

The Innovation, Volume 4

Supplemental Information

Targeted protein degradation in cancers: Orthodox PROTACs and beyond

Jin Li, Xinxin Chen, Aiping Lu, and Chao Liang

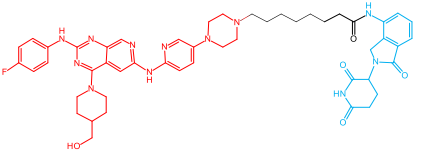
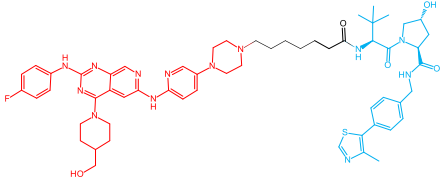
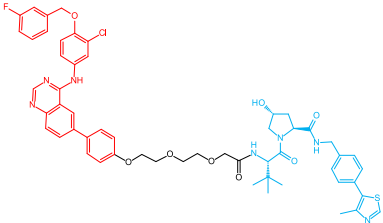
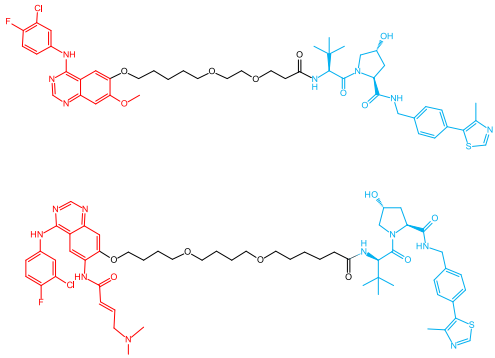
Supplemental Information

Targeted Protein Degradation in Cancers: Orthodox PROTACs and Beyond

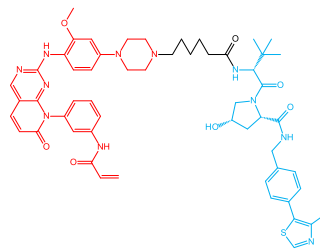
Jin Li, Xinxin Chen, Aiping Lu, Chao Liang

Table S1. PROTACs and Related Diseases in Academia

Name	Structure	POI	E3 Ligase	Disease (Related Cell Line)	Reference
Compound B3		ALK	CRBN	NSCLC (H3122)	1
MS4077		ALK	CRBN	NHL (SU-DHL-1), NSCLC (NCI-H2228)	2
MS4078		ALK	CRBN	NHL (SU-DHL-1), NSCLC (NCI-H2228)	2
Degradar 17		ALK	CRBN	NSCLC (A549), Human Fetal Lung Fibroblast (HFL-1)	3

Compound 2		EGFR ^{Del19}	CRBN	NSCLC (HCC827)	4
Compound 10		EGFR ^{Del19}	VHL	NSCLC (HCC827)	4
PROTAC 1		EGFR ^{Ex20Ins}	VHL	Human Ovarian Carcinoma (OVAR8), Cervical Cancer (HeLa)	5
PROTACs 3/4		EGFR ^{Del19} , EGFR ^{L858R/T790M}	VHL	NSCLC (HCC827, H1975)	5

14o



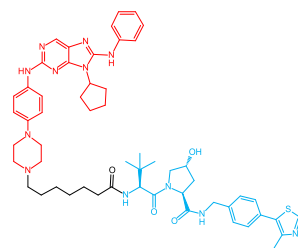
EGFR
L858R/T790M

VHL

NSCLC (H1975)

6

Compound P3



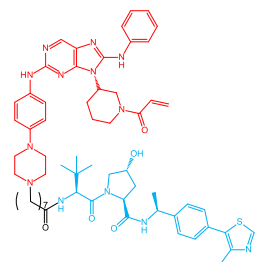
EGFR^{Del19},
EGFR L858R/T790M

VHL

NSCLC
(HCC827, H1975)

7

CP17



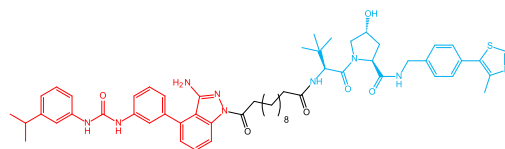
EGFR^{Del19},
EGFR L858R/T790M

VHL

NSCLC
(HCC827, H1975)

8

PROTACs-2/5



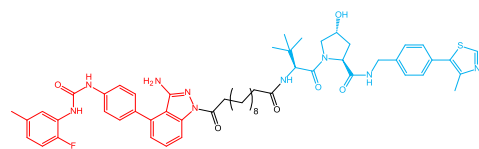
VEGFR-2

VHL

HUVEC
(EA.hy926)

9

CG416



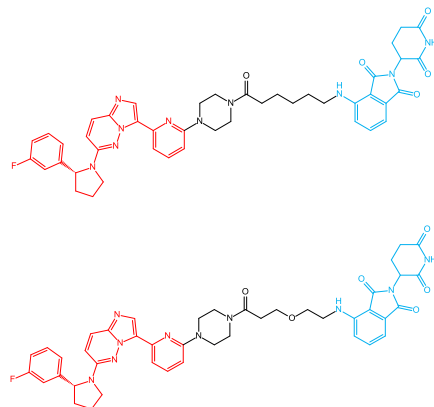
TPM3-TrkA
Fusion Protein,
Wild Type TRKA

CRBN

CRC (KM12)

