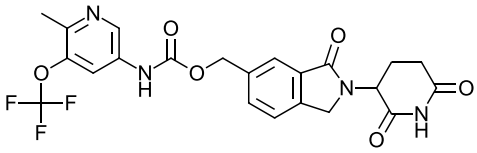
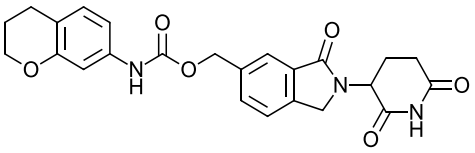
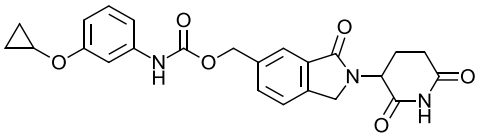
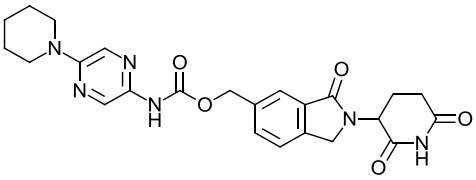
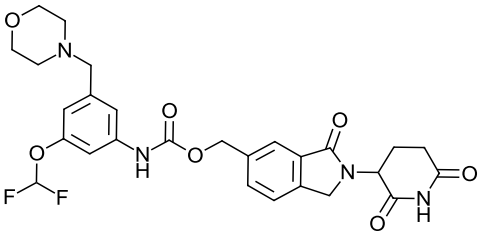
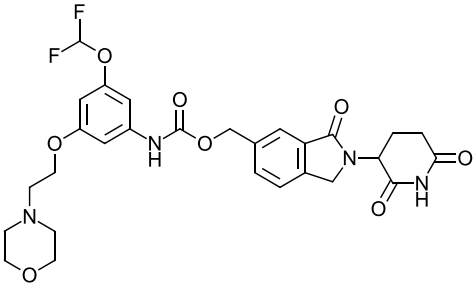
	**13**		**14**
	**15**		**16**
	**17**		**18**
	**19**		**20**
	**21**		**22**
	**23**		**24**
	**25**		**26**

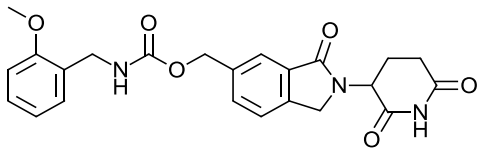
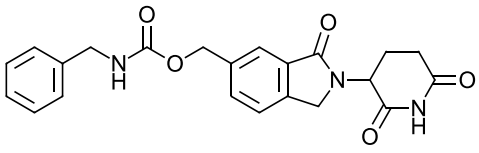
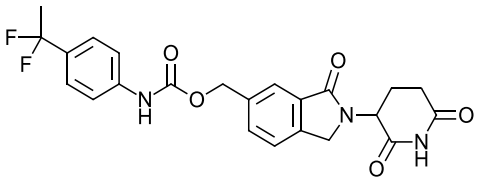
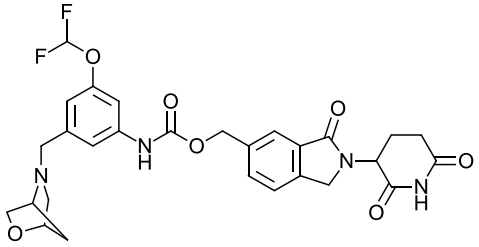
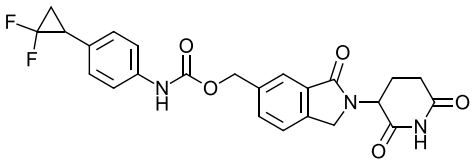
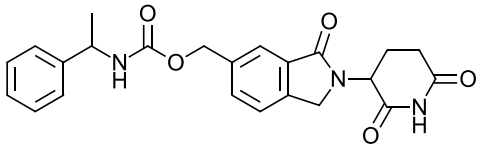
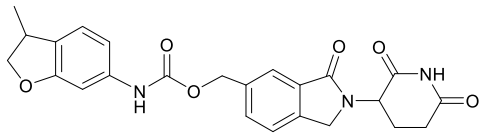
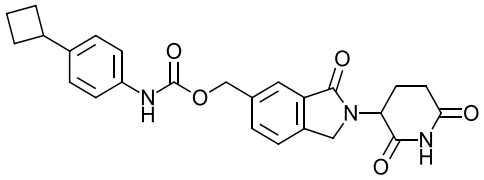
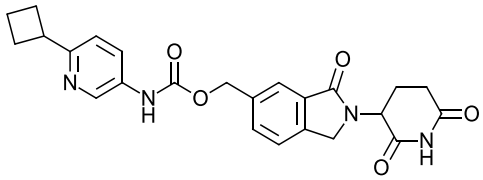
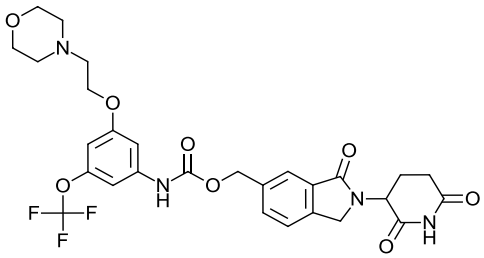
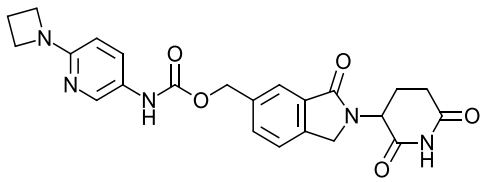
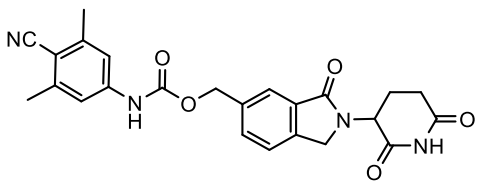
	**27**		**28**
	**29**		**30**
	**31**		**32**
	**33**		**34**
	**35**		**36**
	**37**		**38**
	**39**		**40**

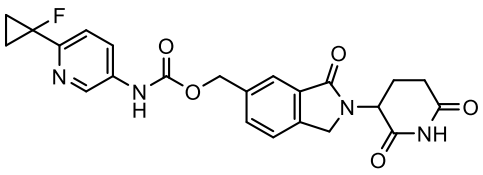
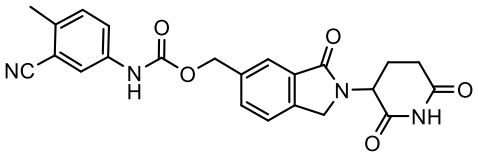
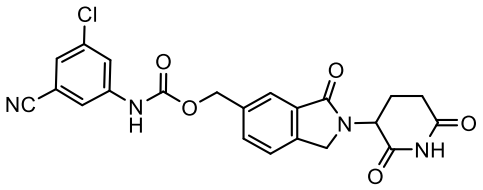
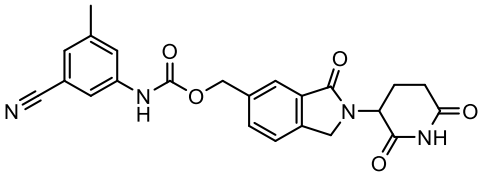
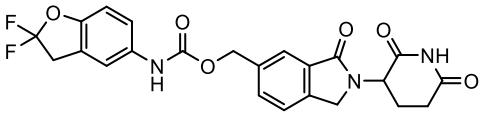
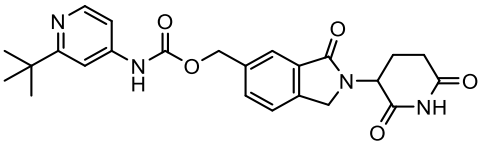
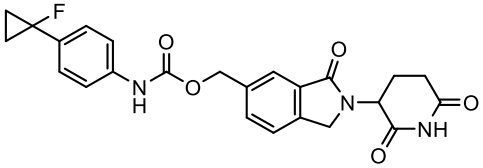
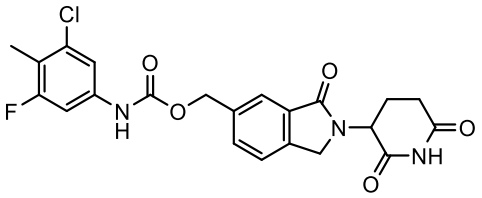
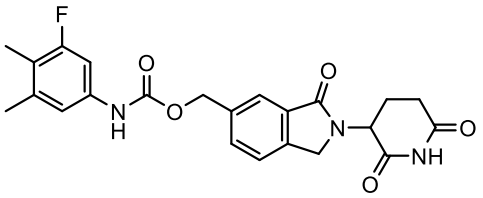
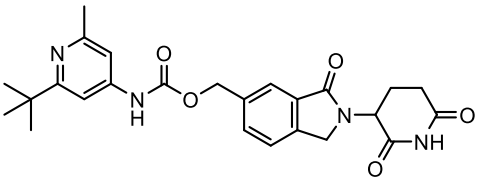
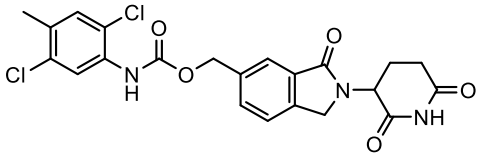
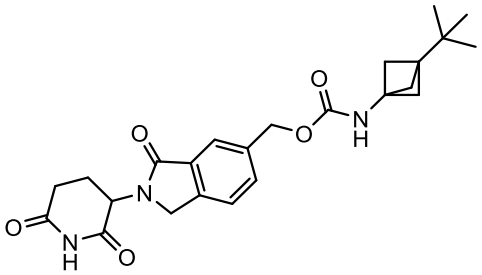
	**41**		**42**
	**43**		**44**
	**45**		**46**
	**47**		**48**
	**49**		**50**
	**51**		**52**
	**53**		**54**

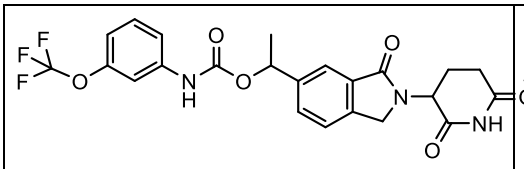
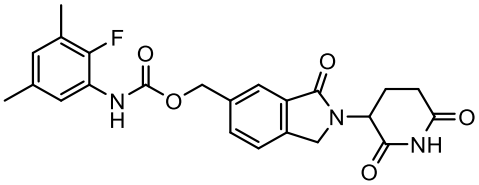
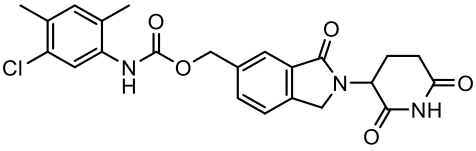
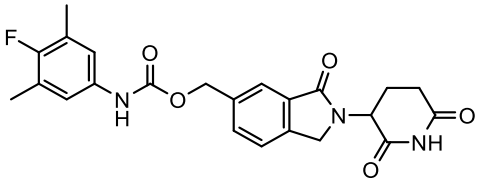
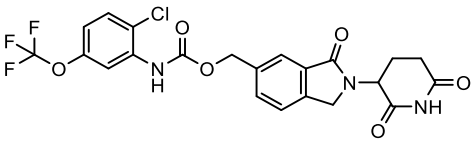
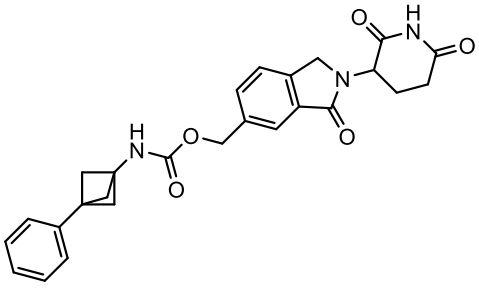
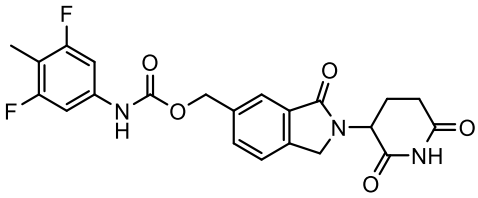
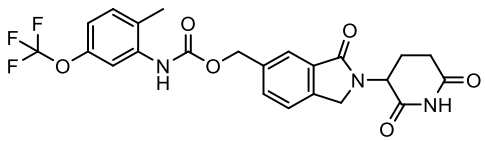
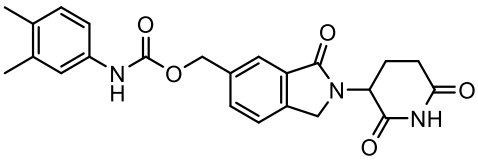
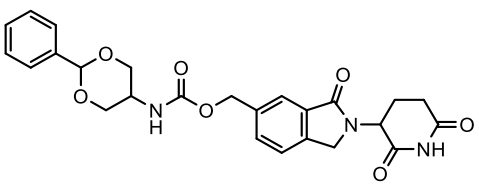
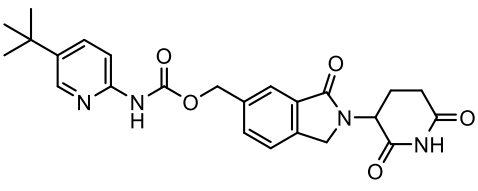
	55		56
	57		58
	59		60
	61		62
	63		64
	65		66
	67		68

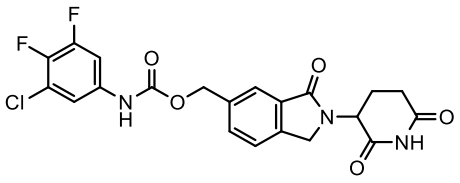
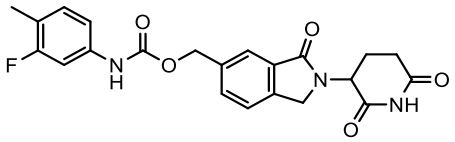
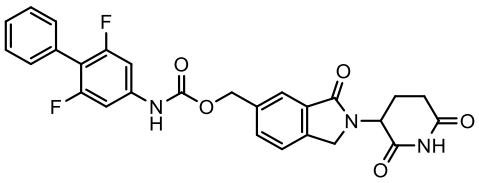
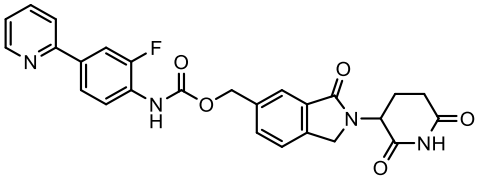
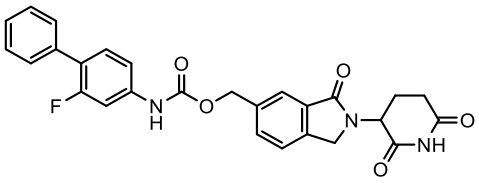
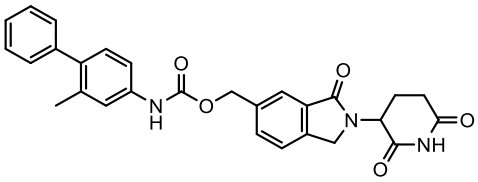
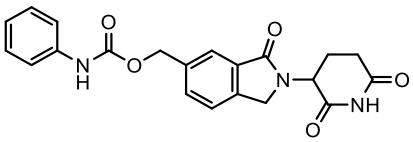
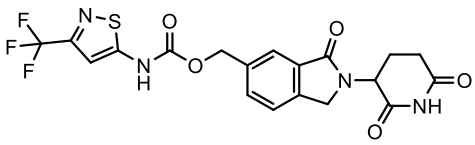
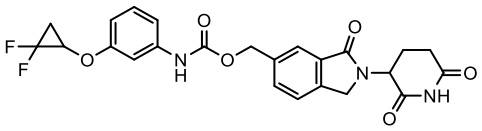
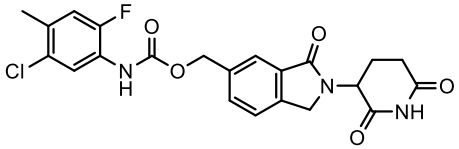
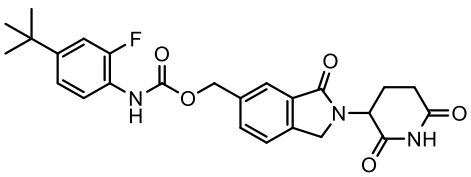
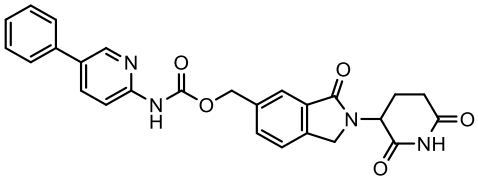
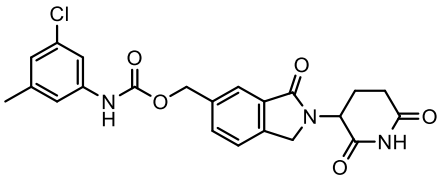
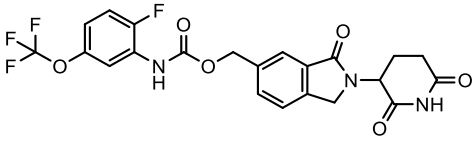
	**69**		**70**
	**71**		**72**
	**73**		**74**
	**75**		**76**
	**77**		**78**
	**79**		**80**
	**81**		**82**

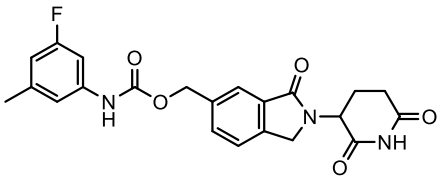
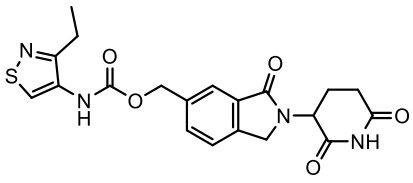
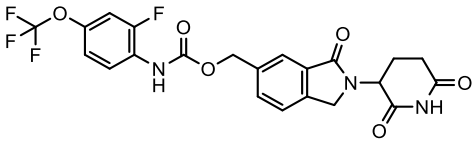
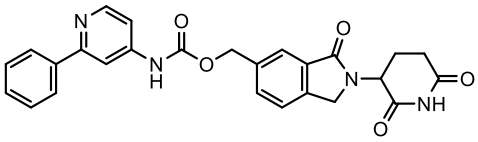
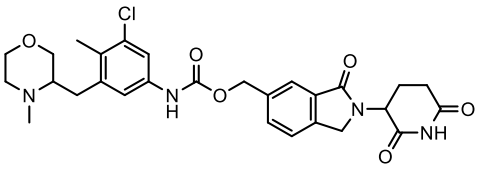
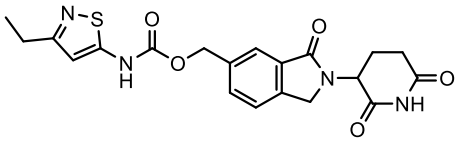
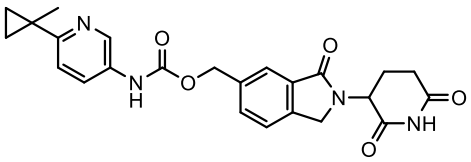
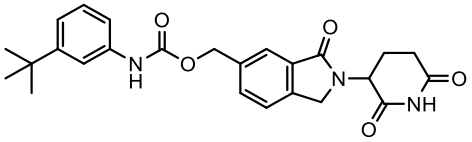
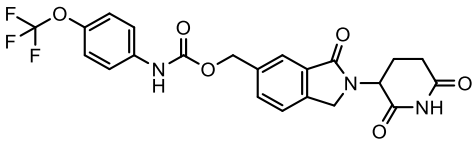
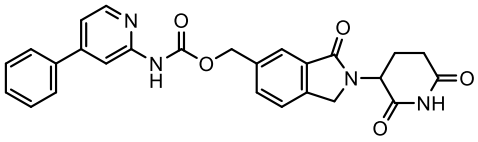
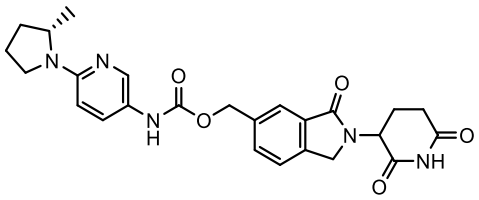
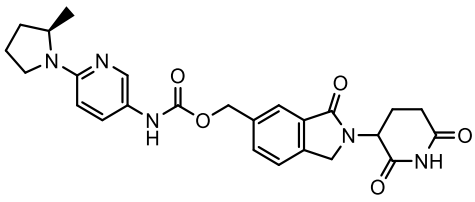
	**83**		**84**
	**85**		**86**
	**87**		**88**
	**89**		**90**
	**91**		**92**
	**93**		**94**
	**95**		**96**

