pathways is implicated in cancer, autoimmune diseases, rheumatoid arthritis, asthma, diabetes, and other human diseases. *See, e.g.*, Miklossy *et al*., *Nat Rev Drug Discov 12*:611-629 (2013).

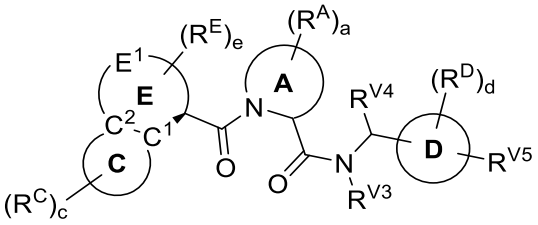
[0006] The STAT protein family is composed of seven members: STAT1, STAT2, STAT3, STAT4, STAT5A, STAT5B, and STAT6. Structurally, they share five domains: an amino-terminal domain, a coiled-coil domain, a DNA-binding domain, an SH2 domain, and a carboxy-terminal transactivation domain. The transactivation domain contains one or two amino acid residues that are crucial for the activity of the STAT protein. In particular, phosphorylation of a particular tyrosine residue promotes dimerization, whereas phosphorylation of a particular serine residue enhances transcriptional activation.

[0007] STAT proteins promote fundamental cellular processes, including cell growth and differentiation, development, apoptosis, immune responses, and inflammation. In particular, STAT3 function may be abnormal in the context of cancer, and this abnormality represents an underlying mechanism of STAT3 for promoting malignant transformation and progression. Constitutively active STAT3 is detected in numerous malignancies, including breast, melanoma, prostate, head and neck squamous cell carcinoma (HNSCC), multiple myeloma, pancreatic, ovarian, and brain tumors. Aberrant STAT3 signaling promotes tumorigenesis and tumor progression partly through dysregulating the expression of critical genes that control cell growth and survival, angiogenesis, migration, invasion, or metastasis. These genes include those that encode $p21^{WAF1/CIP2}$, cyclin D1, MYC, BCL-X, BCL-2, vascular endothelial growth factor (VEGF), matrix metalloproteinase 1 (MMP1), MMP7 and MMP9, and survivin. STAT3 may also play a role in the suppression of tumor immune surveillance. Consequently, the genetic and pharmacological modulation of persistently active STAT3 was shown to control the tumor phenotype and to lead to tumor regression *in vivo*.

[0008] There exists a need in the art for STAT3 inhibitors and STAT3 degraders having physical and pharmacological properties that allow them to be used in therapeutic applications for treating disease.

SUMMARY

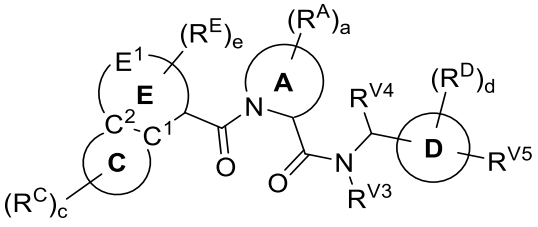
[0009] The present disclosure provides compounds or conjugates of Formula **I**:



(**I**),

and pharmaceutically acceptable salts, solvates, or stereoisomers thereof, wherein each of the variables in Formulae **I** is described, embodied, and exemplified herein.

[0009a] In an aspect, the present disclosure provides a compound of Formula **I**:



(**I**),

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

Ring A is 5- to 7-membered heterocycle;

each R^A is independently oxo, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

a is an integer selected from 0 to 10, as valency permits;

Ring C is C_6 aryl or 5- to 6-membered heteroaryl;

C^1 and C^2 are independently C or N;

each R^C is independently hydrogen, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

c is an integer selected from 0 to 5, as valency permits;

Ring D is C_6 aryl or 5- to 6-membered heteroaryl;

each R^D is independently halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

d is an integer selected from 0 to 4;

Ring E is C_{5-12} carbocycle or 5- to 12-membered heterocycle, wherein the carbocycle or heterocycle is optionally substituted with one or more R^E;