10

CG428



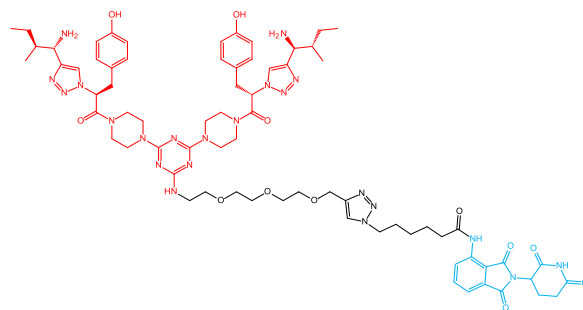
TPM3-TrkA
fusion protein, Wild
Type TrkA

CRBN

CRC (KM12)

10

Degrader 4



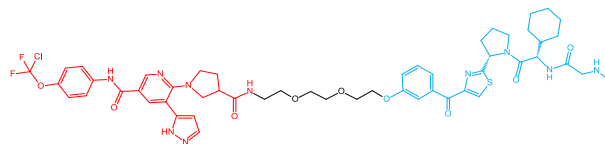
TrkC

CRBN

BC (Hs578t and
MDA-MB-231)

11

SNIPER(ABL)-
62



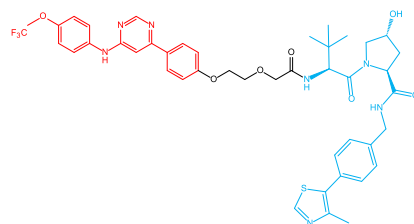
BCR-ABL

clAP1

CML (K562)

12

GMB-475



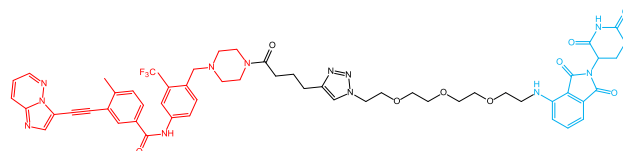
BCR-ABL

VHL

CML (K562)

13

P19P and P22D



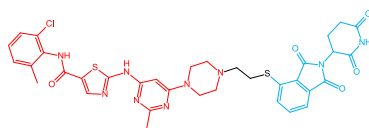
BCR-ABL

CRBN

CML (K562)

14

Degrader 17



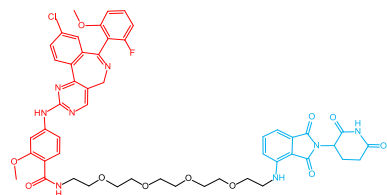
BCR-ABL

CRBN

CML (K562)

15

PROTAC-D



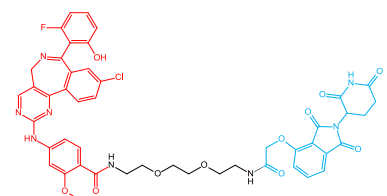
AURKA

CRBN

Osteosarcoma
(U2OS)

16

JB170



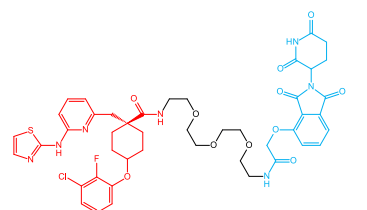
AURKA

CRBN

AML(MV4;11)

17

JB301



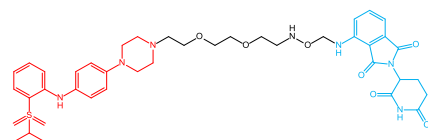
AURKA

CRBN

AML(MV4;11)

18

TL12-186



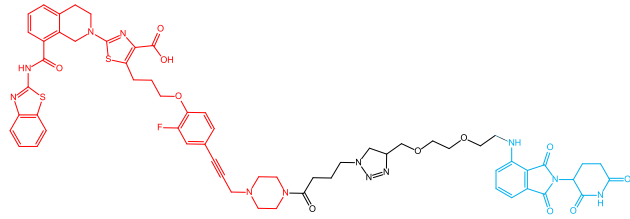
AURKA and
Other Proteins

CRBN

AML(MOLM14)
and ALL(MOLT-4)

19

XZ424



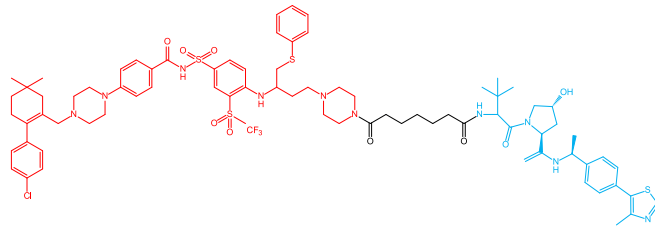
BCL-xL

VHL

ALL(MOLT-4)

20

DT2216



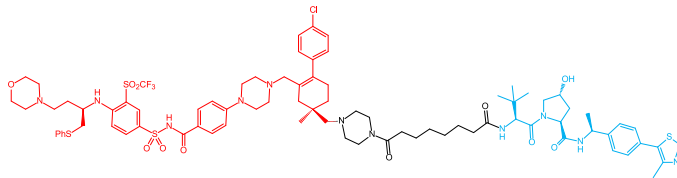
BCL-xL

VHL

ALL(MOLT-4)

21,22

753b



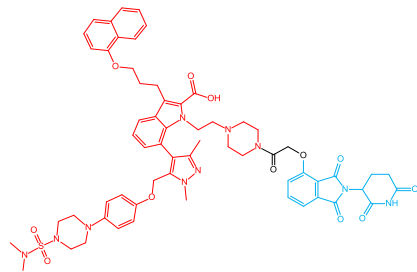
BCL-2/BCL-xL

VHL

AML (Kasumi-1)

23

dMCL 1-2

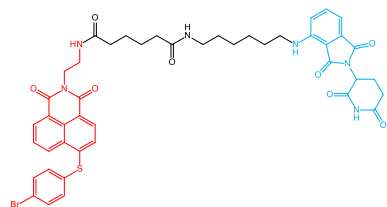


MCL-1

CRBN

MM (OPM2)