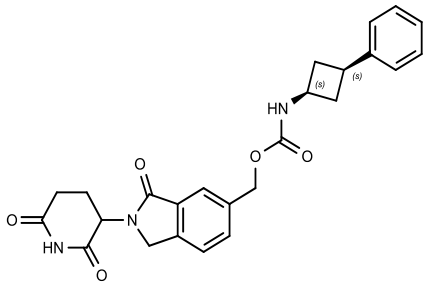
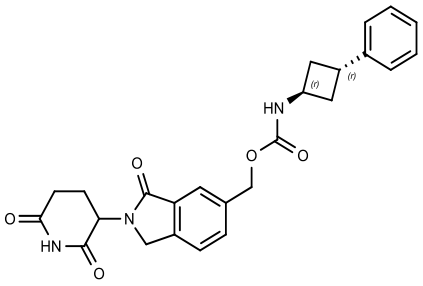
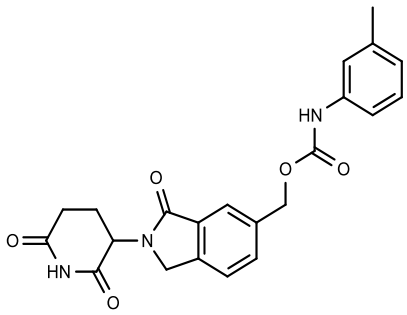
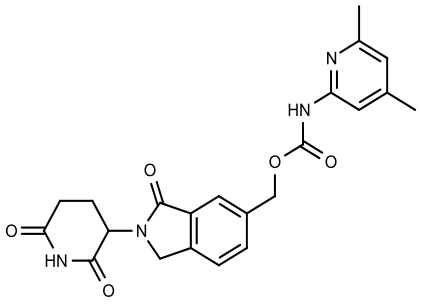
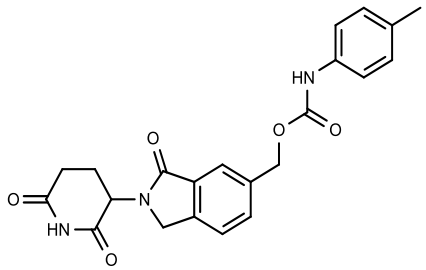
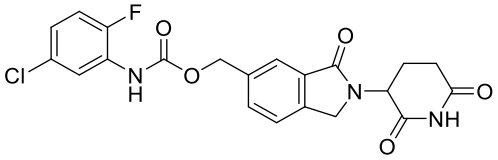
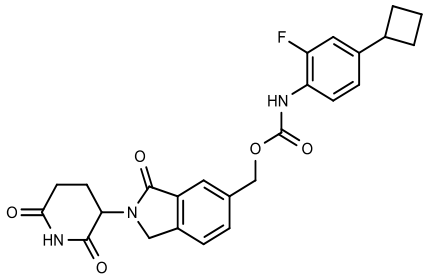
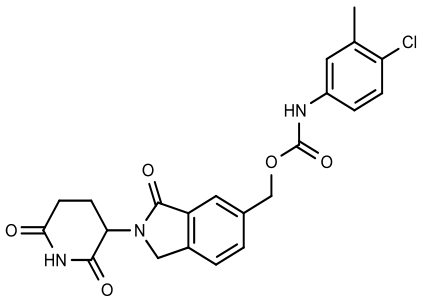
	**97**		**98**
	**99**		**100**
	**101**		**102**
	**103**		**104**
	**105**		**106**
	**107**		**108**

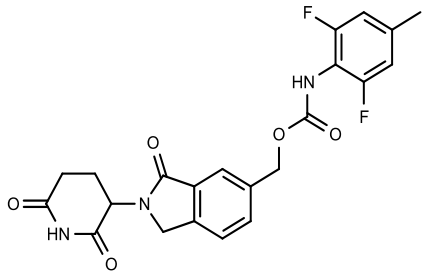
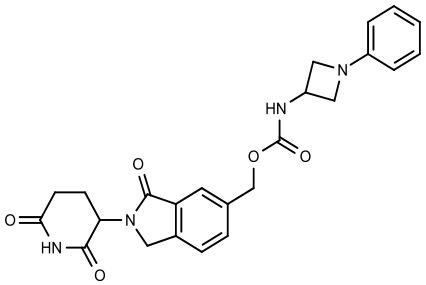
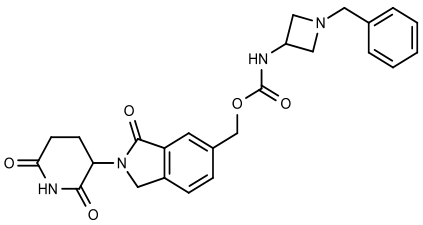
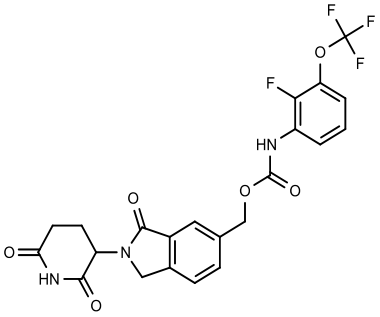
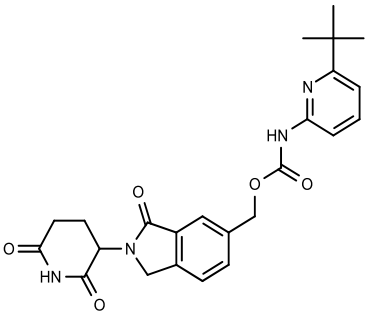
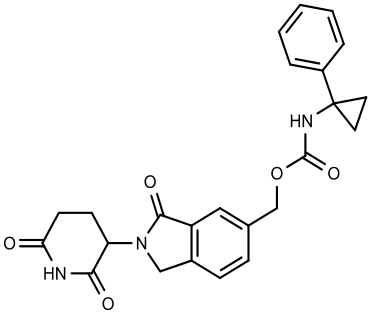
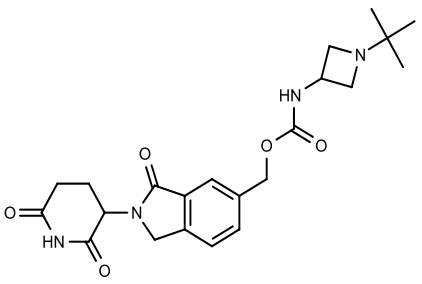
	**109**		**110**
	**111**		**112**
	**113**		**114**
	**115**		**116**
	**117**		**118**
	**119**		**120**

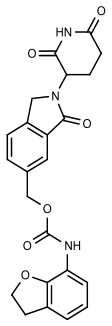
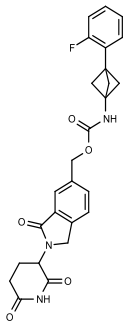
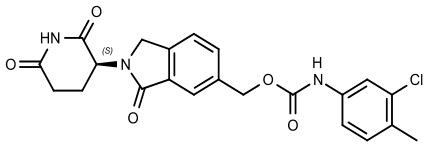
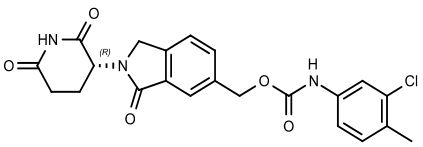
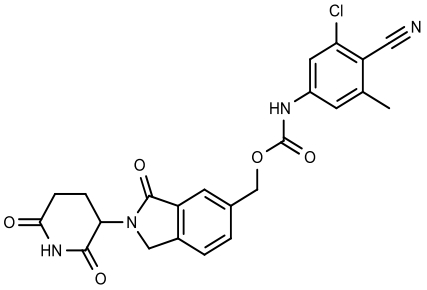
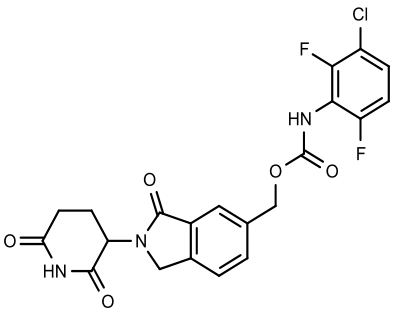
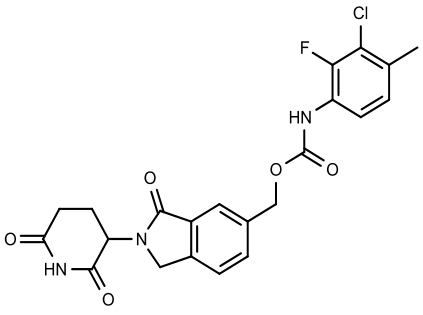
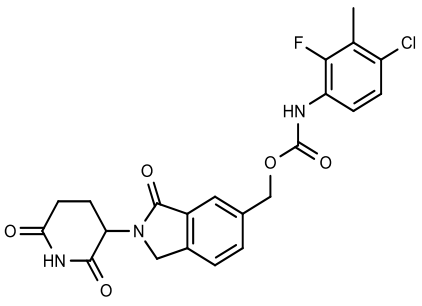
	121		
	122		123
	124		125
	126		127
	128		129
	130		131

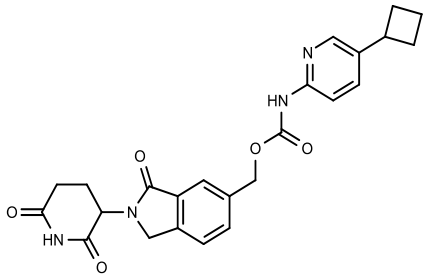
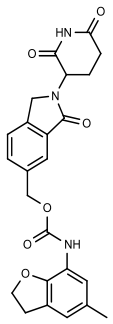
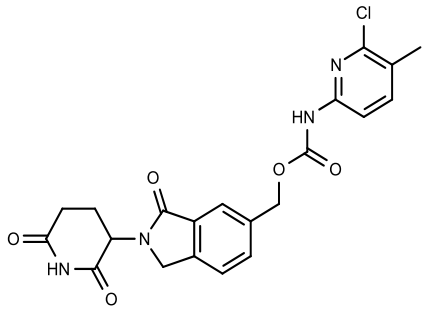
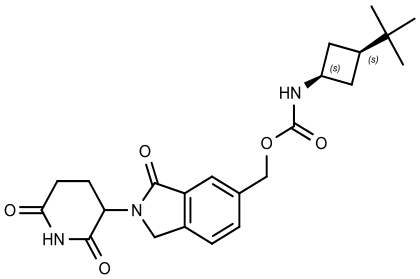
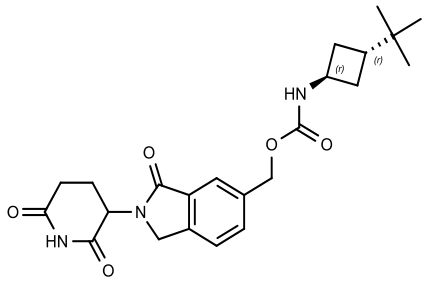
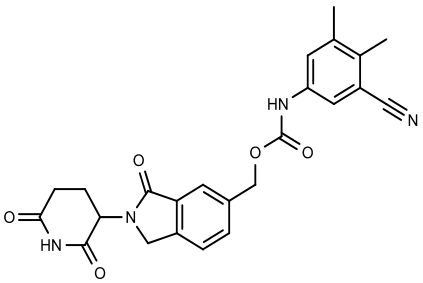
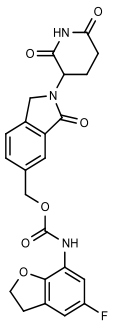
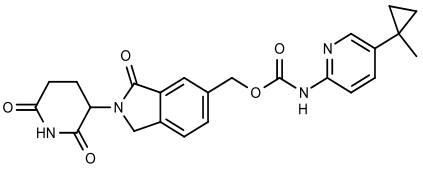
	**132**		**133**
	**134**		**135**
	**136**		**137**
	**138**		**139**
	**140**		**141**
	**142**		**143**
	**144**		**145**

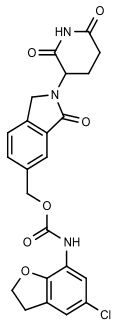
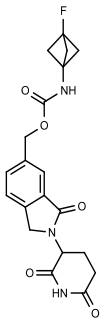
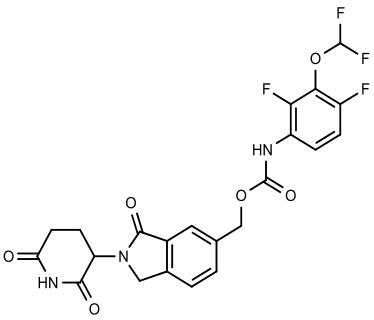
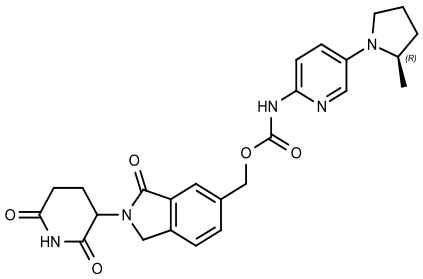
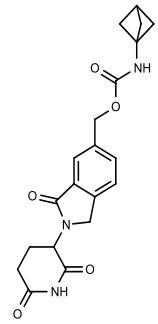
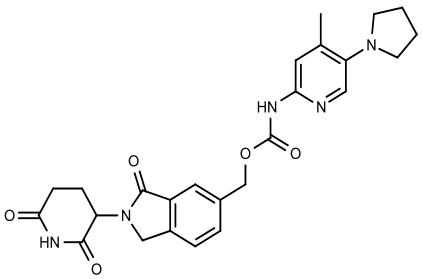
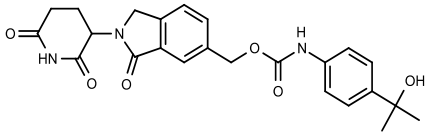
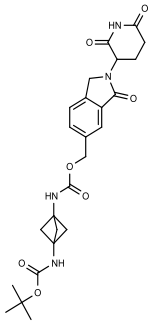
	**146**		**147**
	**148**		**149**
	**150**		**151**
	**152**		**153**
	**154**		**155**
	**156**		**157**

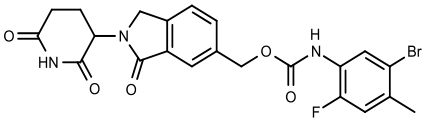
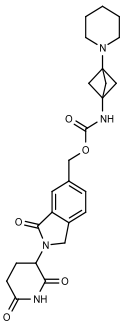
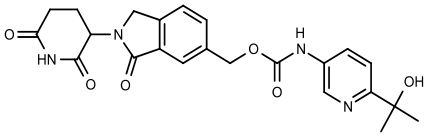
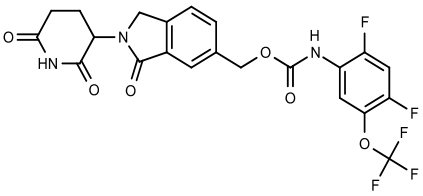
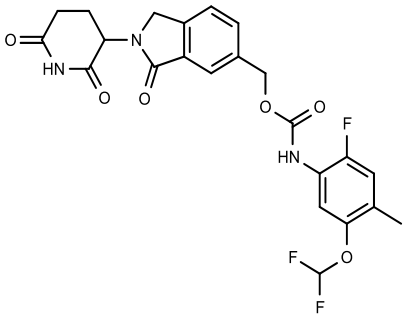
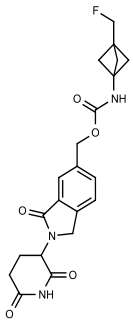
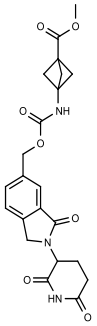
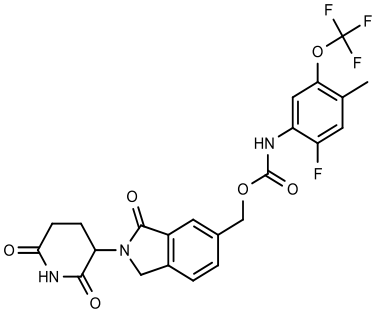
	158		159
	160		161
	162		163
	164		165

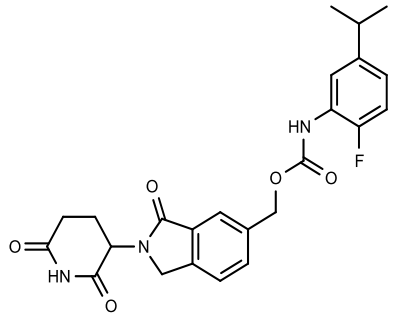
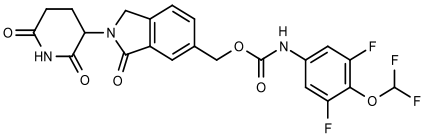
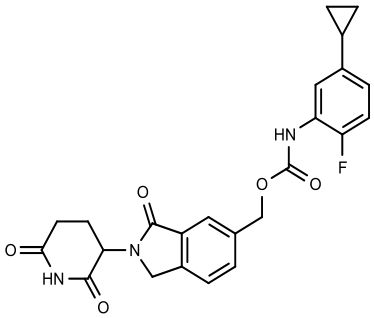
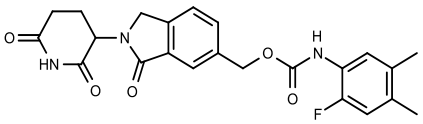
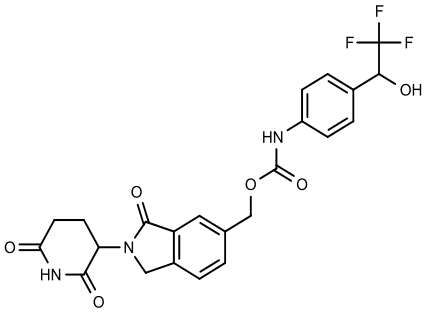
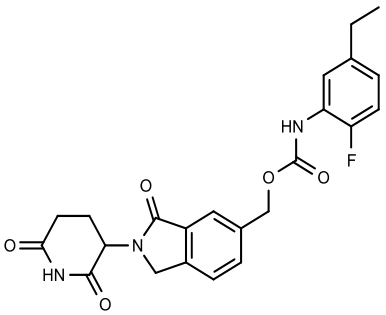
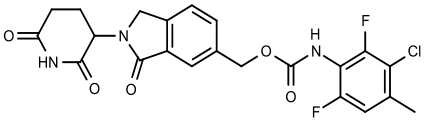
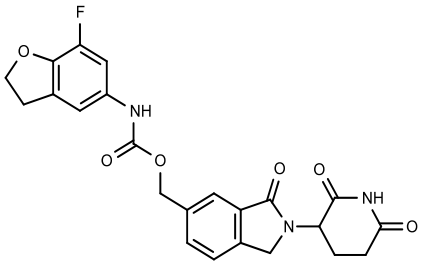
	166		167
			168
	169		170
	171		172