E^1 is $C(R^{E1'})_2$, $NR^{E1''}$, O, or S;

each $R^{E1'}$ is independently halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{3-6} carbocyclyl, or 3- to 6-membered heterocyclyl, wherein the alkyl, alkoxy, alkylamino, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

$R^{E1''}$ is an amino-protecting group, hydrogen, C_{1-6} alkyl, C_{3-6} carbocyclyl, 3- to 6-membered heterocyclyl, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$; wherein the alkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

each R^E is independently oxo, hydrogen, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u; or

two geminal R^E, together with the carbon atom to which they are bonded, form C_{3-6} carbocycle or 3- to 6-membered heterocycle, wherein the carbocycle or heterocycle is optionally substituted with one or more R^u;

e is an integer selected from 0 to 6;

R^{V3} is hydrogen, C_{1-6} alkyl, C_{3-6} carbocyclyl, 3- to 6-membered heterocyclyl, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$; wherein the alkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

R^{V4} is hydrogen, C_{1-6} alkyl, or C_{1-8} heteroalkyl, wherein the alkyl or heteroalkyl is optionally substituted with one or more R^u; and

R^{V5} is hydrogen, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -C(=O)OR^b, or -C(=O)NR^cR^d, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u,

wherein:

each R^u is independently oxo, halogen, -N_3, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -S(=O)R^a, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -C(=O)R^a, -C(=O)OR^b, or -C(=O)NR^cR^d; wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more substituents selected from oxo, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} carbocyclyl, and 3- to 6-membered heterocyclyl; or

two R^u, together with the one or more intervening atoms, form C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl;

each R^a is independently C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl;

each R^b is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl; and

each R^c and R^d is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl; or

R^c and R^d, together with the nitrogen atom to which they are attached, form 3- to 12-membered heterocyclyl,

wherein each occurrence of R^a, R^b, R^c, and R^d is independently and optionally substituted with one or more R^z; and

each R^z is independently oxo, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} carbocyclyl, or 3- to 6-membered heterocyclyl.

[0010] In certain examples, the present disclosure provides pharmaceutical compositions comprising a compound disclosed herein, and a pharmaceutically acceptable excipient.

[0011] In certain examples, the present disclosure provides methods of binding VHL E3 ubiquitin ligase protein complex in a subject or biological sample comprising administering the compound disclosed herein or contacting the biological sample with the compound disclosed herein.

[0012] In certain examples, the present disclosure provides uses of the compound disclosed herein in the manufacture of a medicament for binding VHL E3 ubiquitin ligase protein complex in a subject or biological sample.

[0013] In certain examples, the present disclosure provides compounds disclosed herein for use in binding VHL E3 ubiquitin ligase protein complex in a subject or biological sample.

[0014] In certain examples, the present disclosure provides methods of degrading a protein in a subject or biological sample comprising administering a compound or conjugate disclosed herein to the subject or contacting the biological sample with the compound disclosed herein.

[0015] In certain examples, the present disclosure provides uses of a compound or conjugate disclosed herein in the manufacture of a medicament for degrading a protein in a subject or biological sample.

[0016] In certain examples, the present disclosure provides compounds or conjugates disclosed herein for use in degrading a protein in a subject or biological sample.

[0017] In certain examples, the present disclosure provides methods of treating or preventing a disease or disorder in a subject in need thereof, comprising administering to the subject a compound or conjugate disclosed herein.

[0018] In certain examples, the present disclosure provides methods of treating a disease or disorder in a subject in need thereof, comprising administering to the subject a compound or conjugate disclosed herein.

[0019] In certain examples, the present disclosure provides uses of a compound or conjugate disclosed herein in the manufacture of a medicament for treating or preventing a disease or disorder in a subject in need thereof.

[0020] In certain examples, the present disclosure provides uses of a compound or conjugate disclosed herein in the manufacture of a medicament for treating a disease or disorder in a subject in need thereof.