24



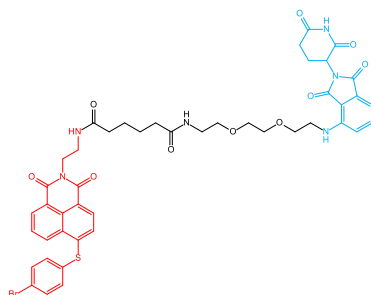
C3/5

MCL-1/BCL-2

CRBN

NSCLC (H23)

25



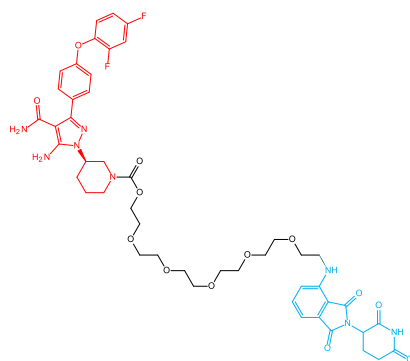
PROTAC (10)

BTK

CRBN

NHL (Ramos)

26



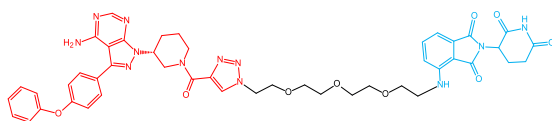
P13I

BTK

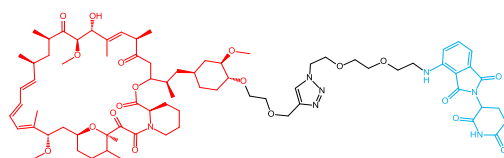
CRBN

NHL (Ramos)

27



RC32

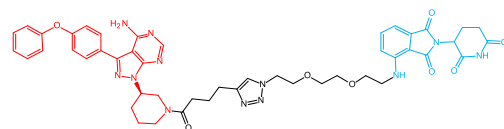


FKBP12

CRBN

28

P13IS

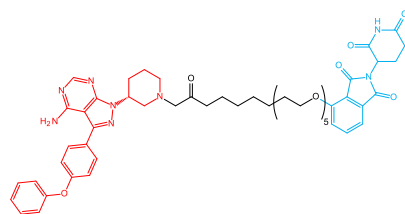


BTK

CRBN

28

NC-1



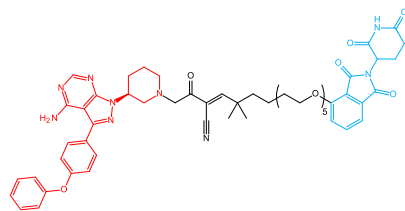
Wild Type BTK
and BTK^{C481S/Y}

CRBN

MCL (Mino),
Osteosarcoma
(U2OS), CLL
(Samples from
patients)

29

RC-3



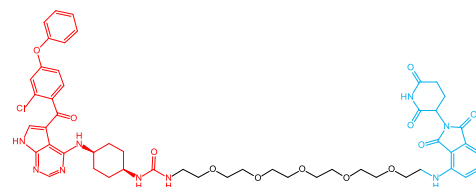
Wild Type BTK
and BTK^{C481S}

CRBN

MCL (Mino),
Osteosarcoma
(U2OS), CLL
(Samples from
patients)

30

6e



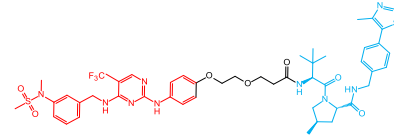
BTK

CRBN

MCL(JeKo-1),
DLBCL (TMD8)

31

PROTAC-3



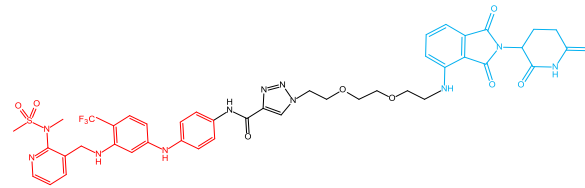
FAK

VHL

PC (PC-3) and
BC (MDA-MB-231)

32

FC-11



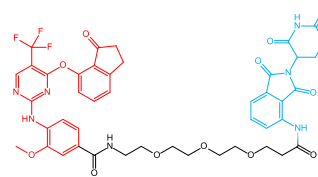
FAK

CRBN

Leydig Cells
(TM3), Primary
Sertoli/Germ Cells

33

PROTAC 6/8



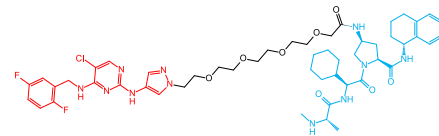
FAK

VHL or CRBN

NSCLC (A549)

34

JP-1 – JP-6

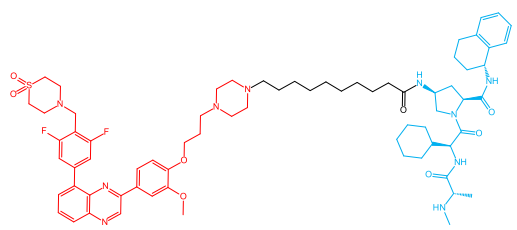
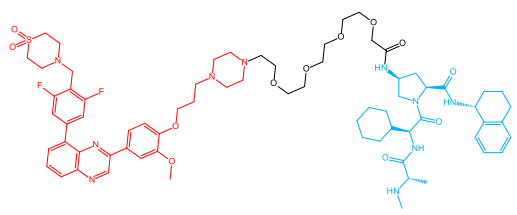
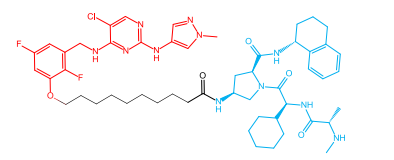
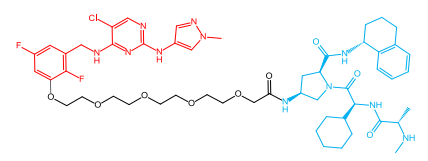
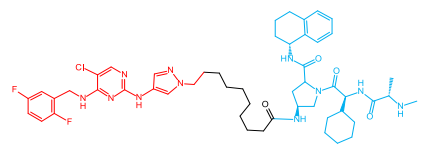