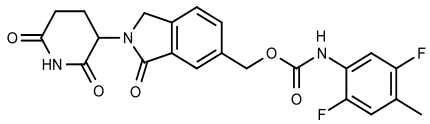
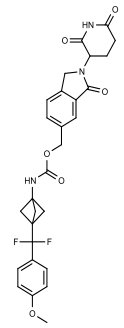
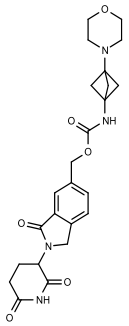
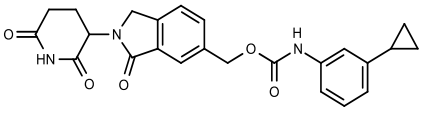
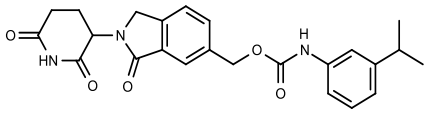
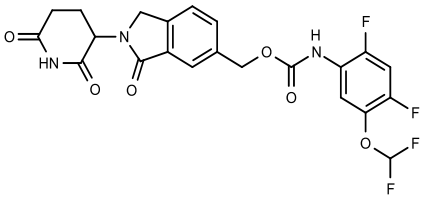
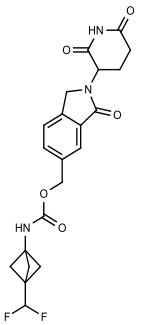
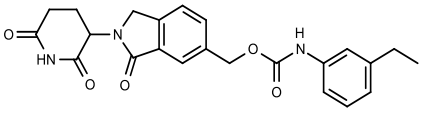
	173		174
	175		176
	177		178
	179		180

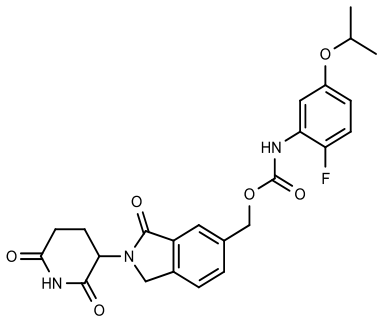
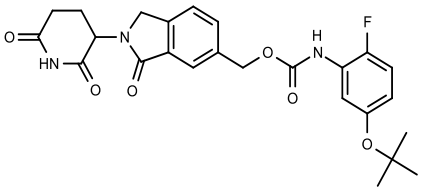
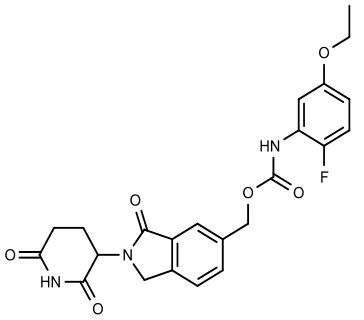
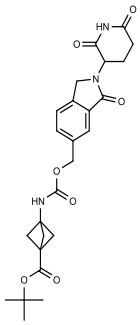
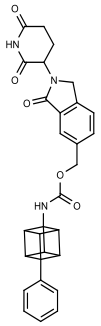
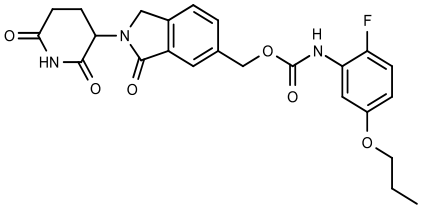
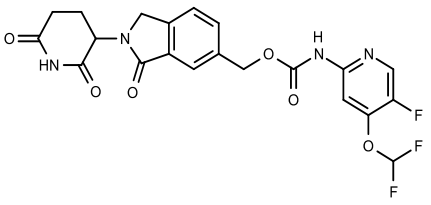
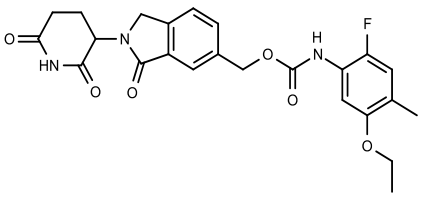
	**181**		**182**
	**183**		**184**
	**185**		**186**
	**187**		**188**

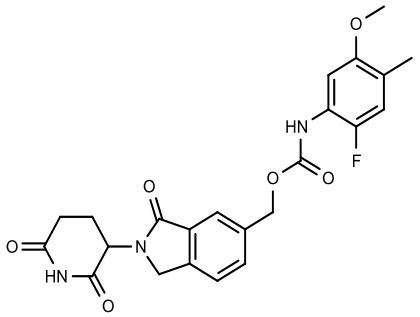
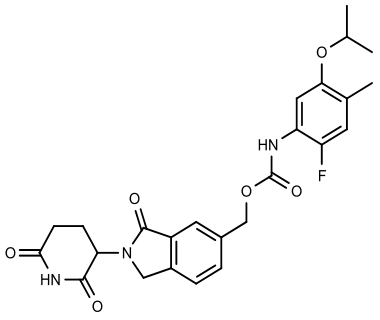
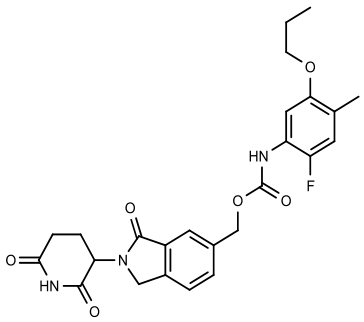
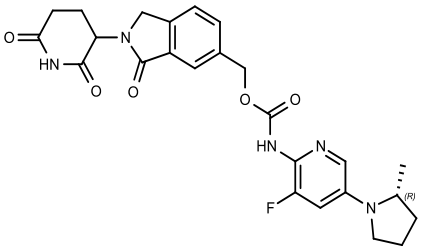
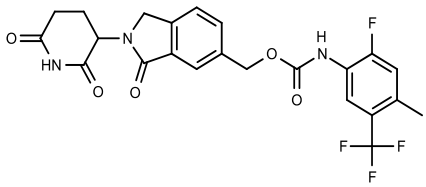
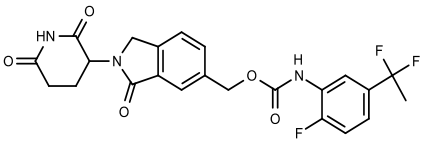
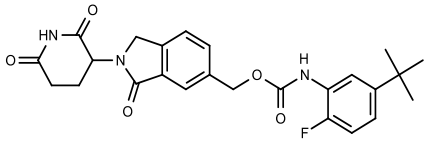
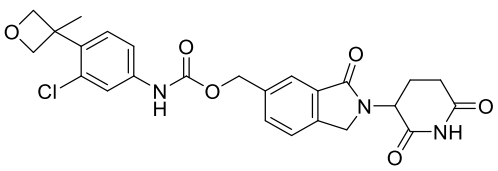
	**189**		**190**
	**191**		**192**
	**193**		**194**
	**195**		**196**

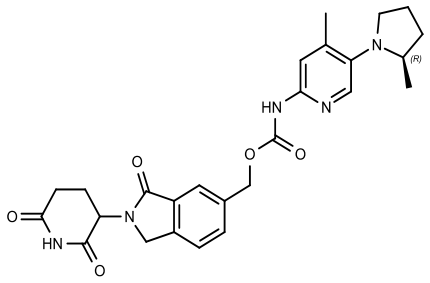
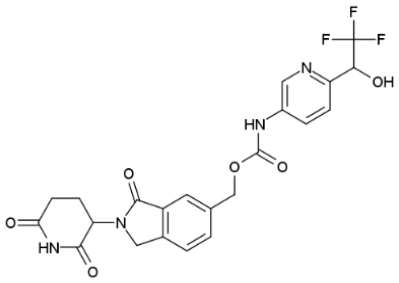
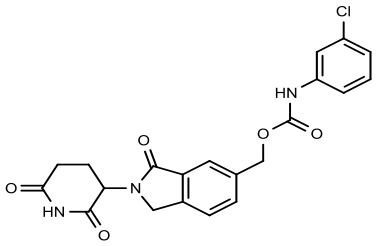
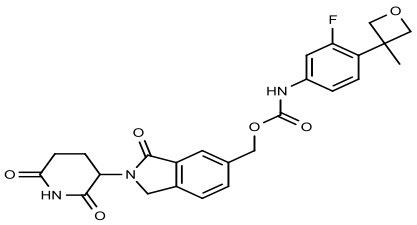
	**197**		**198**
	**199**		**200**
	**201**		**202**
	**203**		**204**

	**205**		**206**
	**207**		**208**
	**209**		**210**
	**211**		**212**

	**213**		**214**
	**215**		**216**
	**217**		**218**
	**219**		**220**

	**221**		**222**
	**223**		**224**
	**225**		**226**
	**227**		**228**

	**229**		**230**
	**231**		**232**
	**233**		**234**
	**235**		**236**

	**237**		**238**
	**239**		**240**

and pharmaceutically acceptable salts and stereoisomers thereof.

In a further aspect of the present disclosure, there is provided a composition comprising the compound as disclosed herein or pharmaceutically acceptable salts or stereoisomers thereof.

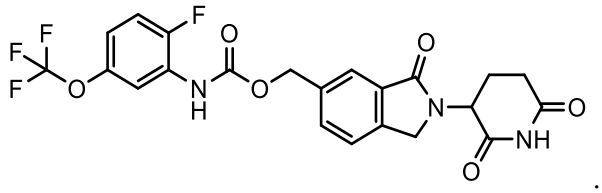
In another aspect of the present disclosure, there is provided a use of the compound as disclosed herein in the manufacture of a medicament for treating cancer, in particular lung cancer, breast cancer and neuroendocrine cancer in a subject.

In a further aspect of the present disclosure, there is provided a use of the compound as disclosed herein in the manufacture of a medicament for treating a Myc-driven cancer in a subject in need thereof.

In another aspect of the present disclosure, there is provided a use of the compound as disclosed herein in the manufacture of a medicament for degrading GSPT1 in a subject suffering from cancer.

In a further aspect of the present disclosure, there is provided a use of the compound as disclosed herein in the manufacture of a medicament for reducing the level of GSPT1 in a subject suffering from cancer.

In another aspect of the present disclosure, there is provided a compound represented by:



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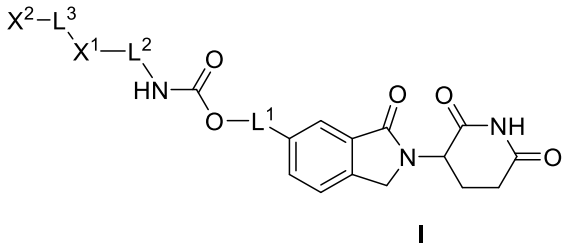
In a further aspect of the present disclosure, there is provided a compound as disclosed herein for use in therapy.

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.

In some examples, 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, 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 example directed towards a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula I:



I

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);

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 examples,

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;

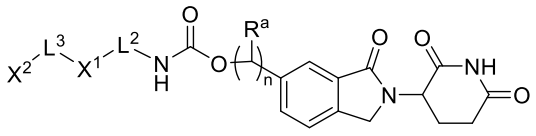
L^2 is a covalent bond, linear or branched C_{1-6} alkyl; and

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

In some examples of a compound of formula I, 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 4-8 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 examples of a compound of formula I, 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.

In some examples, the present disclosure is directed towards a compound 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}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;

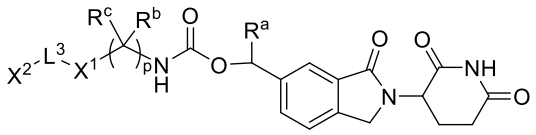
X^2 is H, C$_{3-6}$ cycloalkyl, C$_{6-10}$ aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C$_{1-6}$ alkyl, -C$_{1-4}$ alkoxy, NH_2, NMe_2, halogen, CF_3, CHF_2, $CMeF_2$, -O-$(CH_2)_2$-OMe, OCF_3, $OCHF_2$,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

L^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;

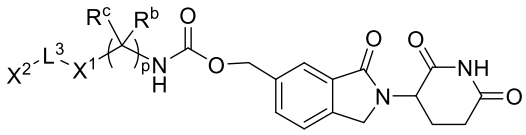
R^a is H or linear or branched C$_{1-4}$ alkyl, such as methyl or ethyl; and n is 1 or 2.

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

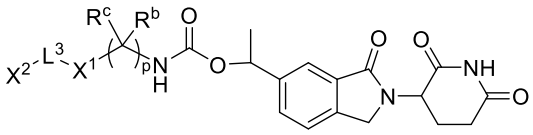
In some examples, the present disclosure is directed towards a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula III, such as IVa or IVb:



III



IVa



IVb

wherein

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$_{1-6}$

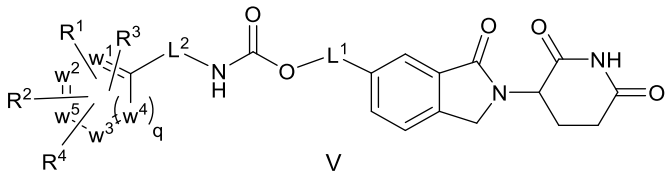
alkyl, CF_3, CHF_2, $CMeF_2$, -O-$(CH_2)_2$-OMe, OCF_3, $OCHF_2$, C_{1-6} alkylamino, -CN, -N(H)C(O)-C_{1-6}alkyl, -OC(O)-C_{1-6}alkyl, -C(O)O-C_{1-6}alkyl, -COOH, -C_{1-6}alkylC(O)OH, -C_{1-6}alkylC(O)O-C_{1-6}alkyl, NH_2, C_{1-4} alkylhydroxy, and C_{1-4} alkoxy;

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;

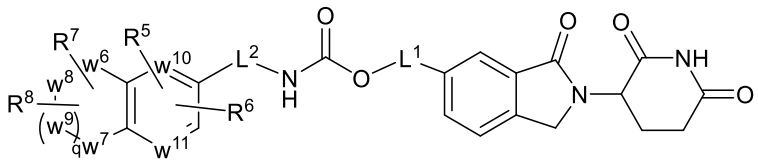
L^3 is a covalent bond, linear or branched C_{1-6} alkyl, -O-, -C_{1-4} alkoxy;

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

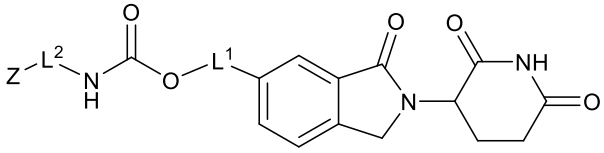
In some examples, a compound of formula I is a compound or pharmaceutically acceptable salts or stereoisomers thereof of formula V, VI or VII:



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; and q is 0 or 1;

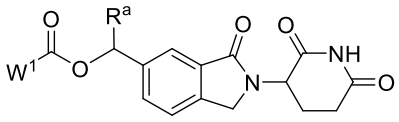
L^1 is a covalent bond, linear or branched C_{1-6} alkyl; L^2 is a covalent bond, linear or branched C_{1-6} alkyl;

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}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;

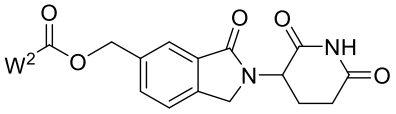
R^5, R^6, R^7 R^8 are independently of each other selected from H, linear or branched C_{1-4} alkyl, such as methyl, and halogen, such as F or Cl, e.g. F;

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 or 1.

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

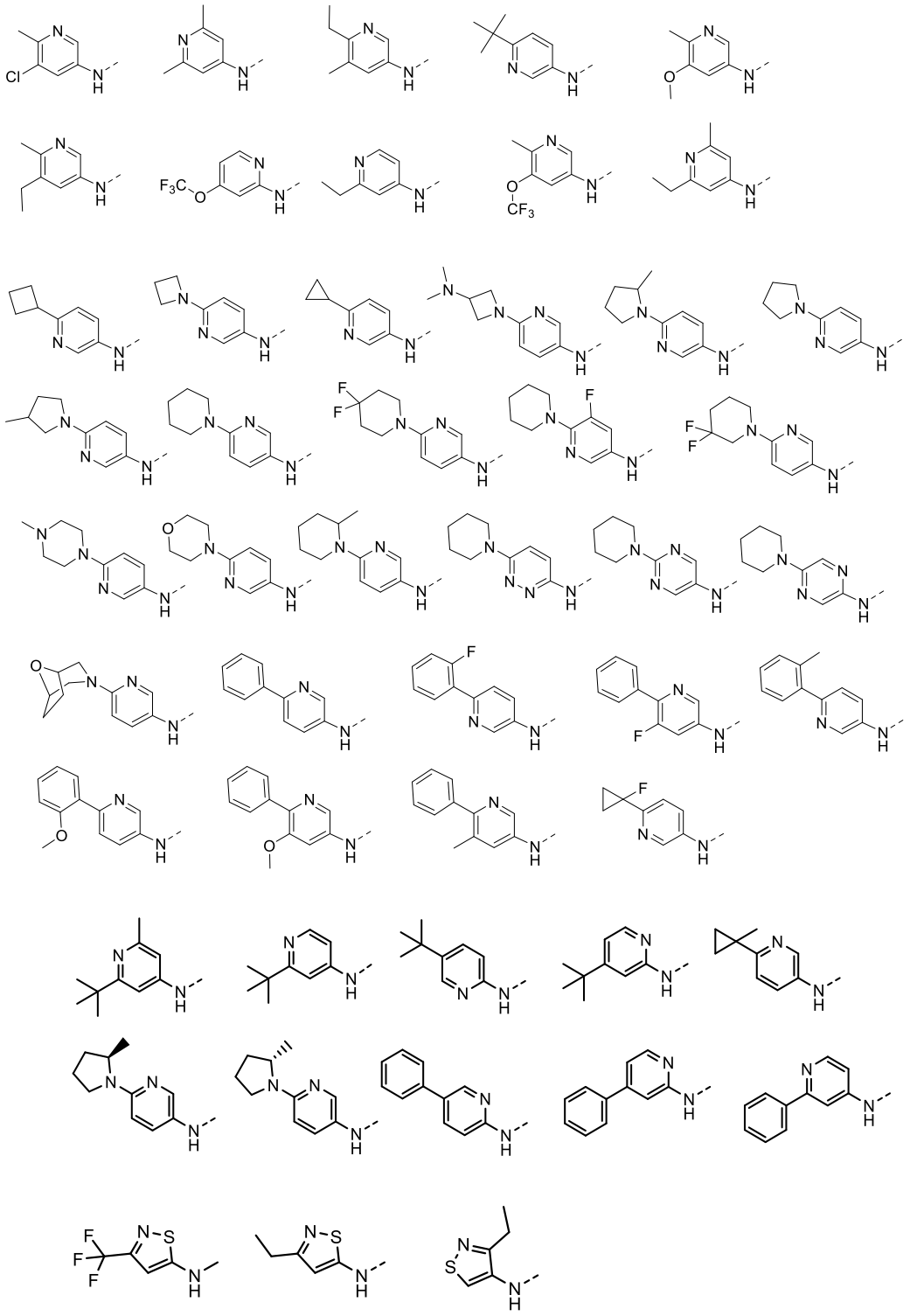


VIII



VIIIa

wherein R^a is H or methyl and W^1 and W^2 are selected from



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

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

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

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

In a fourth example, some examples 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, endrometrium, 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, 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 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 examples comprise the compound or the composition according to any of the examples described herein for use in the treatment of breast cancer.