[0021] In certain examples, the present disclosure provides compounds or conjugates disclosed herein for use in treating or preventing a disease or disorder in a subject in need thereof.

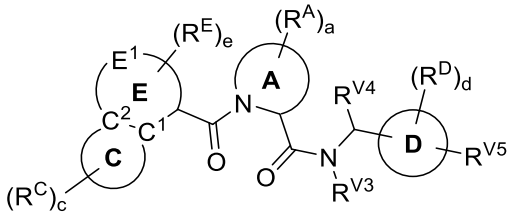
[0022] In certain examples, the present disclosure provides compounds or conjugates disclosed herein for use in treating a disease or disorder in a subject in need thereof.

[0023] In certain examples, the present disclosure provides conjugates of Formula **II**:

T-L-V (II),

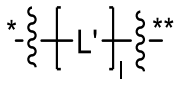
and pharmaceutically acceptable salts, solvates, or stereoisomers thereof, wherein:

V is of Formula **II-1**



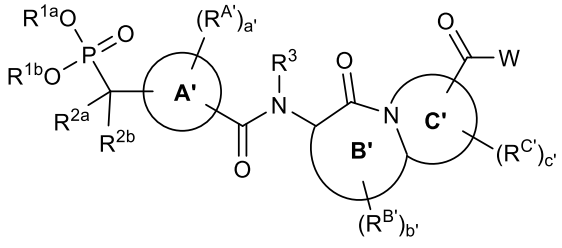
(**II-1**),

L is of Formula **II-2**



(**II-2**), and

T is of Formula **II-3**



(**II-3**),

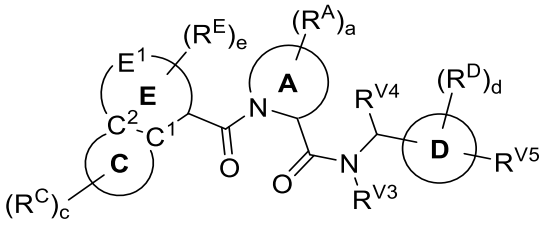
wherein each of the variables in Formulae **II**, **II-1**, **II-2**, and **II-3**, is described, embodied, and exemplified herein.

[0023a] In another aspect, the present disclosure provides a conjugate of Formula **II**:

T-L-V (II),

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

V is of Formula **II-1**



(**II-1**),

wherein:

Ring A is 5- to 7-membered heterocycle;

each R^A is independently oxo, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

a is an integer selected from 0 to 10, as valency permits;

Ring C is C_6 aryl or 5- to 6-membered heteroaryl;

C^1 and C^2 are independently C or N;

each R^C is independently $-\S^{**}$, hydrogen, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

c is an integer selected from 0 to 5, as valency permits;

Ring D is C_6 aryl or 5- to 6-membered heteroaryl;

each R^D is independently $-\S^{**}$, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -

$C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

d is an integer selected from 0 to 4;

Ring E is C_{5-12} carbocycle or 5- to 12-membered heterocycle, wherein the carbocycle or heterocycle is optionally substituted with one or more R^E;

E^1 is $C(R^{E1'})_2$, $NR^{E1''}$, O, or S;

each $R^{E1'}$ is independently halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{3-6} carbocyclyl, or 3- to 6-membered heterocyclyl, wherein the alkyl, alkoxy, alkylamino, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

$R^{E1''}$ is an amino-protecting group, hydrogen, C_{1-6} alkyl, C_{3-6} carbocyclyl, 3- to 6-membered heterocyclyl, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$; wherein the alkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

each R^E is independently $-\S^{**}$, oxo, hydrogen, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u; or

two geminal R^E, together with the carbon atom to which they are bonded, form C_{3-6} carbocycle or 3- to 6-membered heterocycle, wherein the carbocycle or heterocycle is optionally substituted with one or more R^u;

e is an integer selected from 0 to 6;