JAK

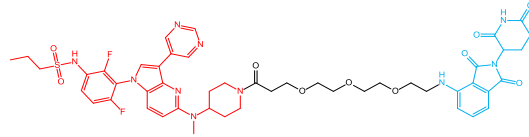
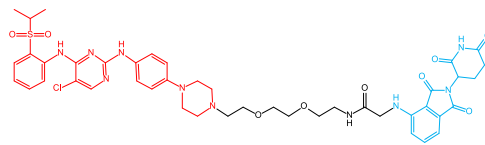
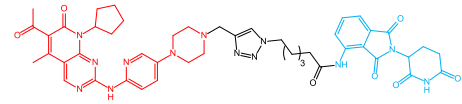
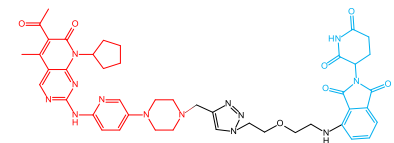
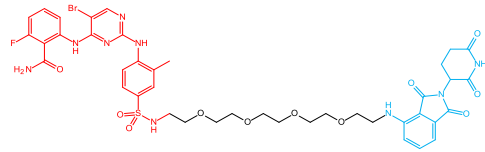
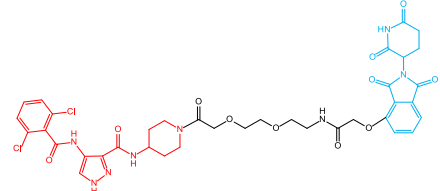
IAP

AML (THP-1)

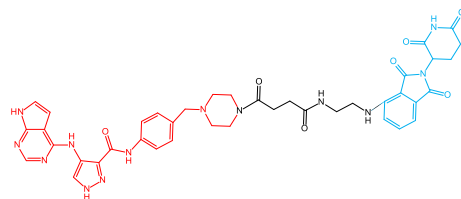
35



SHP2-D26		SHP2	VHL	ESCC (KYSE-520), AML(MV4;11)	36
ZB-S-29		SHP2	CRBN	AML(MV4;11)	37
SJF-0628		BRAF mutations	VHL	Various Cancers	38
P4B		BRAF ^{V600E}	CRBN	MM (A375)	39
Compounds 12/23		BRAF ^{V600E}	CRBN	MM (A375)	40

					
TL12-186		CDK	CRBN	HEK293	41
Pal-pom		CDK4/6	CRBN	BC (MDA-MB-231)	42
CP-10		Wild Type and mutated CDK6	CRBN	MM (MM.1S)	43
TMX-2172		CDK2/4/5/6/7/9	CRBN	Human Ovarian Carcinoma (OVAR8)	44
A9		CDK2	CRBN	PC (PC-3)	45

F3



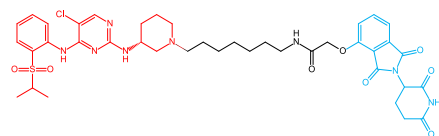
CDK2/9

CRBN

PC (PC-3)

45

BSJ-4-116



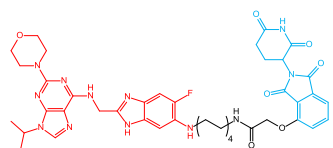
CDK12

CRBN

ALL (Jurkat,
MOLT-4)

46

PP-C8



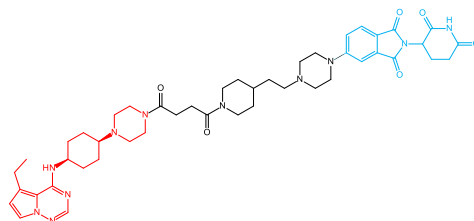
CDK12

CRBN

BC (MDA-MB-
231), HCC (Bel-
7402)

47

PROTAC 23



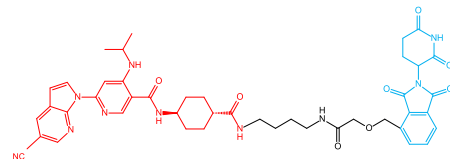
IRAK3

CRBN

AML (THP-1)

48

Degraders 3/5

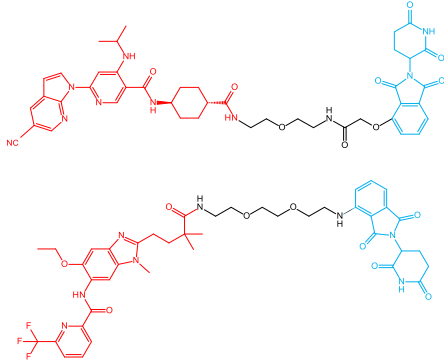
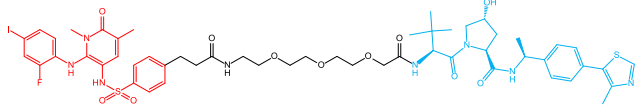
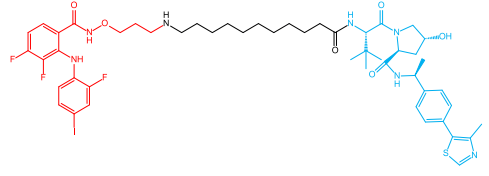
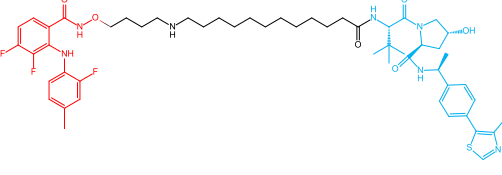