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

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

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

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

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

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

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

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

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

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

In a sixth example, 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 examples as described herein.

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

In a seventh example, 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 eigth example, the 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 example, 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

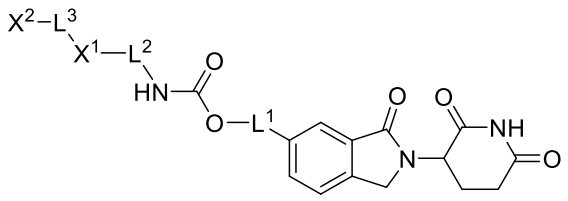
Figure 1: Figure 1A shows that cells treated with 0.3 μM compound 10 induces complete degradation of GSPT1, while no induction of degradation of IKZF1, IKZF3, SALL4, CK1alpha was observed at concentrations up to 30 μM. Figure 1B shows that based on a mass spectrometry-based proteomics analysis of a cancer cell line treated with compound 10, GSPT1 was the most statistically significant downregulated protein (x-axys represents the 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 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-axys represents μM concentration of compound 10; y-axis represents the viability in %). In both cell lines, we observed complete degradation of GSPT1, Figure 2B illustrates that compound 10 degrades GSPT1 in a concentration dependent manner (x-axys represents μM 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 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-axys represents days post treatment initiation [days]; y-axis represents tumor volume [mm^3], mean ±SEM; empty circles O: vehicle, PO, QD; filled 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).

CLAIMS

1. A compound or pharmaceutically acceptable salts or stereoisomers thereof of formula I:



I

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);

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

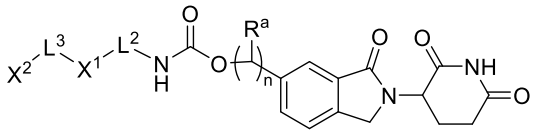
L^3 is a covalent bond, linear or branched C_{1-6} alkyl, -O-, or -C_{1-4} alkoxy, wherein linear or branched C_{1-6} alkyl is unsubstituted or substituted with one or more of halogen.

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}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^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.

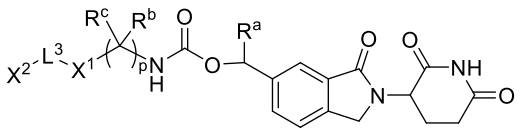
6. The compound of claim 5 or pharmaceutically acceptable salts or stereoisomers thereof, wherein n is 1 and R^a is H or methyl.

7. The compound of claim 5 or pharmaceutically acceptable salts or stereoisomers thereof, wherein p is 0.

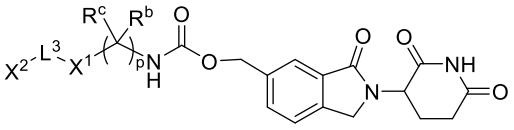
8. The compound of claim 5 or pharmaceutically acceptable salts or stereoisomers thereof, wherein p is 1 and R^b, R^c are H or wherein p is 1, R^b is methyl and R^c is H.

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-.

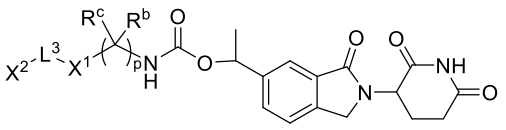
10. The compound of claim 1 or pharmaceutically acceptable salts or stereoisomers thereof, of formula III, such as IVa or IVb:



III



IVa



IVb

wherein

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

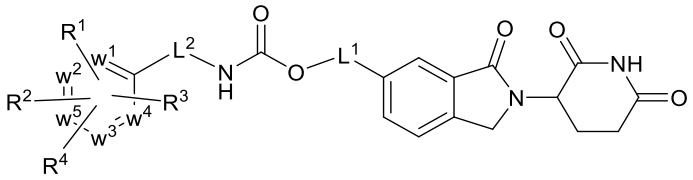
R^a, R^b, R^c are independently of each other H, linear or branched C_{1-4} alkyl, such as methyl;

p is 0 or 1.

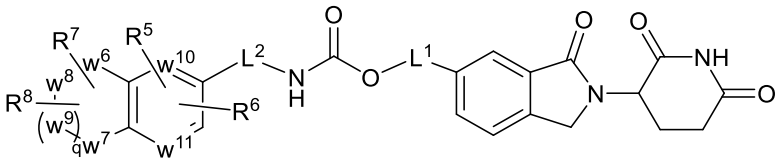
11. The compound of claim 10 or pharmaceutically acceptable salts or stereoisomers thereof, wherein p is 0.

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.

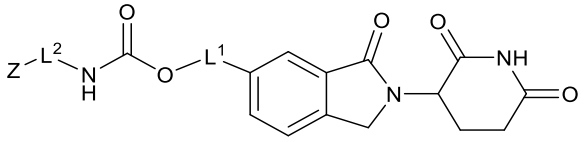
13. The compound of claim 1 or pharmaceutically acceptable salts or stereoisomers thereof, of formula V, VI or VII:



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}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-}

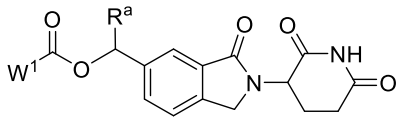
aryl, 5-10 membered heteroaryl, 4-8 membered heterocycloalkyl, wherein X^2 is unsubstituted or substituted with one or more of linear or branched C_{1-6} alkyl, -C_{1-4} alkoxy, NH_2, NMe_2, halogen, CF_3, CHF_2, $CMeF_2$, -O-$(CH_2)_2$-OMe, OCF_3, $OCHF_2$, and -C_{1-4} alkylhydroxy;

R^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;

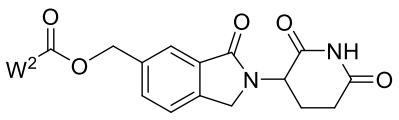
Z is linear or branched -C_{1-6} alkyl, -C_{3-6} cycloalkyl, 4-8 membered heterocycloalkyl, wherein Z is unsubstituted or substituted with C_{1-4} alkyl, C_6 aryl, C_6 aryloxy, 6 membered heteroaryl or CF_3; or Z together with the N atom of the carbamate forms a 4-8 membered heterocycloalkyl, which is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

q is 0, 1.

14. The compound of claim 1 or pharmaceutically acceptable salts or stereoisomers thereof, of formula VIII or VIIIa

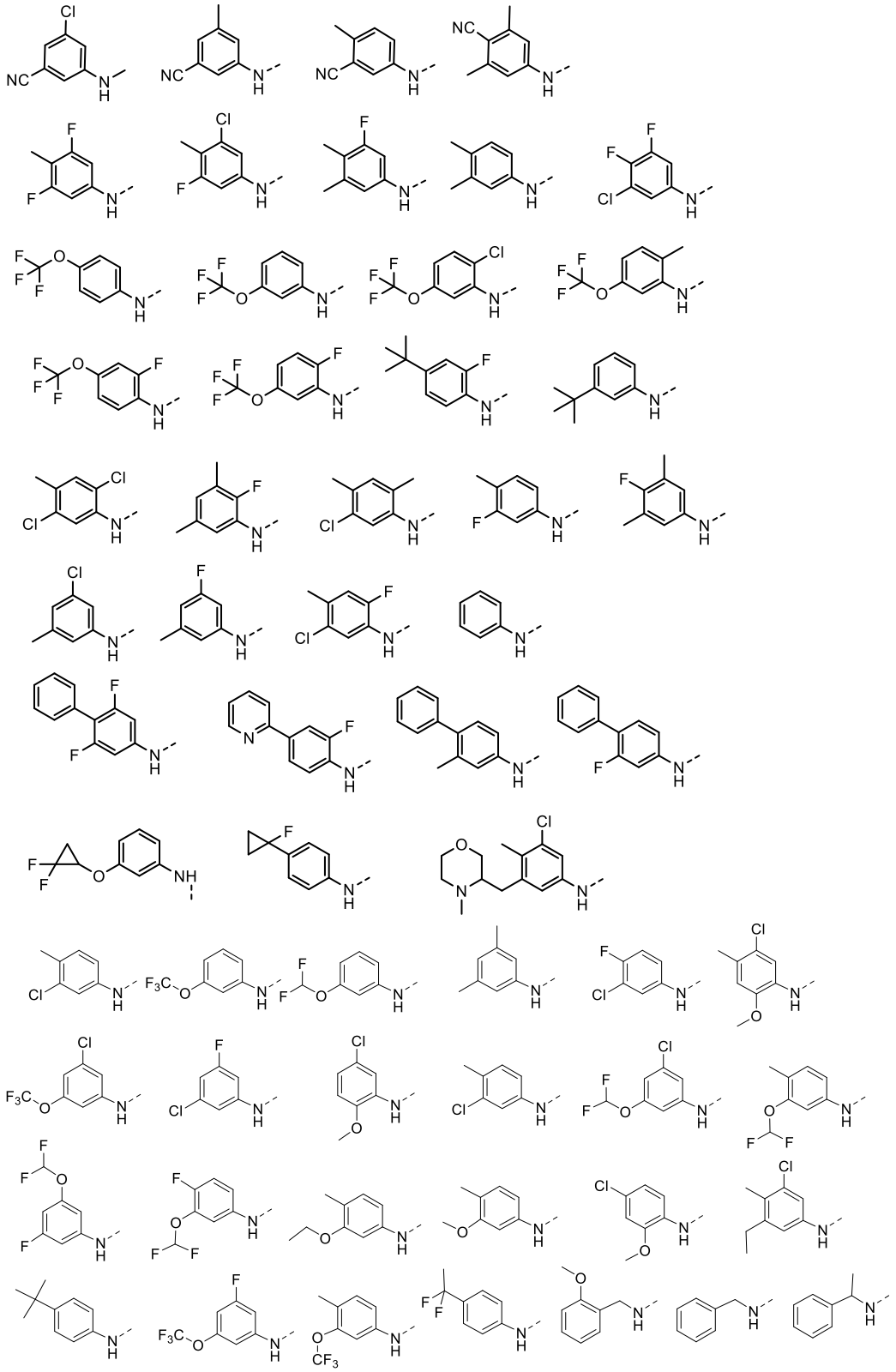


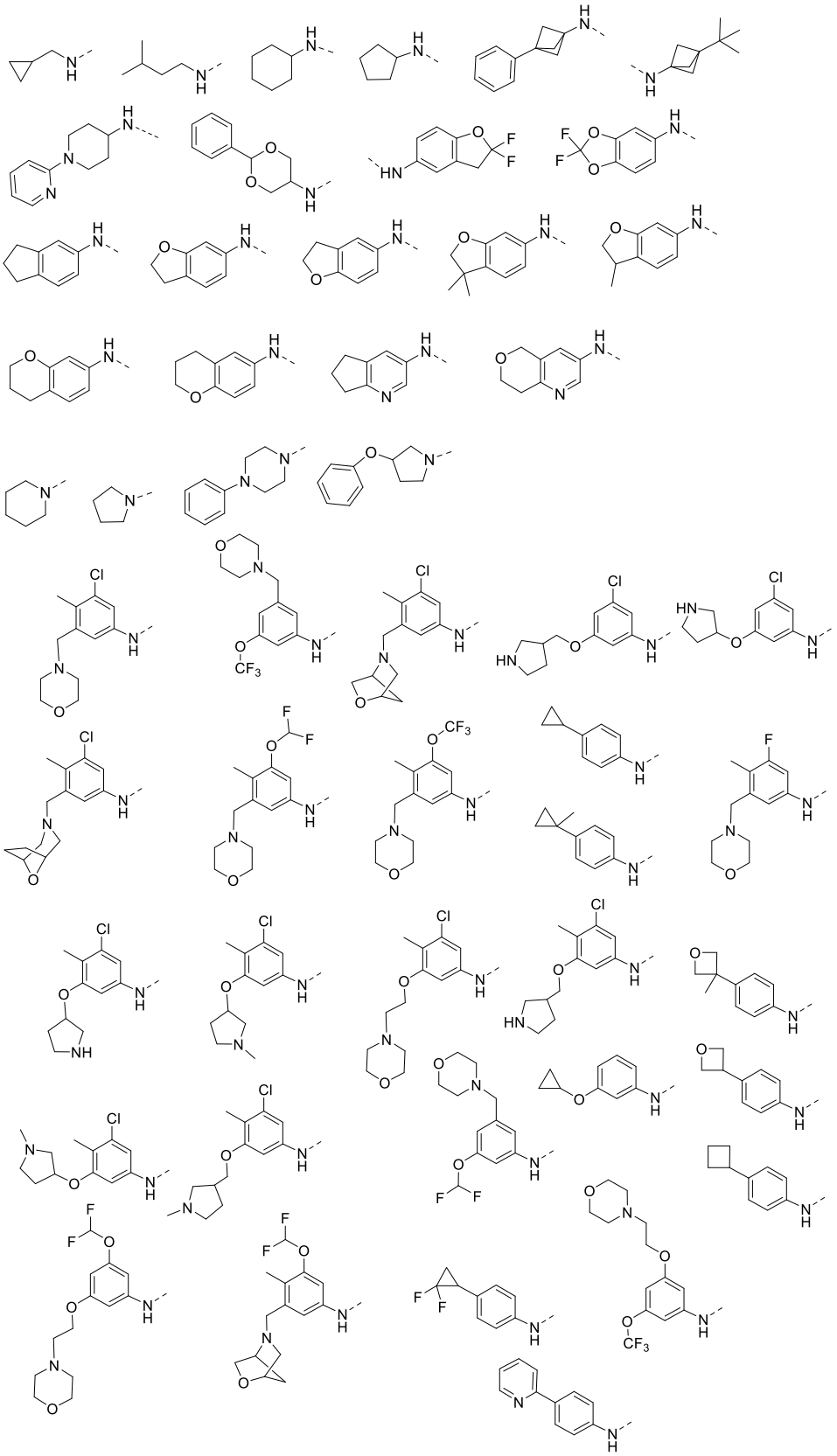
VIII

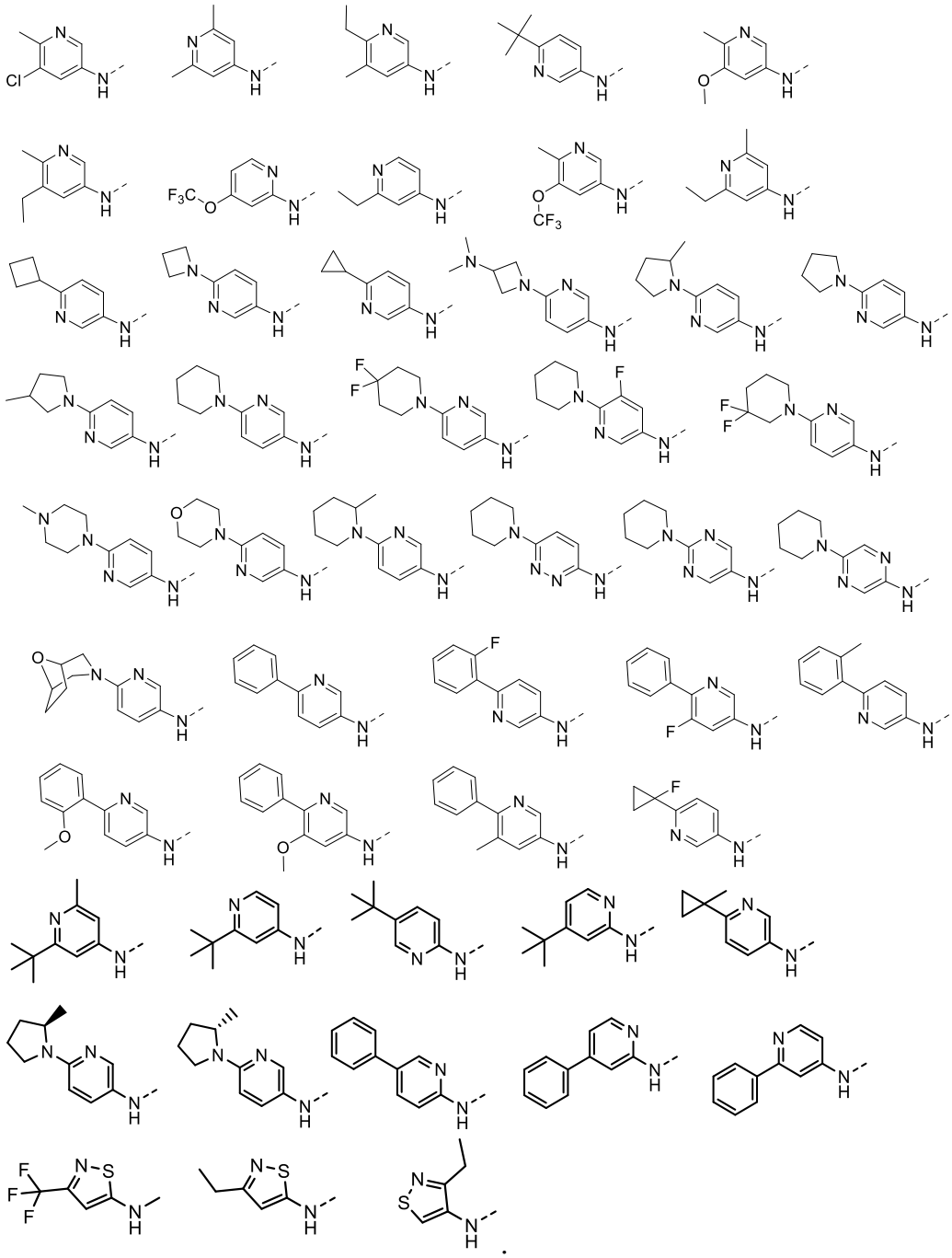


VIIIa

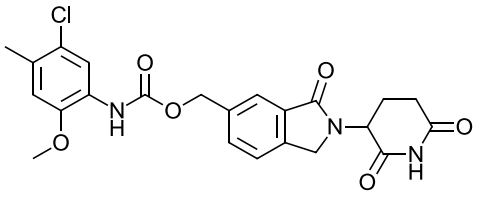
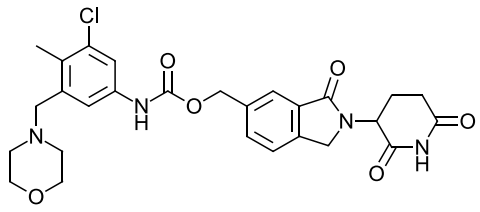
wherein R^a is H or methyl and W^1 and W^2 are selected from