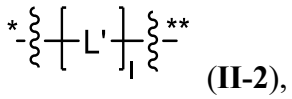
R^{V3} is hydrogen, C_{1-6} alkyl, C_{3-6} carbocyclyl, 3- to 6-membered heterocyclyl, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$; wherein the alkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

R^{V4} is $-\S^{**}$, hydrogen, C_{1-6} alkyl, or C_{1-8} heteroalkyl, wherein the alkyl or heteroalkyl is optionally substituted with one or more R^u; and

R^{V5} is hydrogen, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u,

wherein one of R^C, R^D, R^E and R^{V4} is $-\S^{**}$, and $-\S^{**}$, denotes attachment to **-L-T**,

L is of Formula **II-2**



(**II-2**),

wherein:

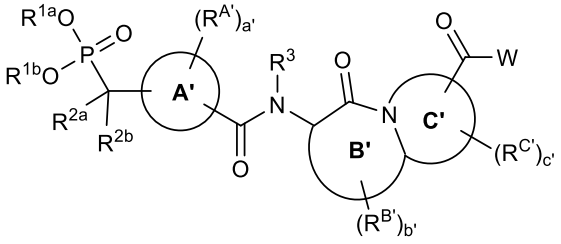
* denotes attachment to **T** and ** denotes attachment to **V**;

each L' is independently C_{1-6} alkylene, C_{1-6} heteroalkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-12} carbocyclylene, 3- to 12-membered heterocyclylene, C_{6-10} arylene, 5- to 10-membered heteroarylene, -C(=O)-, -C(=O)N($R^{L'}$)-, -C(=O)O-, -N($R^{L'}$)-, -O-, -S-, or -S(=O)$_2$-, wherein the alkylene, alkenylene, carbocyclylene, heterocyclylene, arylene, or heteroarylene is optionally substituted with one or more R^u;

each occurrence of $R^{L'}$ is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -S(=O)$_2R^a$, -S(=O)$_2OR^b$, -S(=O)$_2NR^cR^d$, -C(=O)R^a, -C(=O)OR^b, or -C(=O)NR^cR^d, wherein the alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u; and

l is an integer selected from 0 to 6,

T is of Formula **II-3**



(**II-3**),

wherein:

R^{1a} and R^{1b} are independently hydrogen or C_{1-6} alkyl optionally substituted with one or more R^u;

R^{2a} and R^{2b} are independently hydrogen or halogen;

R^{2a} and R^{2b} together form an oxo; or

R^{2a} and R^{2b}, together with the carbon atom to which they are attached, form C_{3-6} carbocycle or 3- to 6-membered heterocycle, wherein the carbocycle or heterocycle is optionally substituted with one or more R^u;

Ring A' is C_{6-10} aryl or 5- to 10-membered heteroaryl;

each $R^{A'}$ is independently halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

a' is an integer selected from 0 to 6, as valency permits;

R^3 is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$, wherein the alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

Ring B' is 3- to 12-membered heterocycle;

each $R^{B'}$ is independently $-\S^{*}$, oxo, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

* denotes attachment to **L**;

b' is an integer selected from 0 to 6, as valency permits;

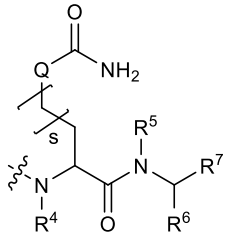
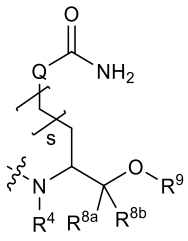
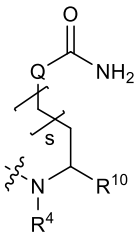
Ring C' is 3- to 8-membered heterocycle;

each $R^{C'}$ is independently oxo, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -

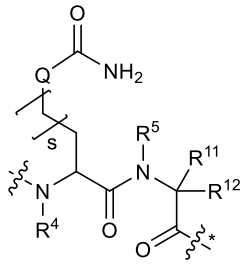
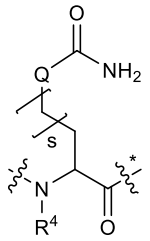
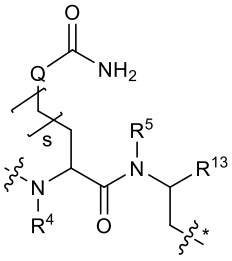
C(=O)NR^{c}R^d, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