IRAK4

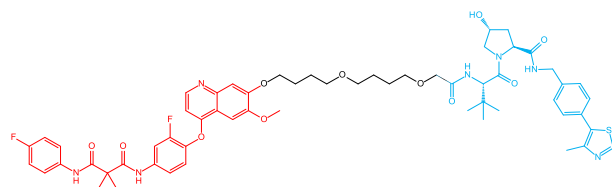
CRBN

AML (THP-1)

49

Compound 9		IRAK4	CRBN	ABC-DLBCL (OCI-LY10, TMD8)	50
Compound 3		MEK	VHK	MM (A375)	51
MS423		MEK	VHL	CRC(HT29) and MM(SK-MEL-28)	52
MS934		MEK	CRBN	CRC(HT29) and MM(SK-MEL-28)	53

SJF α and SJF δ



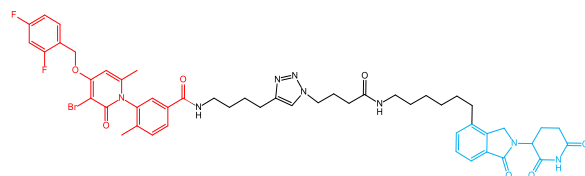
p38 α and p38 δ

VHL

BC (MDA-MB-231)

54

NR-6a and NR-7h



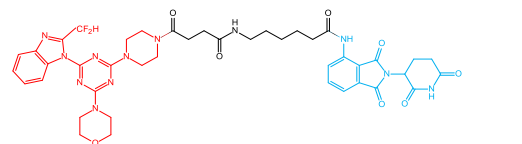
p38 α / β

CRBN

Various Cancers

55

Compound D



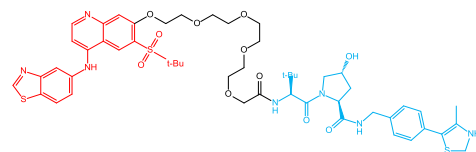
PI3K

CRBN

HCC (HepG2)

56

PROTAC_RIPK2



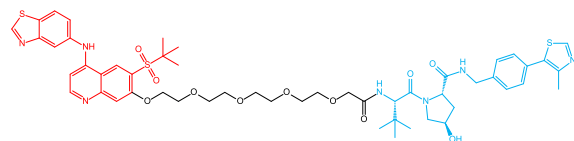
RIPK2

VHL

AML (THP-1)

57

PROTACs 1/2/3



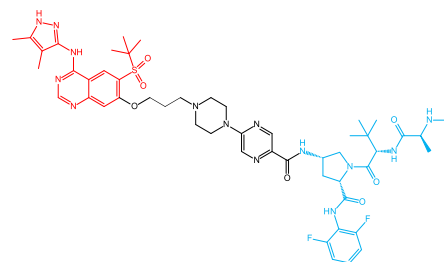
RIPK2

VHL/IAP/CRBN

AML (THP-1)

58

PROTAC 6



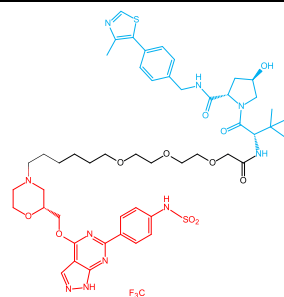
RIPK2

IAP

AML (THP-1)

58

SGK3-
PROTAC1



SGK3

VHL

BC (CAMA-1)

59

ARD-266



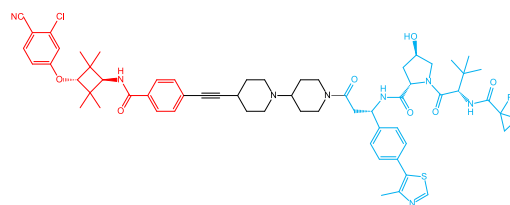
AR

VHL

mCRPC
(LNCaP, VCaP,
22Rv1)

60

ARD-69



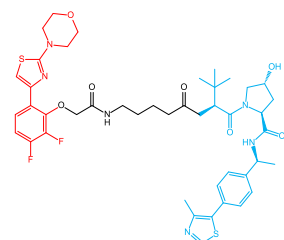
AR

VHL

mCRPC
(LNCaP, VCaP,
22Rv1)

61

MTX-23



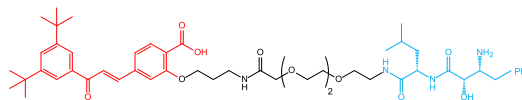
AR

VHL

mCRPC
(LNCaP, VCaP,
22Rv1)

62

SNIPER
Compound 9



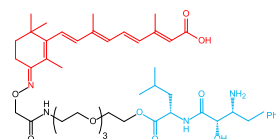
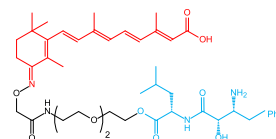
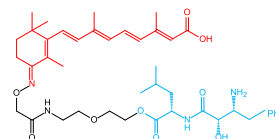
PAR

clAP1

Fibrosarcoma
(HT1080)

63

Compound
4a/4b/4c



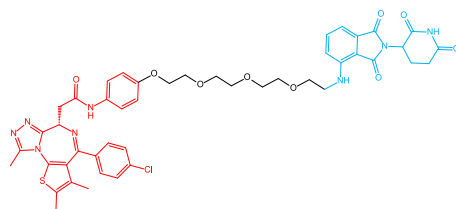
CRABP

clAP1

ALL(MOLT-4),
Fibrosarcoma
(HT1080),
Neuroblastoma
(IMR-32)