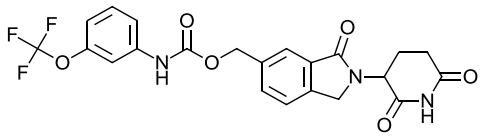
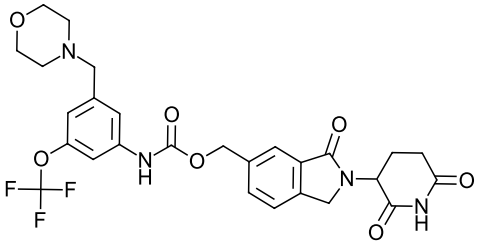
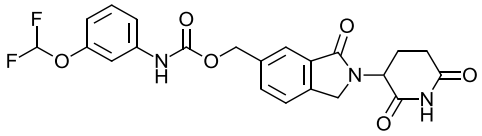
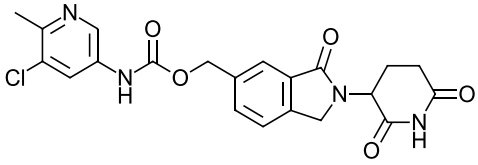
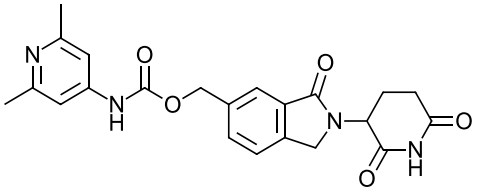
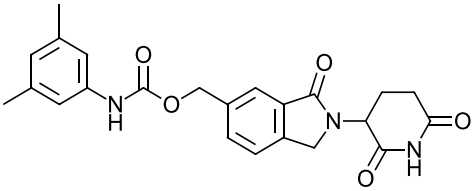
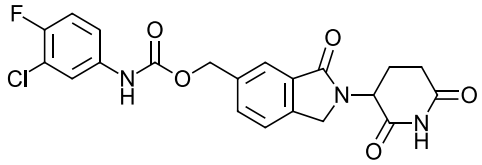
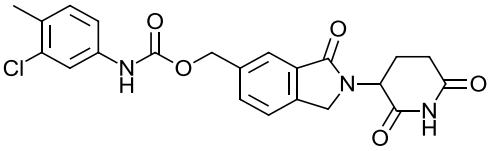
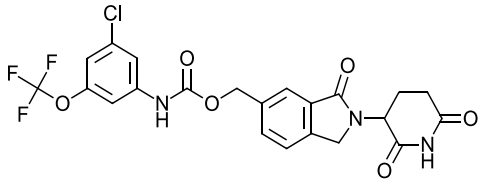
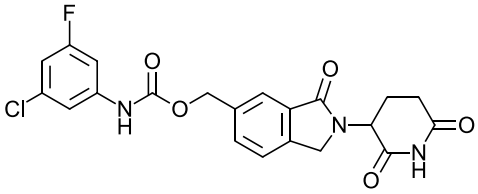
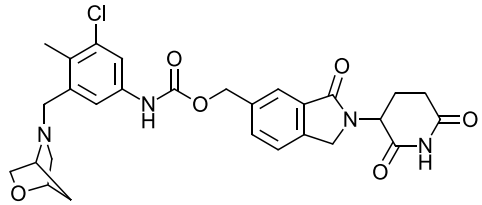
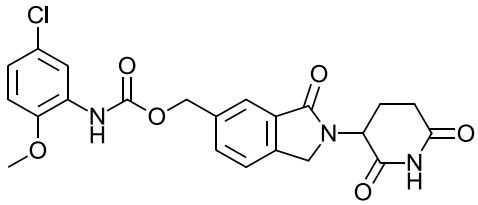
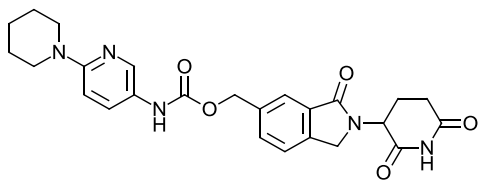
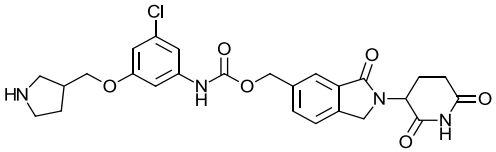
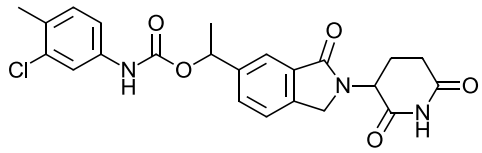
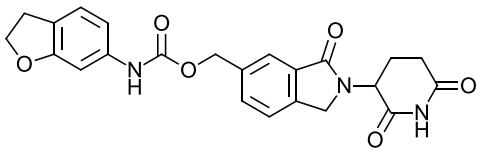
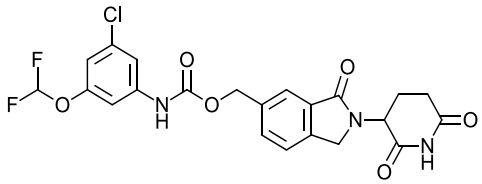
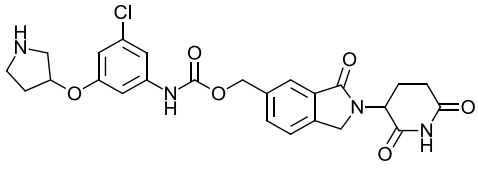


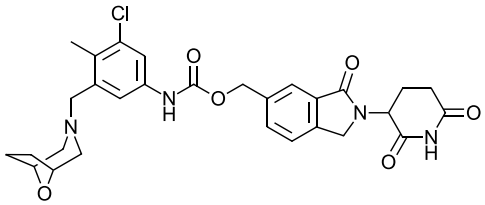
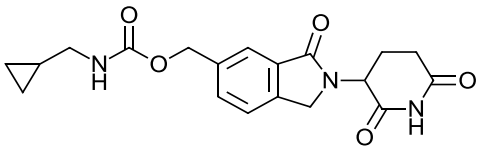
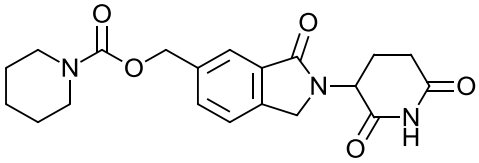
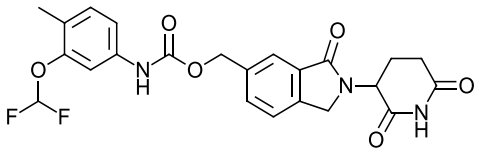
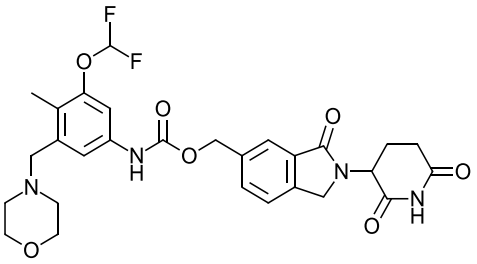
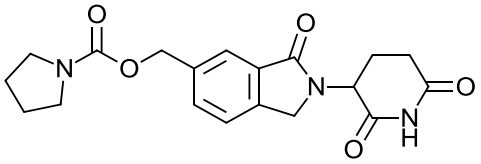
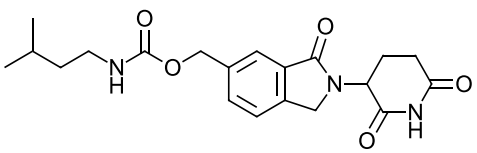
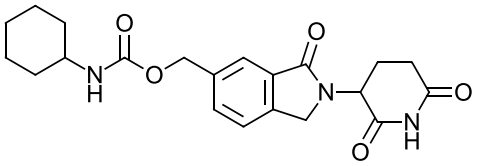
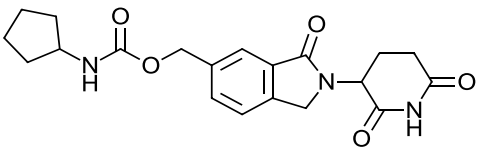
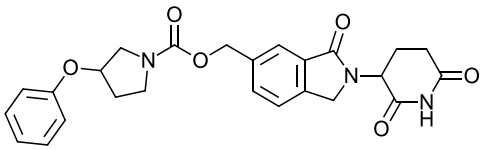
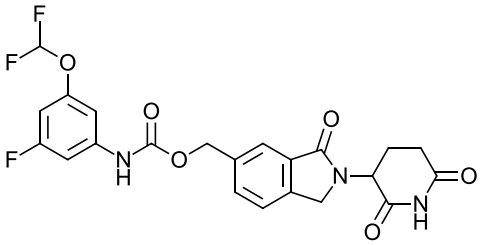
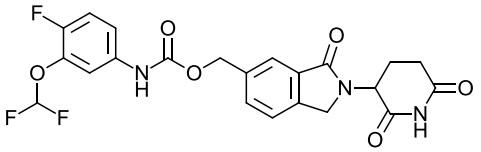
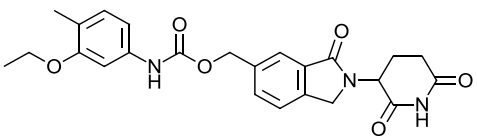
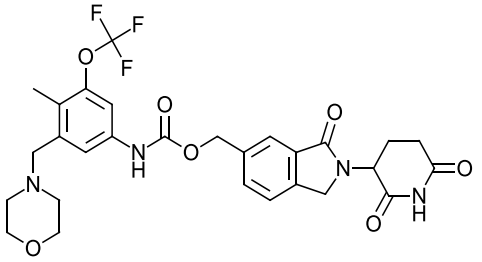
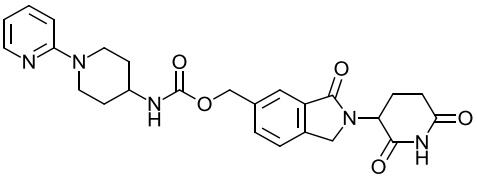
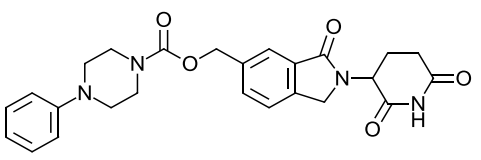


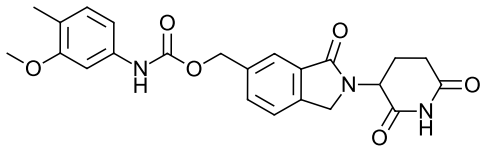
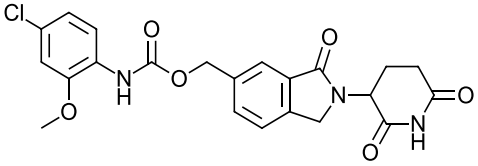
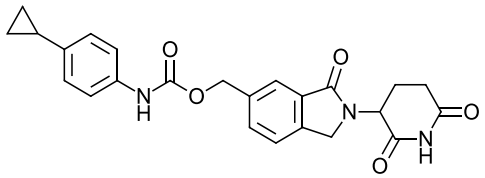
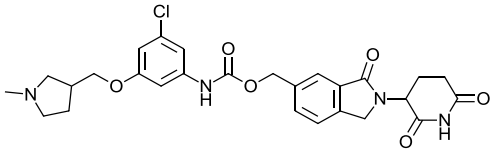
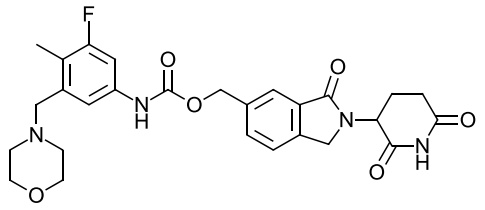
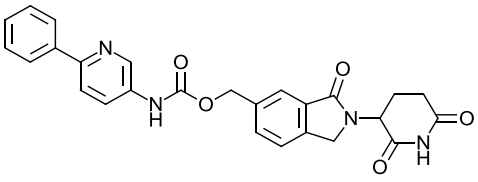
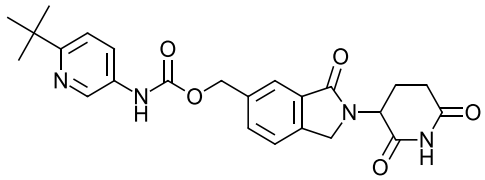
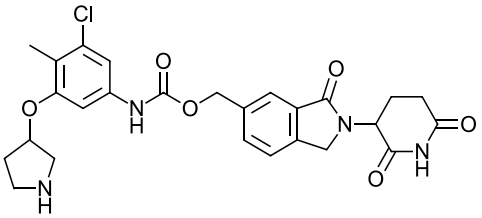
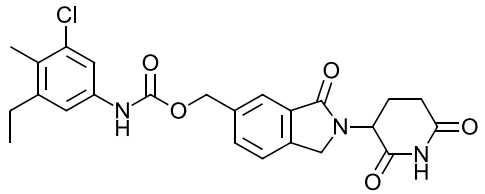
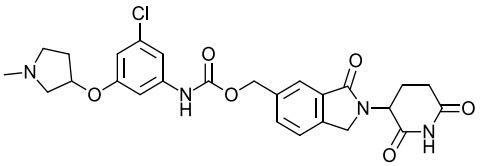
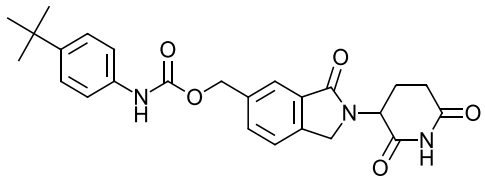
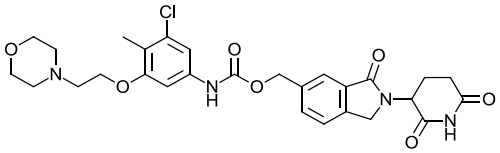
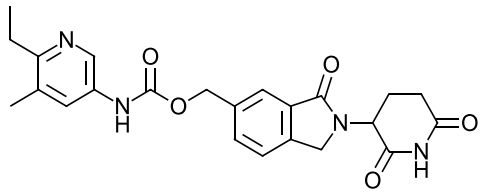
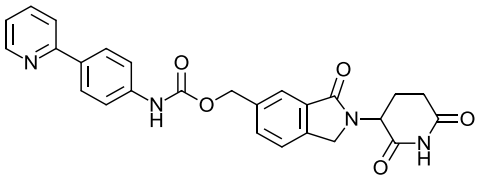
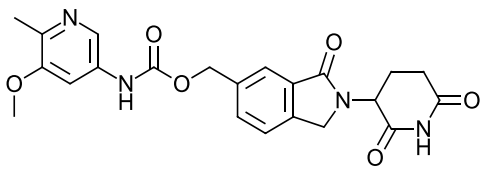
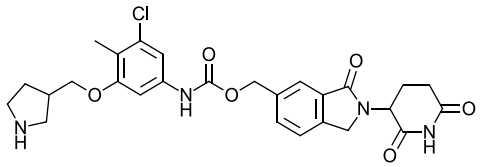
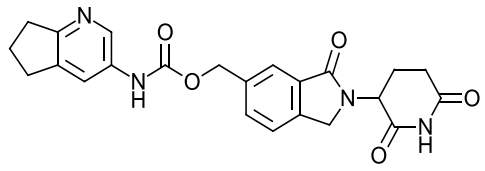
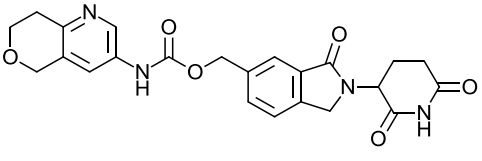


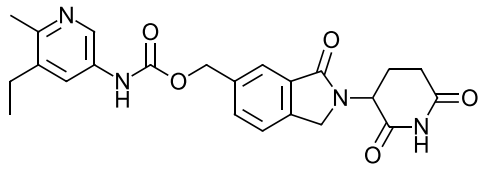
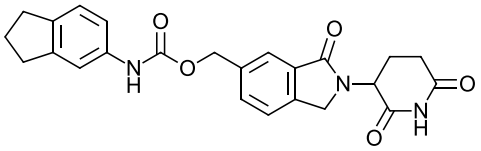
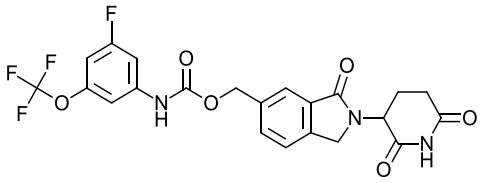
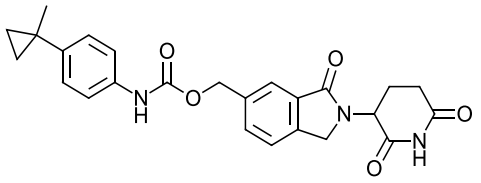
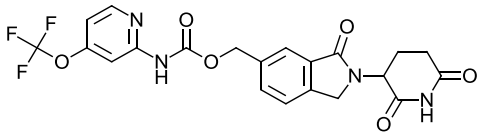
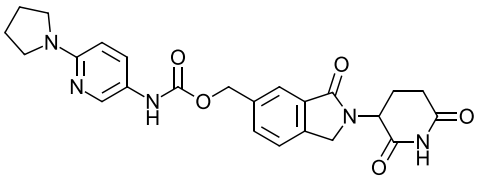
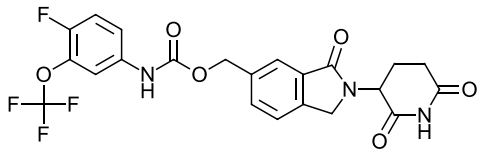
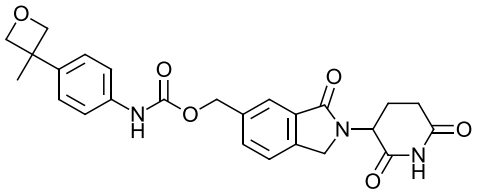
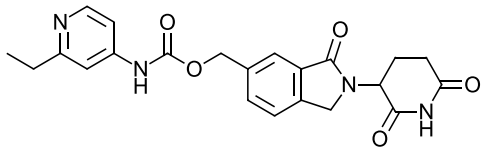
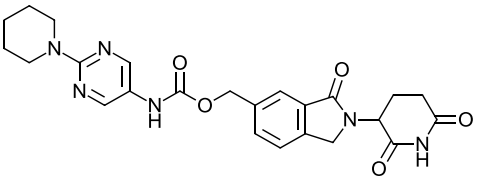
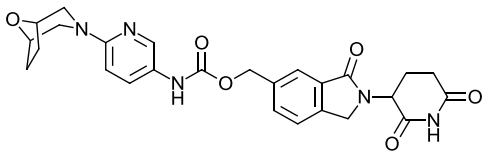
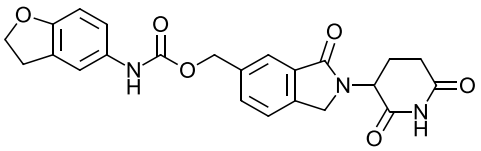
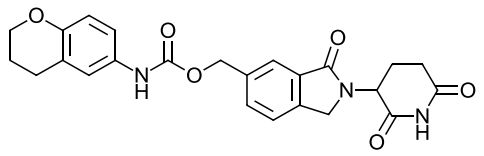
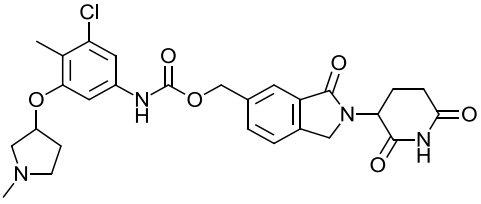
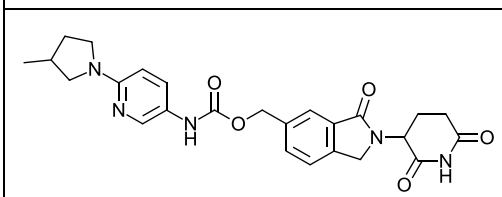
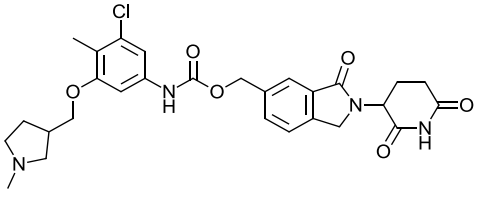
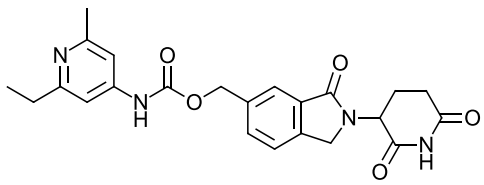
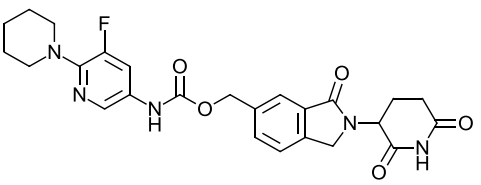
15. A compound selected from the group consisting of:

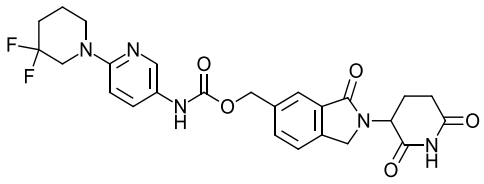
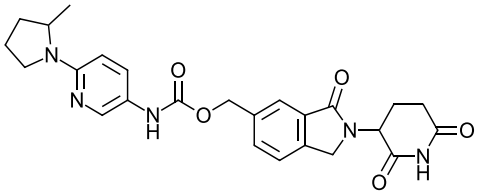
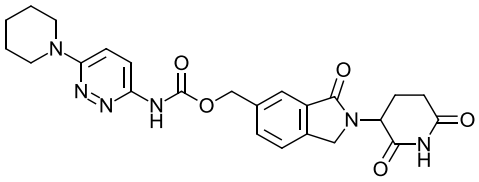
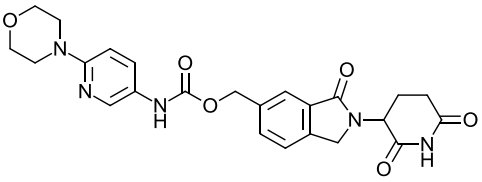
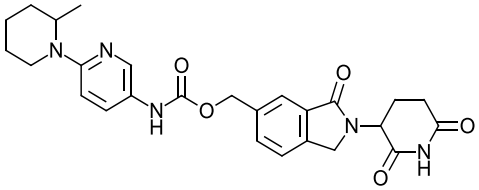
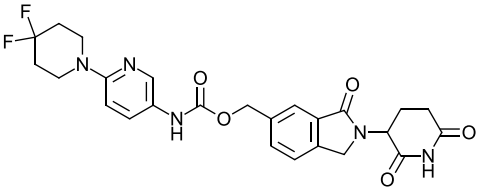
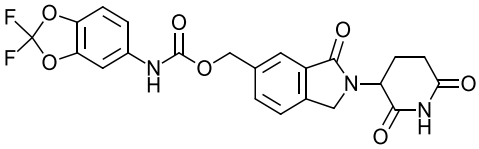
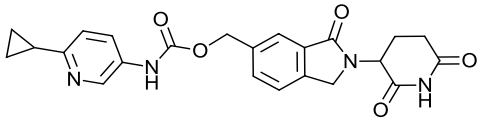
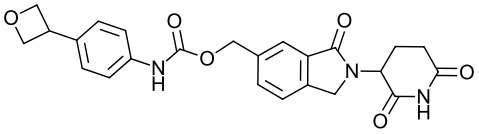
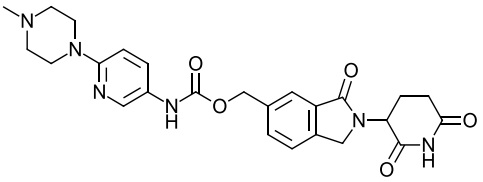
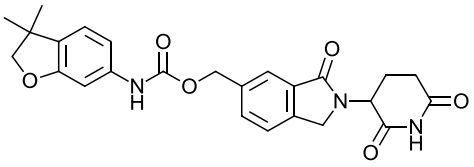
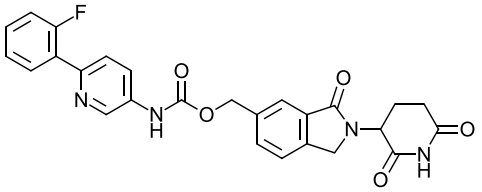
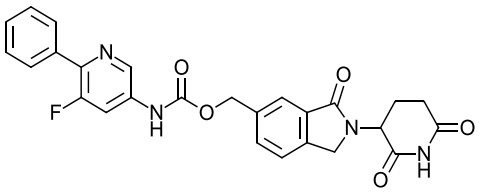
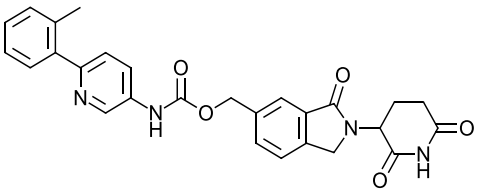
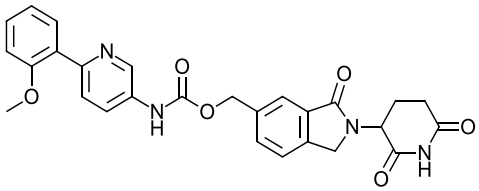
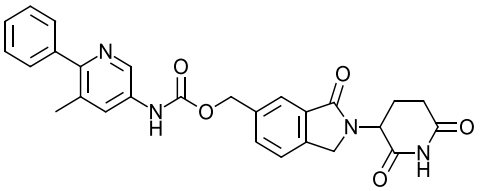
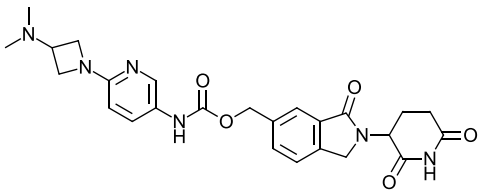
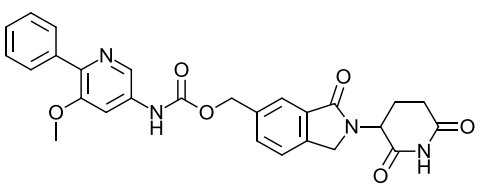
Compound	No.	Compound	No.
	1		2

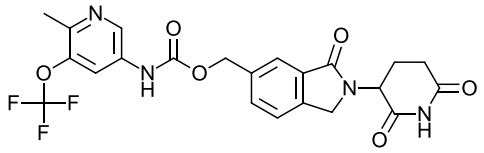
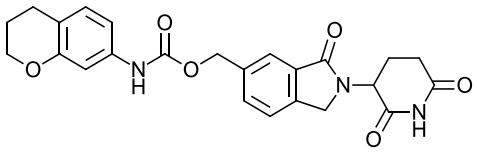
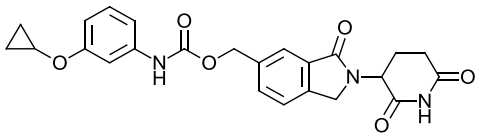
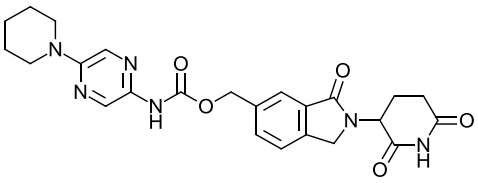
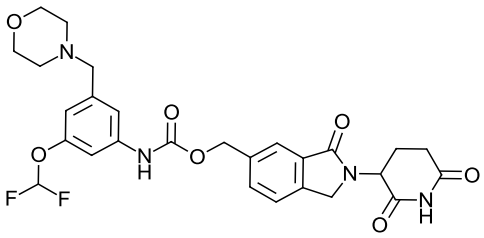
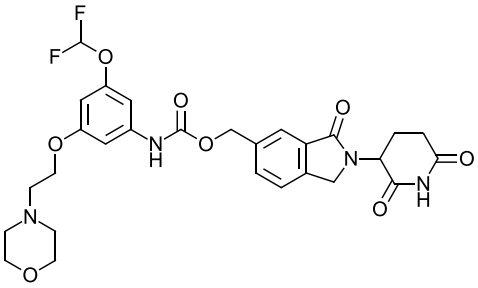
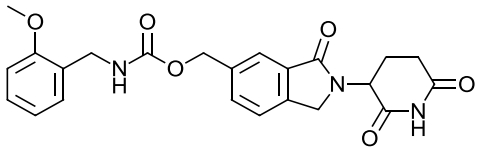
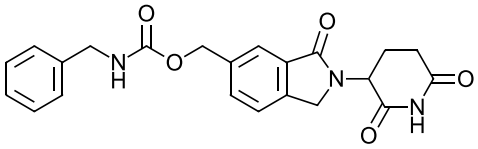
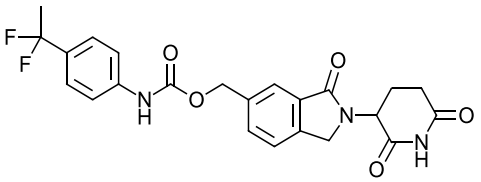
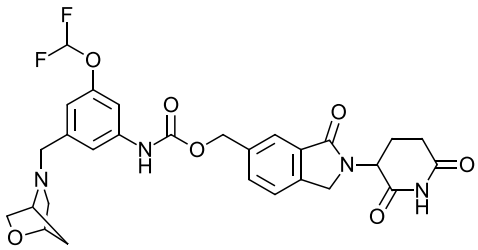
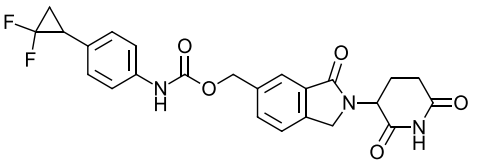
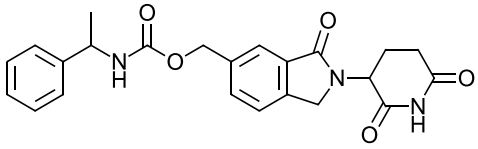
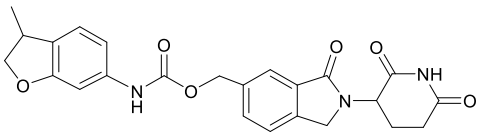
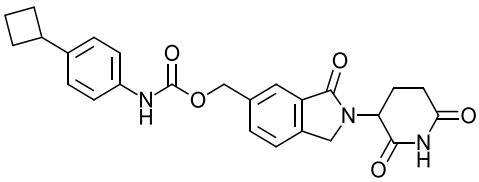
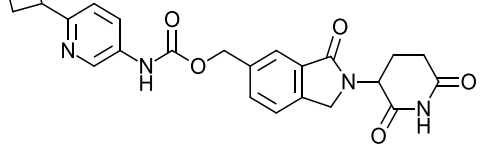
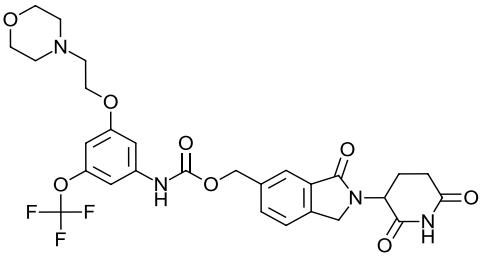
	**3**		**4**
	**5**		**6**
	**7**		**8**
	**9**		**10**
	**11**		**12**
	**13**		**14**
	**15**		**16**
	**17**		**18**
	**19**		**20**

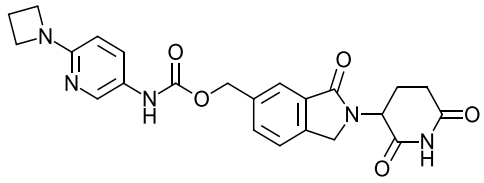
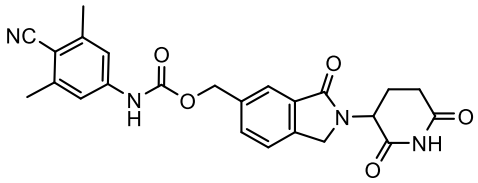
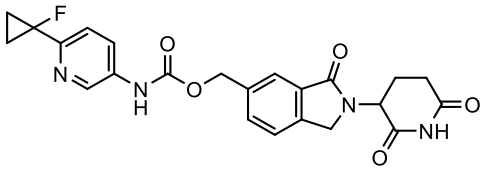
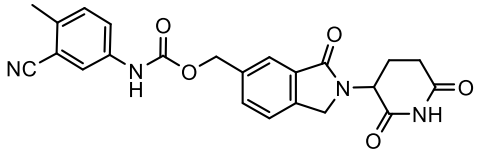
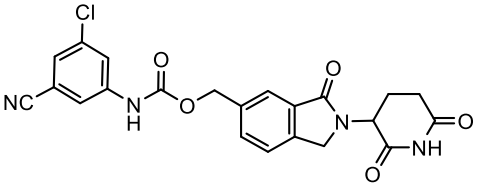
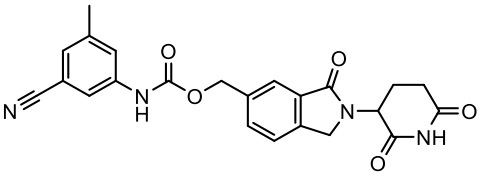
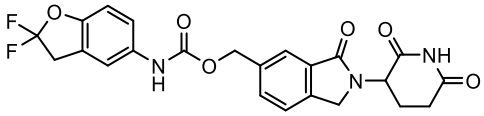
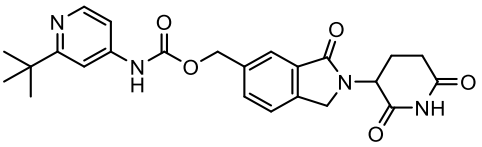
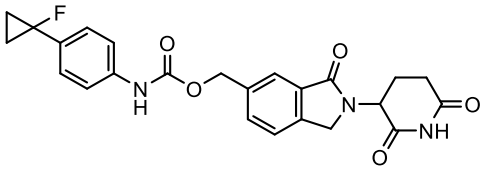
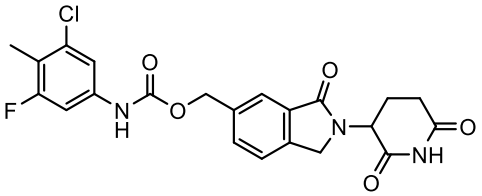
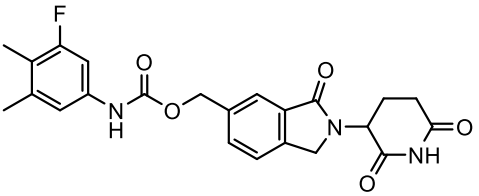
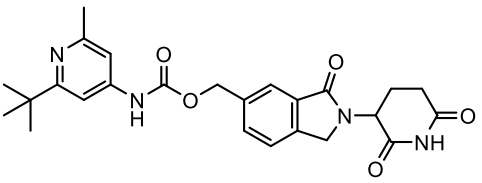
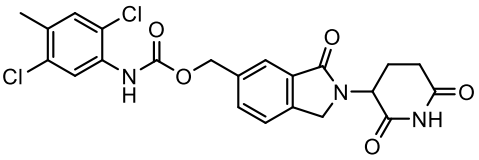
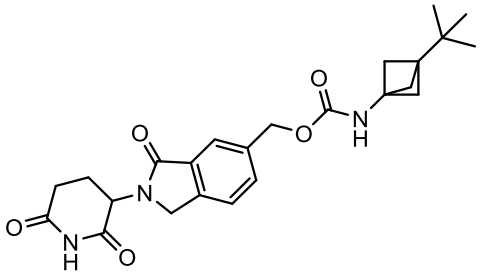
	**21**		**22**
	**23**		**24**
	**25**		**26**
	**27**		**28**
	**29**		**30**
	**31**		**32**
	**33**		**34**
	**35**		**36**

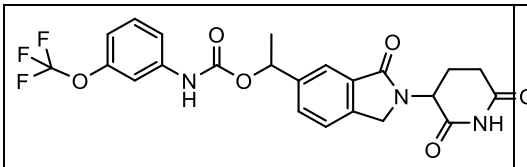
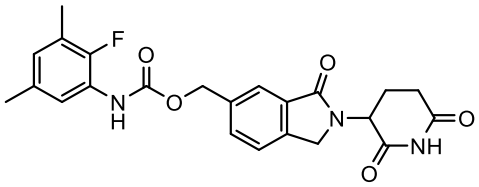
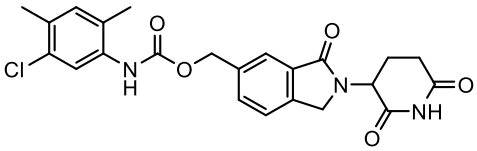
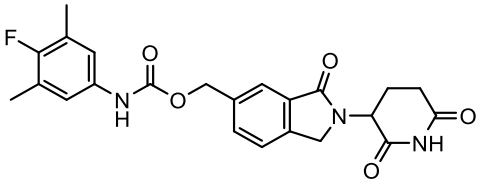
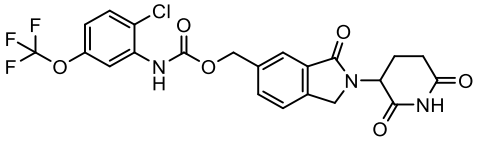
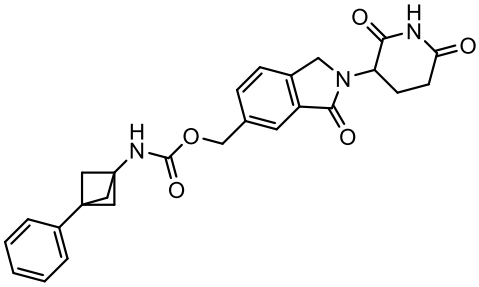
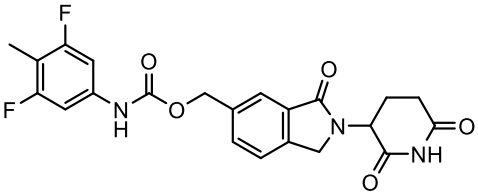
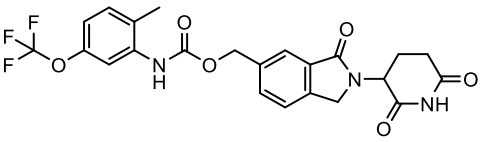
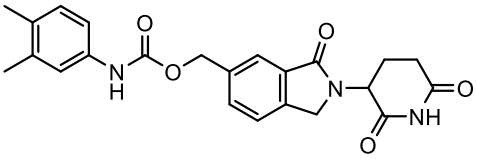
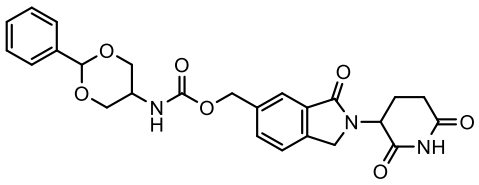
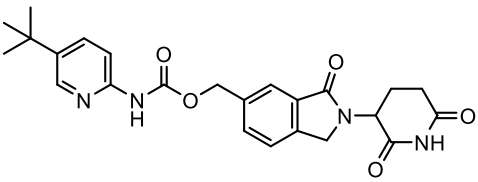
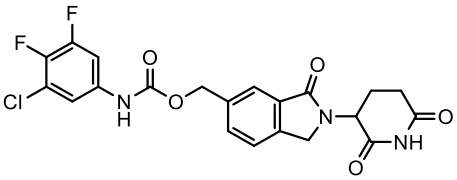
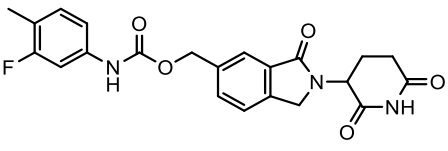
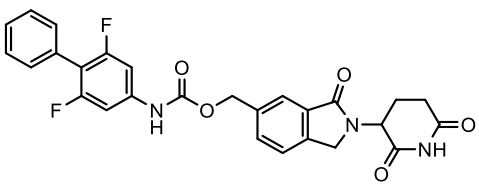
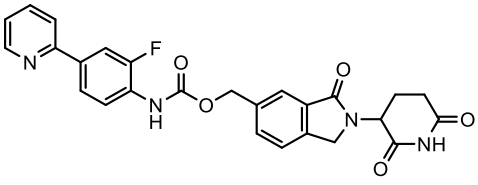
	**37**		**38**
	**39**		**40**
	**41**		**42**
	**43**		**44**
	**45**		**46**
	**47**		**48**
	**49**		**50**
	**51**		**52**
	**53**		**54**