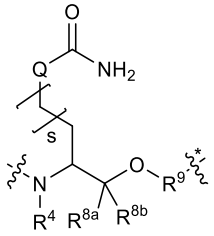
c' is an integer selected from 0 to 6, as valency permits;

W is


(W-1),

(W-2), or

(W-3), or

W is


(W-4)

(W-5),

(W-6), or


(W-7),

wherein:

* denotes attachment to **L**;

Q is absent; or

Q is -C(R^Q)$_2$-, -O-, and -N(R$^{Q'}$)-;

each R^Q is independently hydrogen, halogen, -CN, -NO$_2$, -OH, -NH$_2$, C$_{1-6}$ alkyl, C$_{1-6}$ alkoxy, C$_{1-6}$ alkylamino, C$_{3-6}$ carbocyclyl, or 3- to 6-membered heterocyclyl, wherein the alkyl, alkoxy, alkylamino, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u; or

two R^Q, together with the carbon atom to which they are attached, form C$_{3-6}$ carbocyclyl or 3- to 6-membered heterocyclyl, wherein the carbocyclyl or heterocyclyl is optionally substituted with one or more R^u;

R$^{Q'}$ is hydrogen, C$_{1-6}$ alkyl, C$_{3-6}$ carbocyclyl, 3- to 6-membered heterocyclyl, -S(=O)$_2$R^a, -S(=O)$_2$OR^b, -S(=O)$_2$NR^{c}R^d, -C(=O)R^a, -C(=O)OR^b, or -C(=O)NR^{c}R^d, wherein the alkyl, carbocyclyl or heterocyclyl is optionally substituted with one or more R^u;

s is an integer selected from 0 to 4;

R^4 and R^5 are independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

R^6 and R^7 are independently C_{6-10} aryl or 5- to 10-membered heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more R^{6a} or R^{7a}, respectively;

each R^{6a} and each R^{7a} are independently halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)R^a$, $-NR^cS(=O)_2OR^b$, $-NR^cS(=O)_2NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, $-OS(=O)_2R^a$, $-OS(=O)_2OR^b$, $-OS(=O)_2NR^cR^d$, $-OC(=O)R^a$, $-OC(=O)OR^b$, $-OC(=O)NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

or

R^7 is hydrogen or C_{1-6} alkyl optionally substituted with one or more R^{7b};

each R^{7b} is independently halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

or

R^6 and R^7, together with the carbon atom to which they are attached, form C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

R^{8a} and R^{8b} are independently hydrogen, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkylamino, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

R^9 is C_{6-10} aryl or 5- to 10-membered heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more R^{9a};

each R^{9a} is independently halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

R^{10} is hydrogen, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkylamino, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

R^{11} is hydrogen or C_{1-6} alkyl optionally substituted with one or more R^u;

R^{12} is hydrogen, C_{1-6} alkyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -(C_{1-6} alkylene)-(C_{3-12} carbocyclyl), -(C_{1-6} alkylene)-(3- to 12-membered heterocyclyl), -(C_{1-6} alkylene)-(C_{6-10} aryl), or -(C_{1-6} alkylene)-(5- to 10-membered heteroaryl), wherein the alkyl, alkylene, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^{12a};

each R^{12a} is independently oxo, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

R^{11} and R^{12}, together with the carbon atom to which they are attached, form C_{3-6} carbocyclyl or 3- to 6-membered heterocyclyl, wherein carbocyclyl or heterocyclyl is optionally substituted with one or more R^u; or

R^{11} and R^5, together with the intervening atoms, form 4- to 8-membered heterocyclyl optionally substituted with one or more R^u; and