64

ARV-825

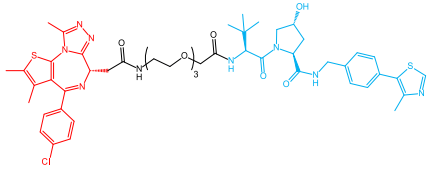
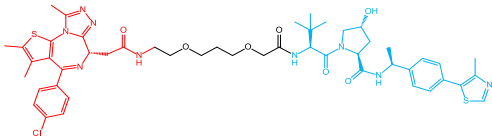
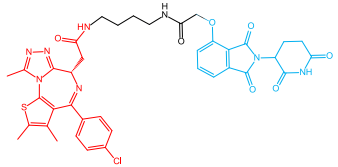
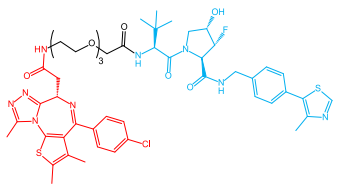
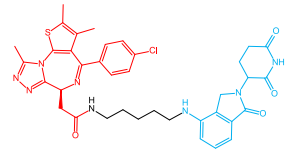


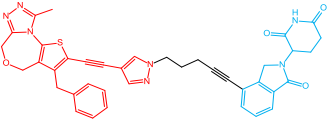
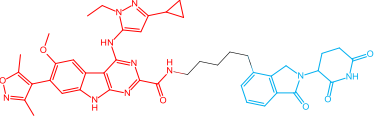
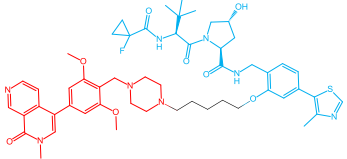
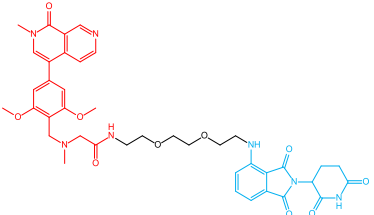
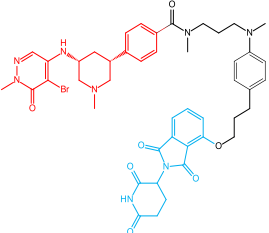
BRD4

CRBN

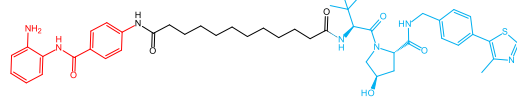
BL (Namalwa),
NHL (Ramos)

65

MZ1		BRD4	VHL	AML(MV4;11)	66-69
ARV-771		BRD2/3/4	VHL	mCRPC (LNCaP95, VCaP, 22Rv1)	70
dBET1		BRD4	CRBN	AML(MV4;11)	71
15a		BRD4	VHL	AML(MV4;11), NSCLC (A549)	72
SIAIS213110		BRD2/3/4	CRBN	MM (MM.1S), AML(MV4;11), TNBC (MDA-MB-468)	73

QCA570		BRD2/3/4	CRBN	ALL (RS4;11), AML(MV4;11)	74
BETd- 260/ZBC260		BRD2/3/4	CRBN	ALL (RS4;11)	75
VZ185		BRD7/9	VHL	AML (EOL-1), Rhabdomyosarcoma (A-204)	76
dBRD9		BRD9	CRBN	AML (EOL-1), ALL (MOLM-13)	77
GSK983		PCAF	CRBN	AML (THP-1)	78

PROTAC 4



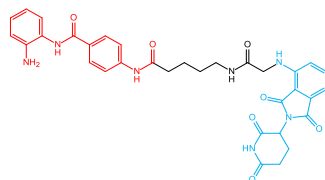
HDAC1/2/3

VHL

E14 mESCs,
CRC (HCT-116)

79

HD-TAC1



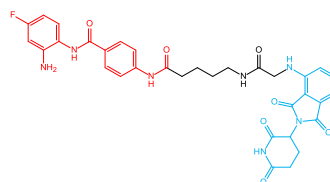
HDAC3

CRBN

Macrophage
(RAW 264.7)

80

HD-TAC7



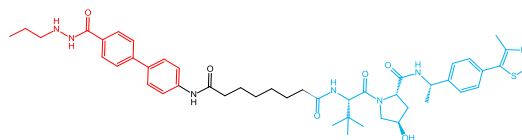
HDAC3

CRBN

Macrophage
(RAW 264.7)

80

XZ9002



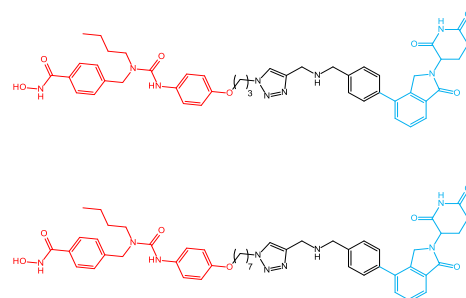
HDAC3

VHL

TNBC (MDA-
MB-468)