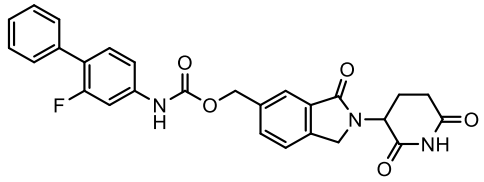
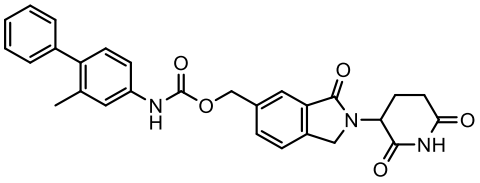
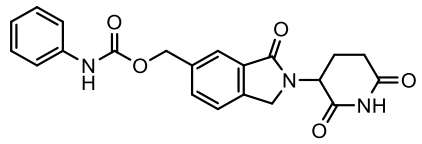
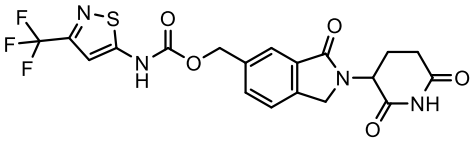
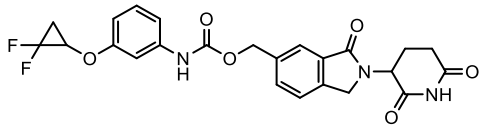
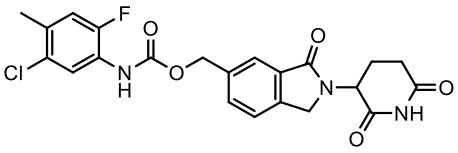
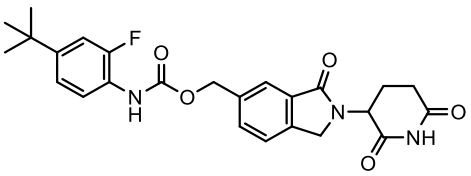
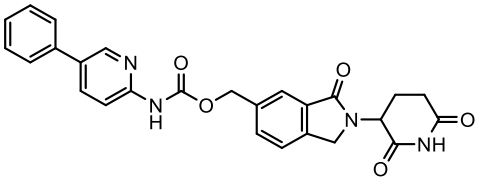
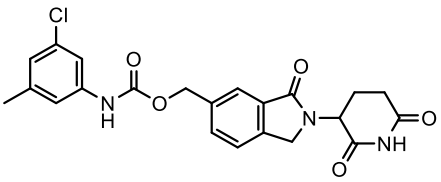
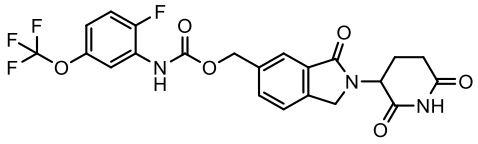
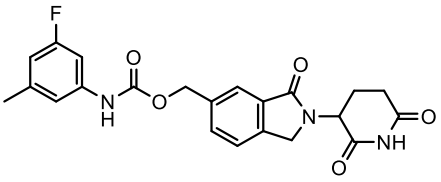
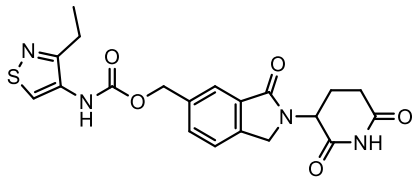
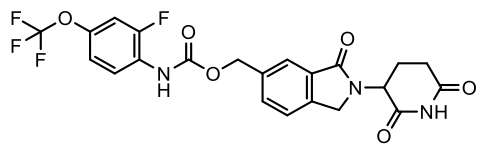
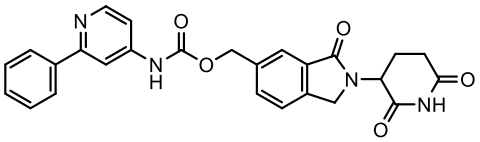
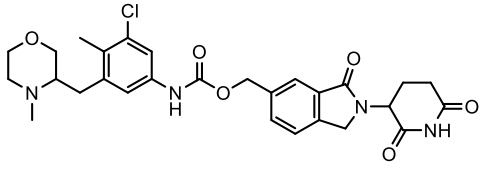
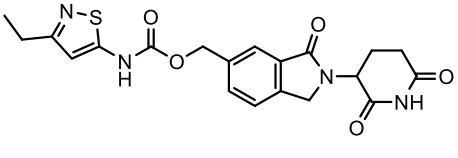
	55		56
	57		58
	59		60
	61		62
	63		64
	65		66
	67		68
	69		70
	71		72

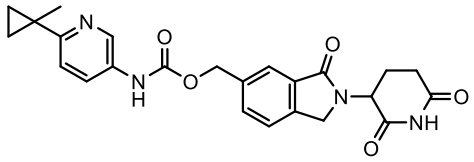
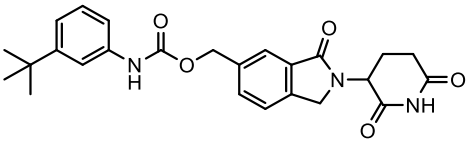
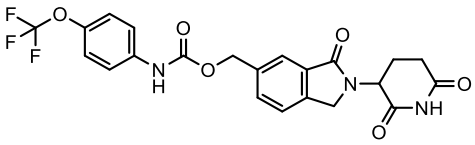
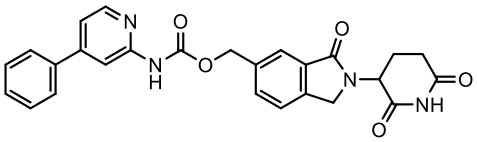
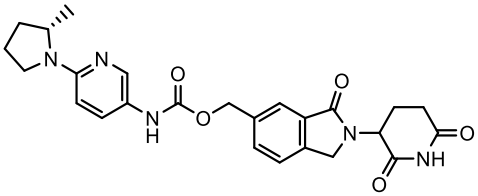
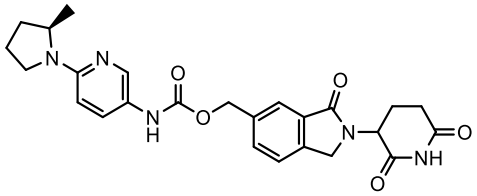
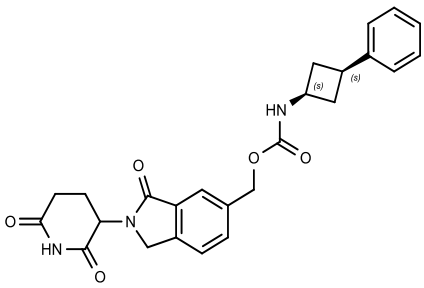
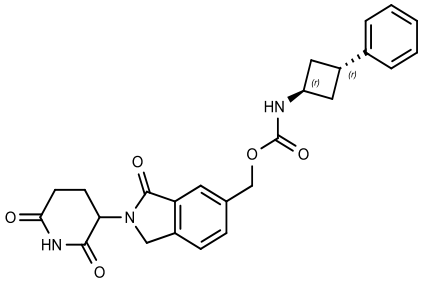
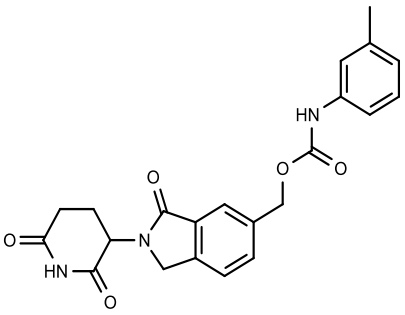
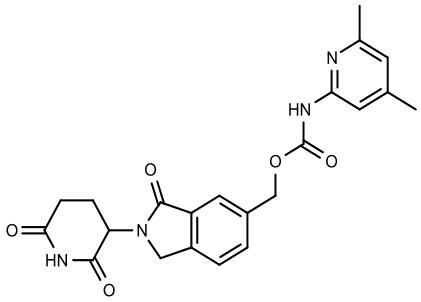
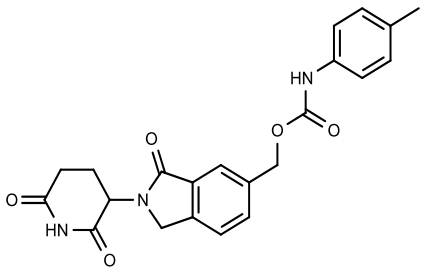
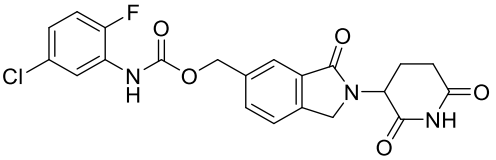
	**73**		**74**
	**75**		**76**
	**77**		**78**
	**79**		**80**
	**81**		**82**
	**83**		**84**
	**85**		**86**
	**87**		**88**
	**89**		**90**

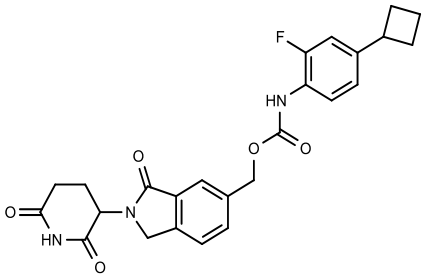
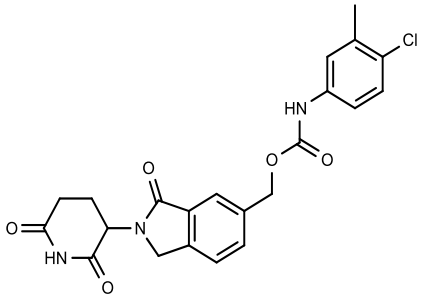
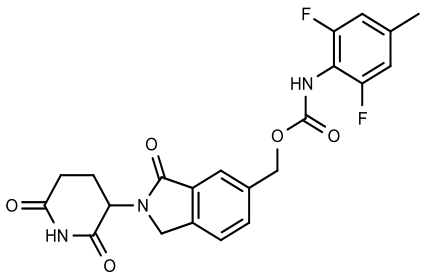
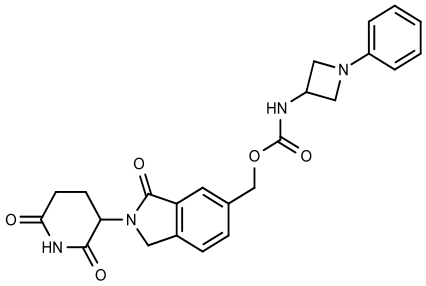
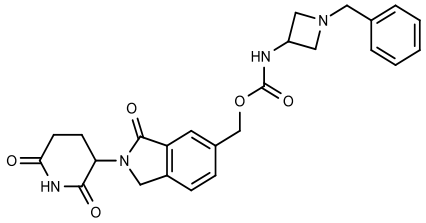
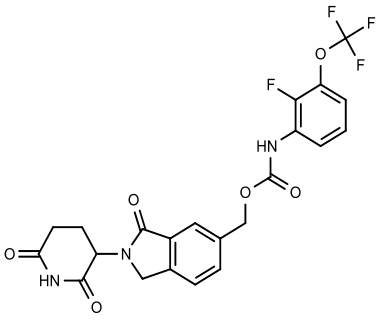
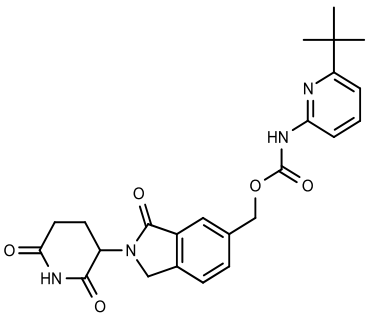
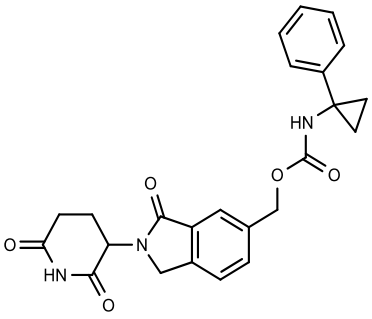
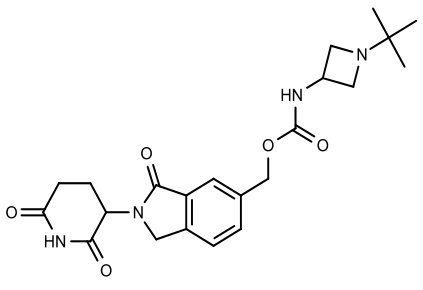
	91		92
	93		94
	95		96
	97		98
	99		100
	101		102
	103		104
	105		106

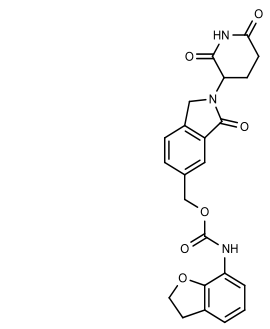
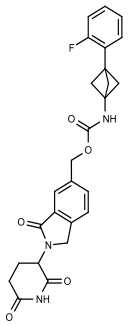
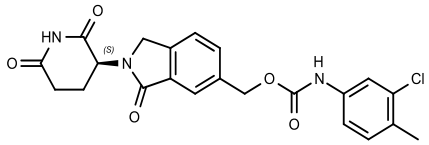
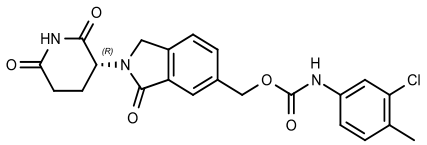
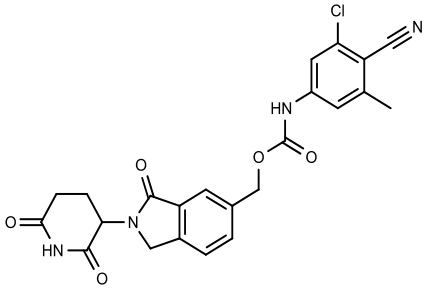
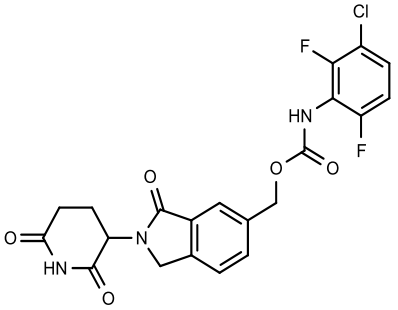
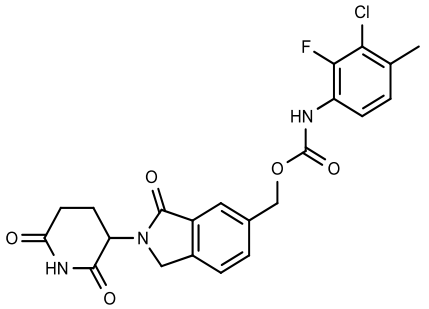
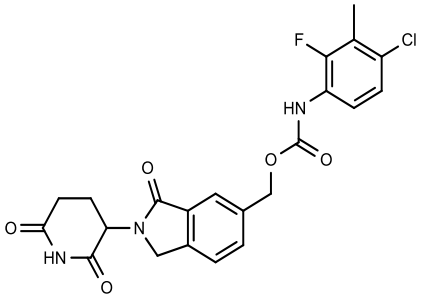
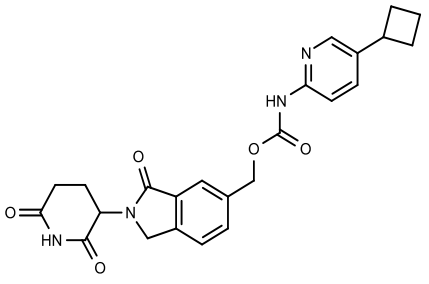
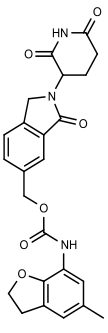
	**107**		**108**
	**109**		**110**
	**111**		**112**
	**113**		**114**
	**115**		**116**
	**117**		**118**
	**119**		**120**

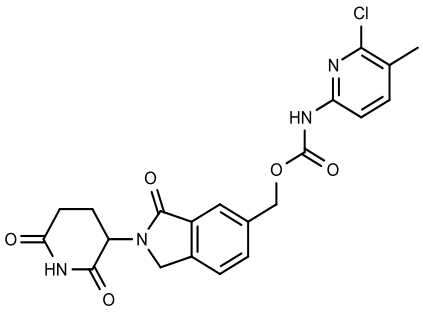
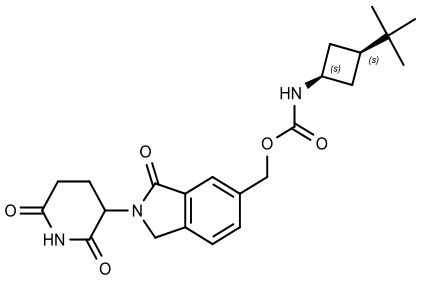
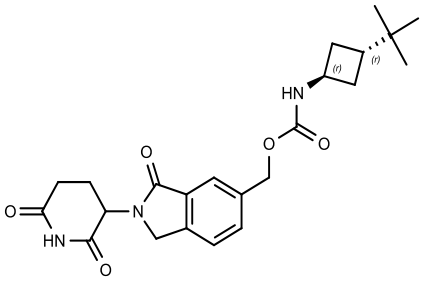
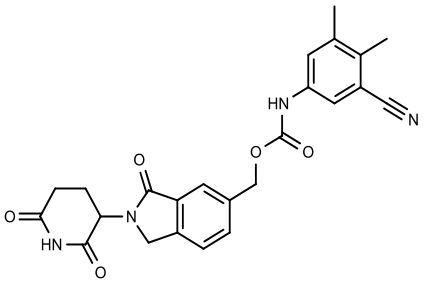
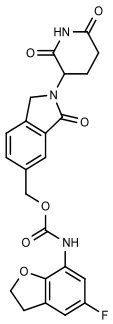
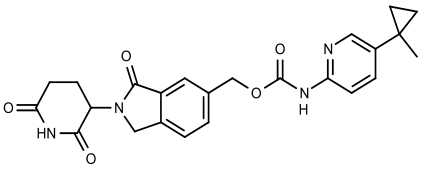
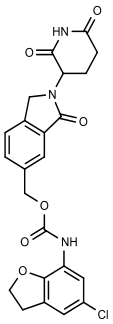
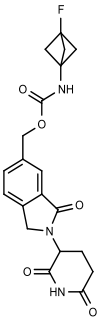
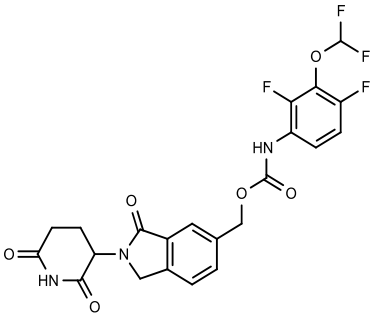
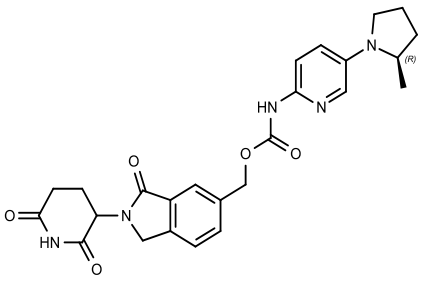
	121		
	122		123
	124		125
	126		127
	128		129
	130		131
	132		133
	134		135