81

WH624, YZ268

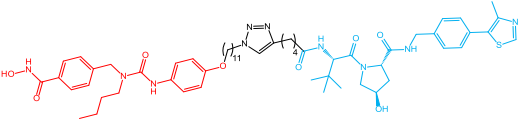
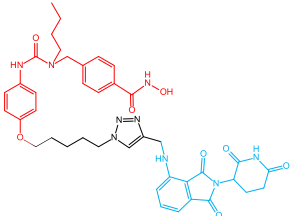
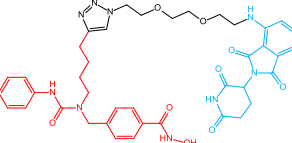
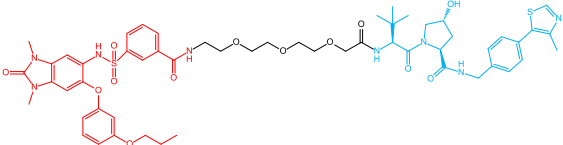
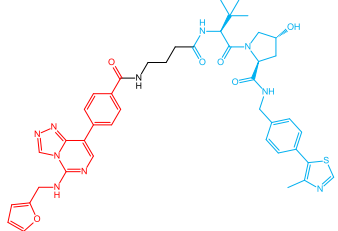


HDAC6

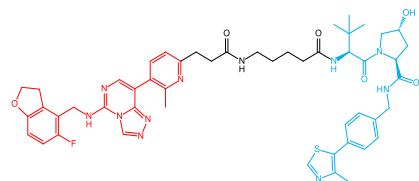
CRBN

MM (MM.1S)

82

Compound 3j		HDAC6	VHL	MM (MM.1S) and Mouse 4935 Cell Line	83
12d		HDAC6	CRBN	MM (MM.1S)	84
NP8		HDAC6	CRBN	MM (MM.1S)	85
dTRIM24		TRIM24	VHL	ALL (MOLM-13)	86
UNC6852		PRC2	VHL	DLBCL (DB, Pfeiffer)	87

PROTAC 1/2



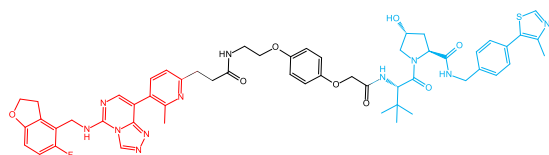
PRC2

VHL

NHL (Karpas-422)

88

SD-36



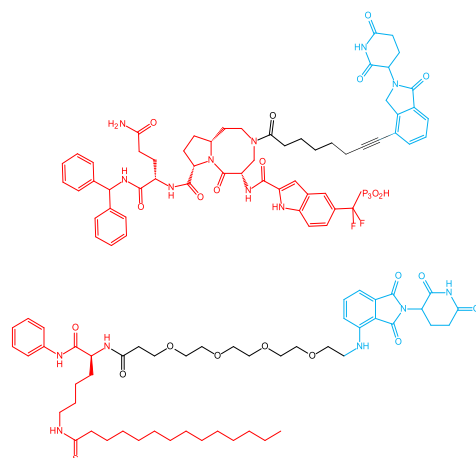
STAT3

CRBN

AML (MOLM-16)

89

TM-P4-Thal



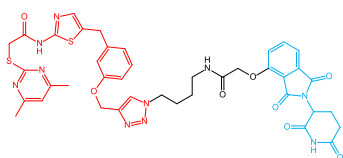
SIRT2

CRBN

BC (MCF-7, BT-549)

90

Compound 12



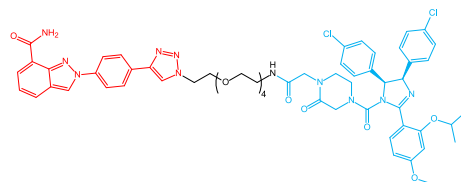
SIRT2

CRBN

Cervical Cancer (HeLa)

91

Compound 3



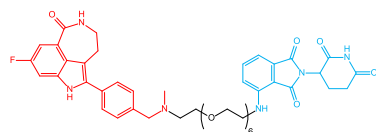
PARP-1

CRBN

BC (MDA-MB-231)

92

iRucaparib-AP6



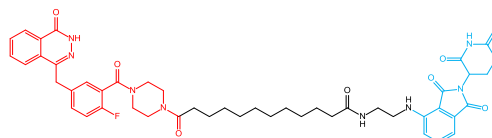
PARP-1

CRBN

Mouse C2C12 Myotubes

93

Degrader SK575



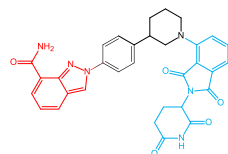
PARP-1

CRBN

CRC (SW620)

94

CN0



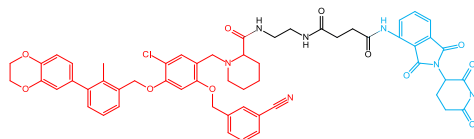
PARP-1

CRBN

BC (MDA-MB-231)

95

P22



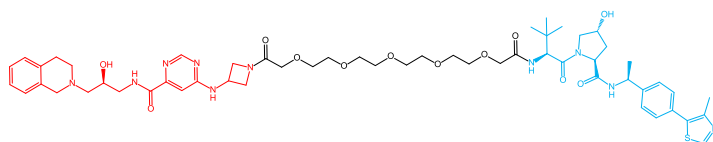
PD-L1

CRBN

BC (MDA-MB-231)

96

Compound 15



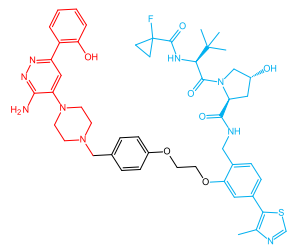
PRMT5

VHL

BC (MCF-7)

97

ACBI1



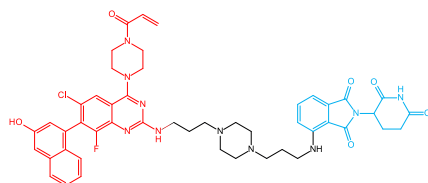
SMARCA2/4,
PBRM1

VHL

AML (MV4;11),
NSCLC (H1568)