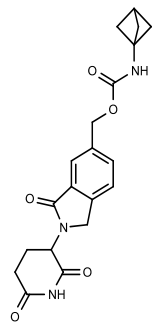
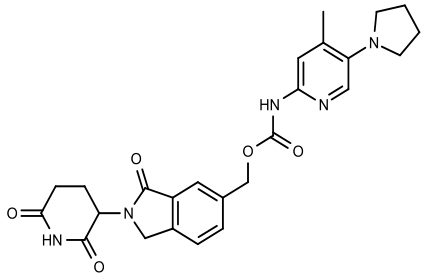
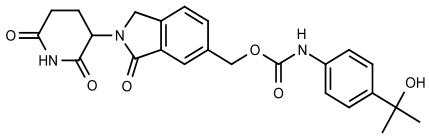
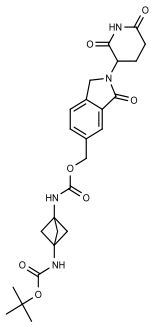
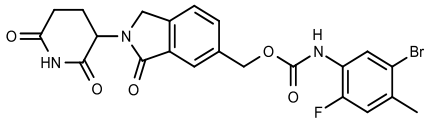
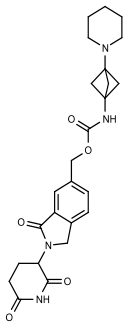
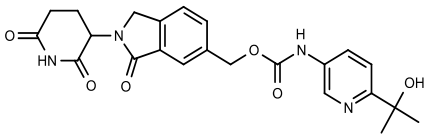
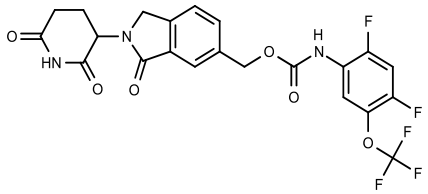
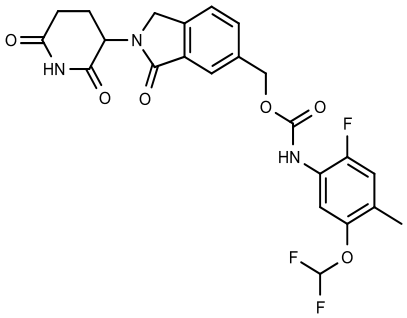
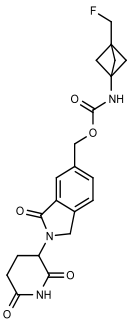
	**136**		**137**
	**138**		**139**
	**140**		**141**
	**142**		**143**
	**144**		**145**
	**146**		**147**
	**148**		**149**
	**150**		**151**

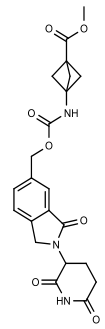
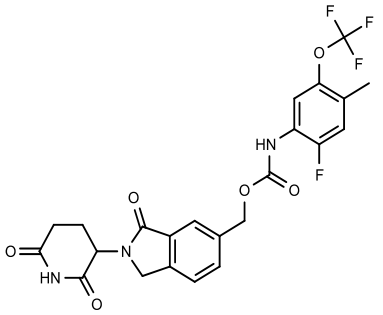
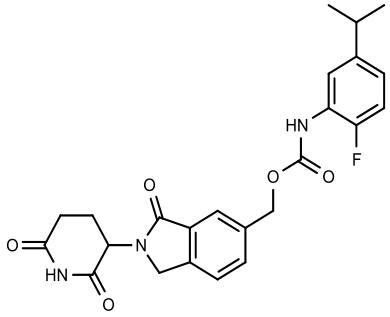
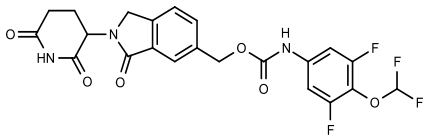
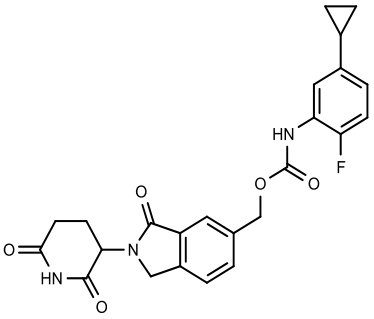
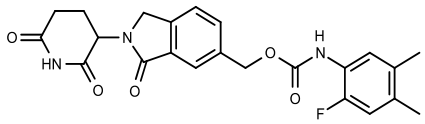
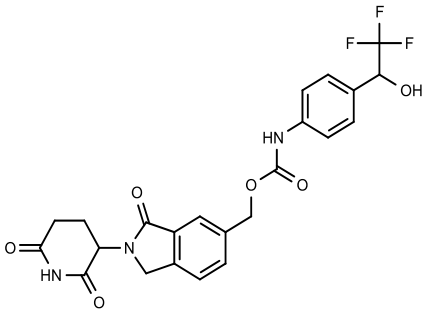
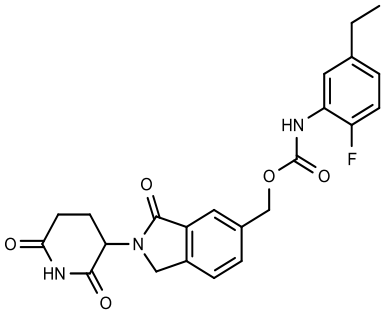
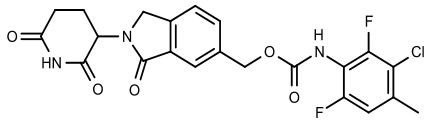
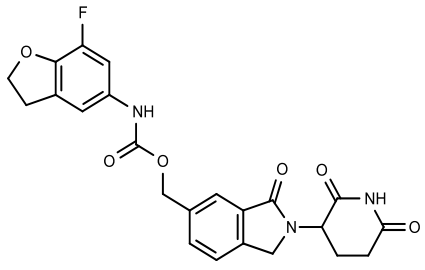
	**152**		**153**
	**154**		**155**
	**156**		**157**
	**158**		**159**
	**160**		**161**
	**162**		**163**

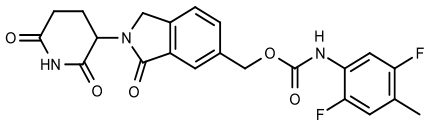
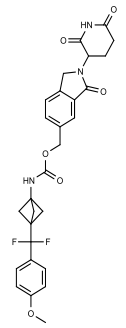
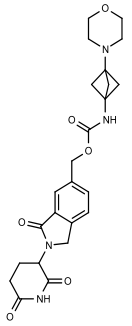
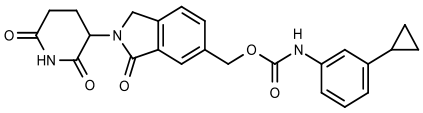
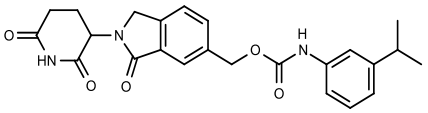
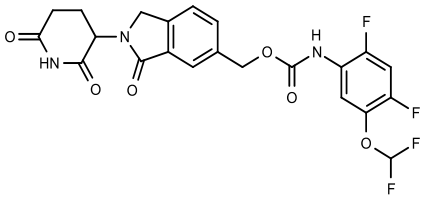
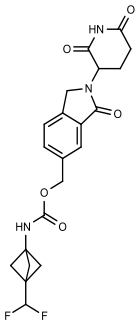
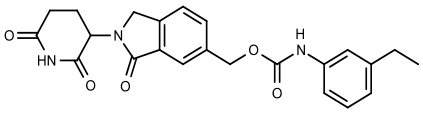
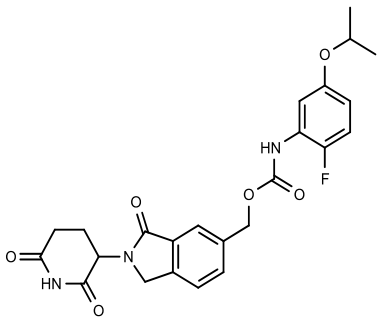
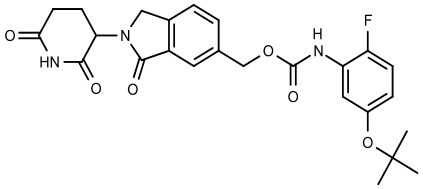
	**164**		**165**
	**166**		**167**
			**168**
	**169**		**170**
	**171**		**172**

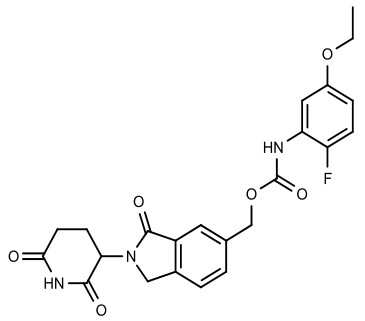
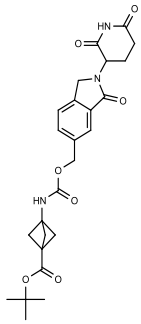
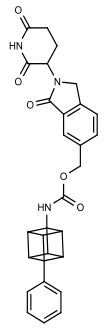
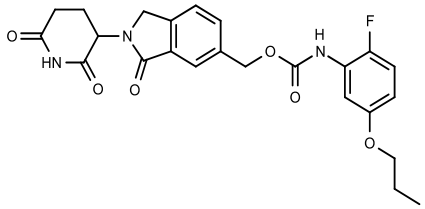
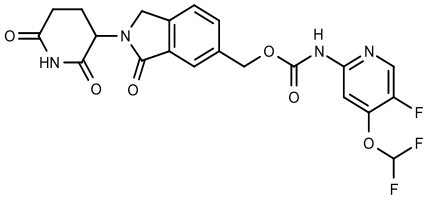
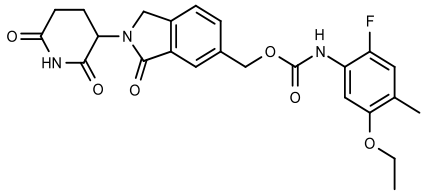
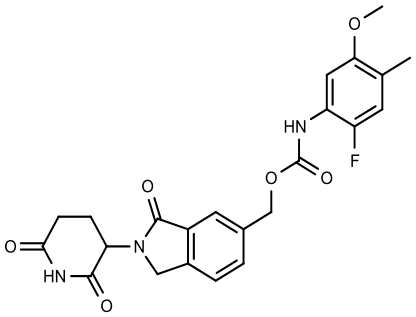
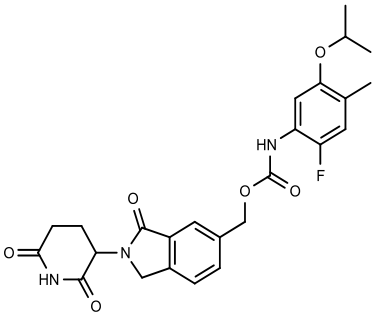
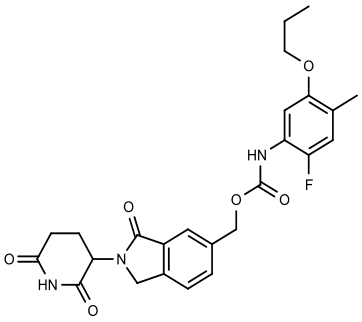
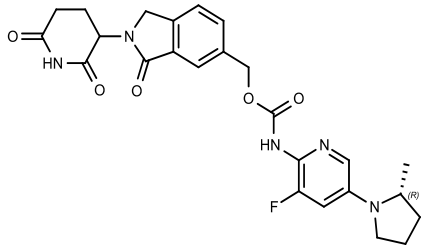
	**173**		**174**
	**175**		**176**
	**177**		**178**
	**179**		**180**
	**181**		**182**

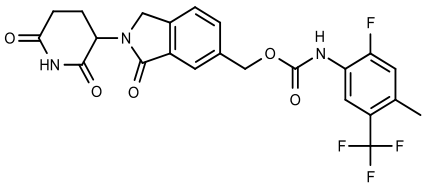
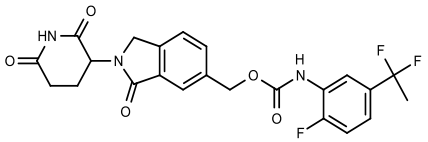
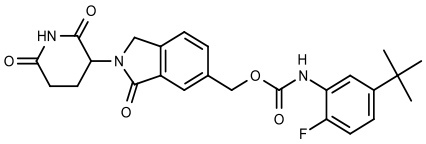
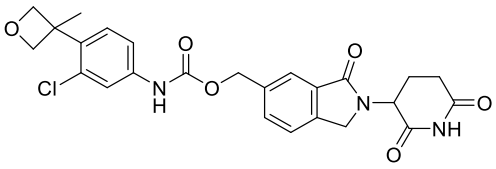
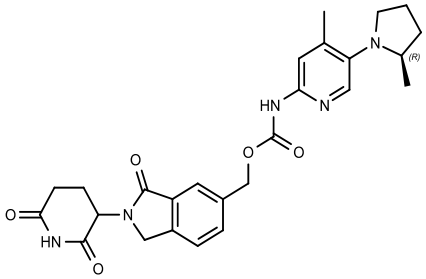
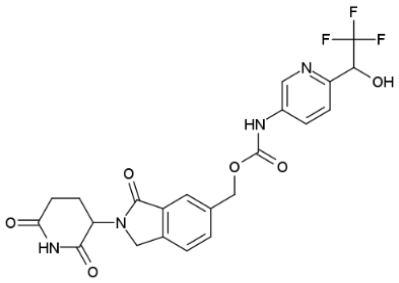
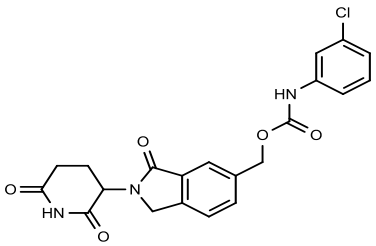
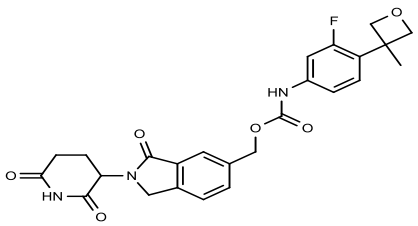
	**183**		**184**
	**185**		**186**
	**187**		**188**
	**189**		**190**
	**191**		**192**

	**193**		**194**
	**195**		**196**
	**197**		**198**
	**199**		**200**
	**201**		**202**

	**203**		**204**
	**205**		**206**
	**207**		**208**
	**209**		**210**
	**211**		**212**

	**213**		**214**
	**215**		**216**
	**217**		**218**
	**219**		**220**
	**221**		**222**

	**223**		**224**
	**225**		**226**
	**227**		**228**
	**229**		**230**
	**231**		**232**

	**233**		**234**
	**235**		**236**
	**237**		**238**
	**239**		**240**

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. Use of the compound of claim 1 in the manufacture of a medicament for treating cancer, in particular lung cancer, breast cancer and neuroendocrine cancer in a subject.

19. Use of the compound of claim 1 in the manufacture of a medicament for treating a Myc-driven cancer in a subject in need thereof.

20. The use of claim 19, wherein the Myc-driven cancer is a Myc-driven lung cancer.

21. The use of claim 19, wherein the Myc-driven cancer is a Myc-driven small cell lung cancer.

22. The use of claim 21, wherein the Myc-driven small cell lung cancer is a high L-Myc small cell lung cancer.

23. The use of claim 19, wherein the Myc-driven cancer is a Myc-driven non-small cell lung cancer.

24. The use of claim 23, wherein the Myc-driven non-small cell lung cancer is a high N-Myc non-small cell lung cancer.

25. The use of claim 19, wherein the compound is to be administered to the subject via oral administration.

26. Use of the compound of claim 1 in the manufacture of a medicament for degrading GSPT1 in a subject suffering from cancer.

27. The use of claim 26, wherein the cancer is a Myc-driven cancer.

28. The use of claim 27, wherein the Myc-driven cancer is a Myc-driven lung cancer.

29. The use of claim 27, wherein the Myc-driven cancer is a Myc-driven small cell lung cancer.

30. The use of claim 29, wherein the Myc-driven small cell lung cancer is a high L-Myc small cell lung cancer.

31. The use of claim 26, wherein the Myc-driven cancer is a Myc-driven non-small cell lung cancer.

32. The use of claim 31, wherein the Myc-driven non-small cell lung cancer is a high N-Myc non-small cell lung cancer.

33. The use of claim 26, wherein the compound is to be administered to the subject via oral administration.

34. Use of the compound of claim 1 in the manufacture of a medicament for reducing the level of GSPT1 in a subject suffering from cancer.

35. The use of claim 34, wherein the cancer is a Myc-driven cancer.

36. The use of claim 35, wherein the Myc-driven cancer is a Myc-driven lung cancer.

37. The use of claim 35, wherein the Myc-driven cancer is a Myc-driven small cell lung cancer.

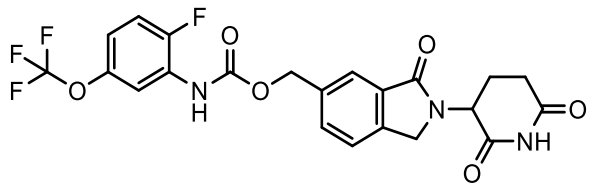
38. The use of claim 37, wherein the Myc-driven small cell lung cancer is a high L-Myc small cell lung cancer.

39. The use of claim 35, wherein the Myc-driven cancer is a Myc-driven non-small cell lung cancer.

40. The use of claim 39, wherein the Myc-driven non-small cell lung cancer is a high N-Myc non-small cell lung cancer.

41. The use of claim 34, wherein the compound is to be administered to the subject via oral administration.

42. A compound represented by:



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43. A compound of claim 1 for use in therapy.