98

XY-4-88



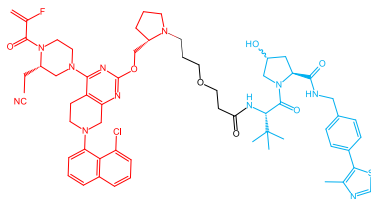
KRASG12C

CRBN

Pancreatic
Cancer (Paca-2),
NSCLC (H358)

99

LC-2



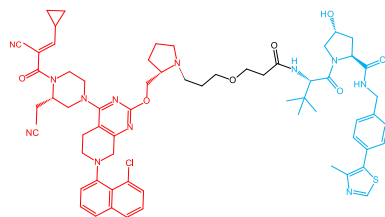
KRASG12C

VHL

NSCLC (H2030,
H23), Pancreatic
Cancer (Paca-2)

100

YF135

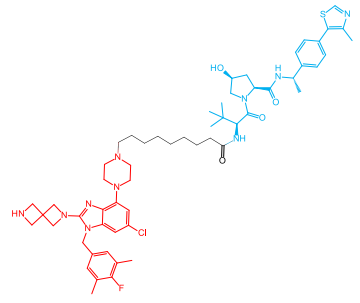
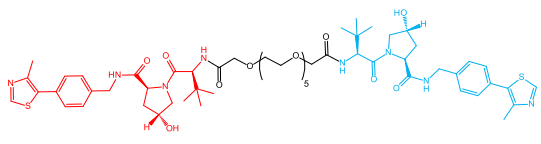
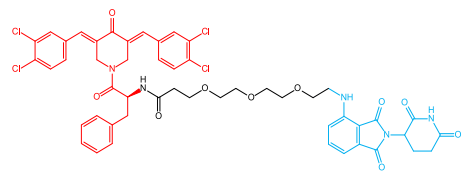
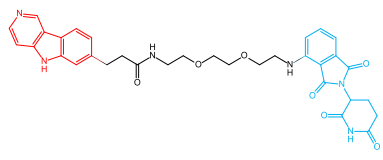
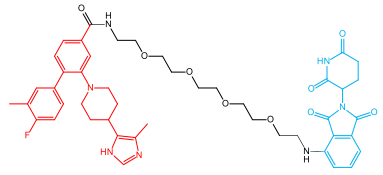


KRAS

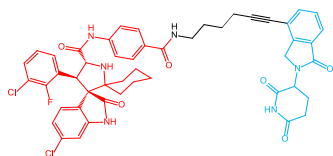
VHL

NSCLC (H358,
A549, H23)

101

9d		SOS1	VHL	NSCLC (H358)	102
CM11		pVHL30	VHL	Cervical Cancer (HeLa), Osteosarcoma (U2OS)	103
WL40		Rpn13	CRBN	MM (MM.1S)	104
QC-01-175		Tau	CRBN	Patient-Derived Frontotemporal Dementia Neuronal Cells (A25T)	105
d9A2		SCL9	CRBN	CML (HAP1, KBM7)	106

MD-224



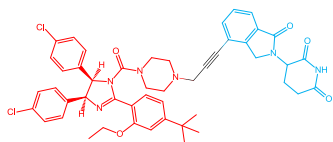
TP53

CRBN

ALL (RS4;11)

107

PROTAC 32



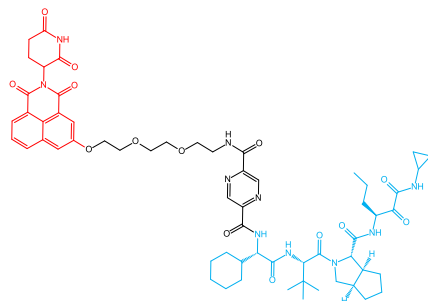
MDM2

CRBN

ALL (RS4;11)

108

DGY-08-097



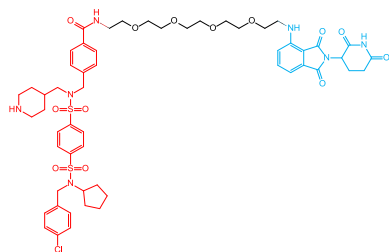
NS3

CRBN

Huh7.5 Cells
Infected with Wild
Type HCV-Jc1

109

PROTACs 3/5

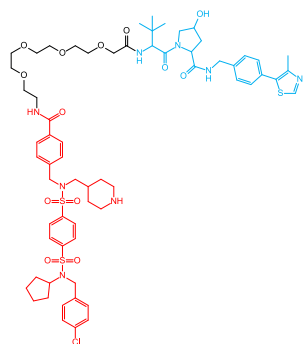


PDEδ

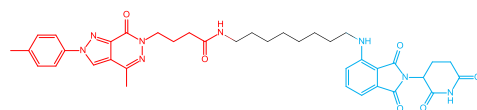
CRBN

ALL (Jurkat)

110



Compound 17f



PDE δ

CRBN

CRC (SW480)

111

ABC-DLBCL, activated B cell-like diffuse large B-cell lymphoma; ALL, acute lymphocytic leukemia; AML, acute myeloid leukemia; BC, breast cancer; BL, Burkitt lymphoma; mESCs, mouse embryonic stem cells; CLL, chronic lymphocytic leukemia; CML, chronic myelogenous leukemia; CRC, colorectal cancer; DLBCL, diffuse large B-cell lymphoma; ESCC, esophageal squamous cell carcinoma; HCC, hepatocellular carcinoma; HUVECs, human umbilical vein endothelial cells; MCL, mantle cell lymphoma, mCRPC, metastatic castration-resistant prostate cancer; MM, multiple myeloma; NHL, non-Hodgkin's lymphoma; NSCLC, non-small-cell Lung cancer; PC, prostate cancer; TNBC, triple-negative breast cancer.

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