R^{13} is hydrogen, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to

10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u,

wherein:

each R^u is independently oxo, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)R^a$, $-NR^cS(=O)_2OR^b$, $-NR^cS(=O)_2NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, $-OS(=O)_2R^a$, $-OS(=O)_2OR^b$, $-OS(=O)_2NR^cR^d$, $-OC(=O)R^a$, $-OC(=O)OR^b$, $-OC(=O)NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$; wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more substituents selected from oxo, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} carbocyclyl, and 3- to 6-membered heterocyclyl;

each R^a is independently C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl;

each R^b is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl; and

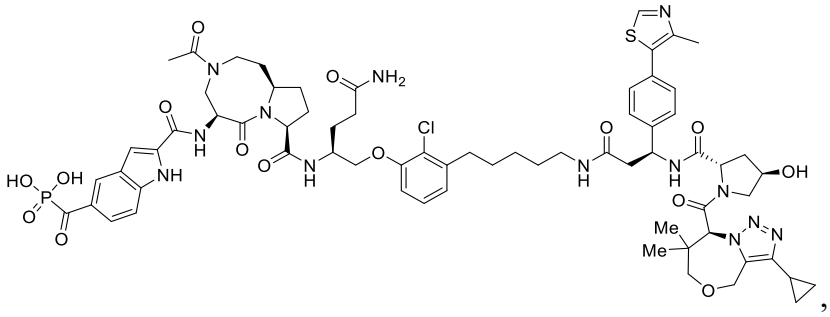
each R^c and R^d is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl; or

R^c and R^d, together with the nitrogen atom to which they are attached, form 3- to 12-membered heterocyclyl,

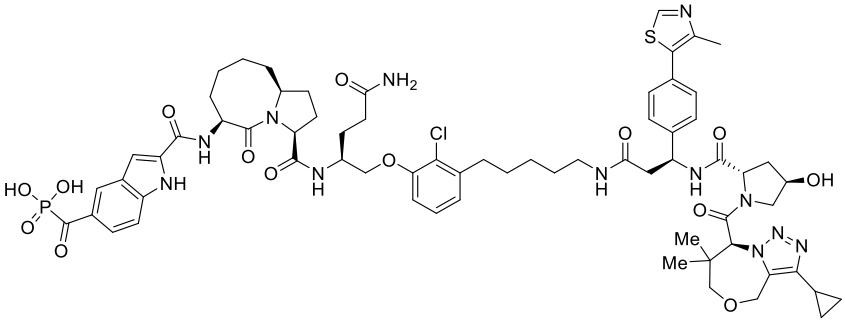
wherein each occurrence of R^a, R^b, R^c, and R^d is independently and optionally substituted with one or more R^z; and

each R^z is independently oxo, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} carbocyclyl, or 3- to 6-membered heterocyclyl.

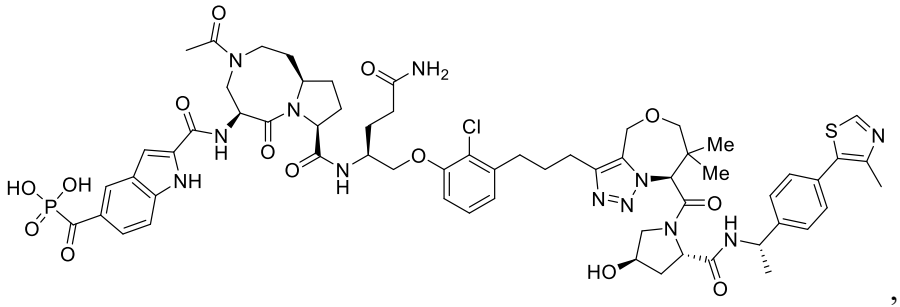
[0023b] In another aspect, the present disclosure provides a conjugate selected from the group consisting of:



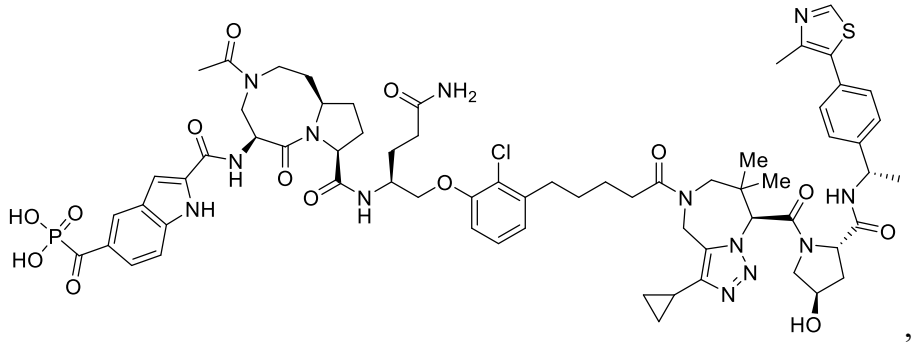
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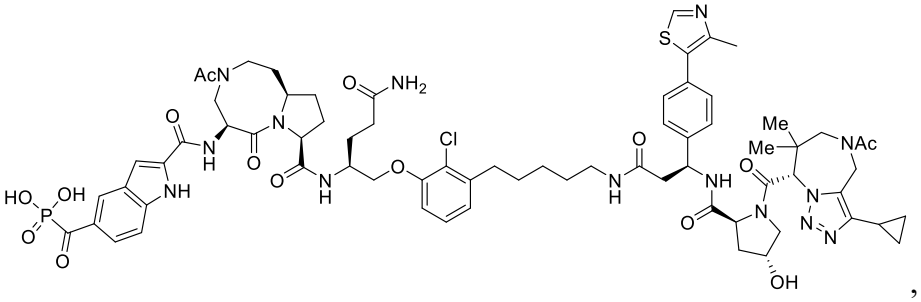
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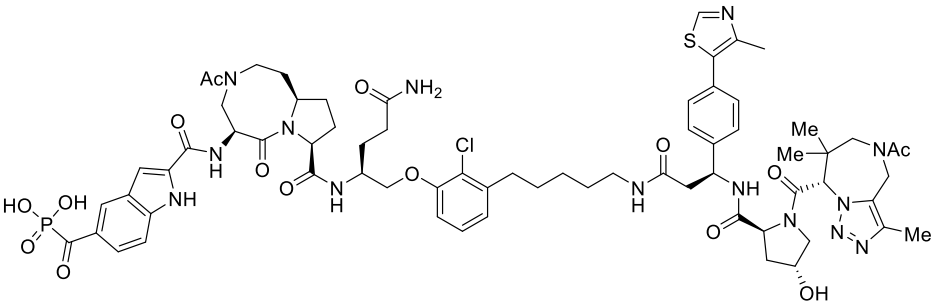
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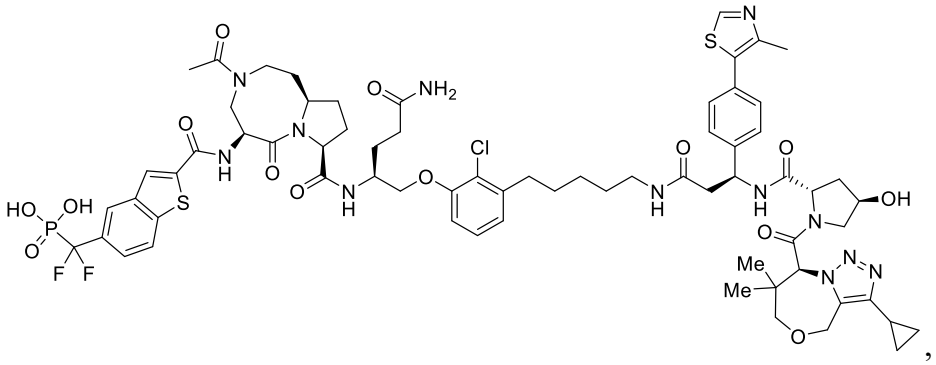
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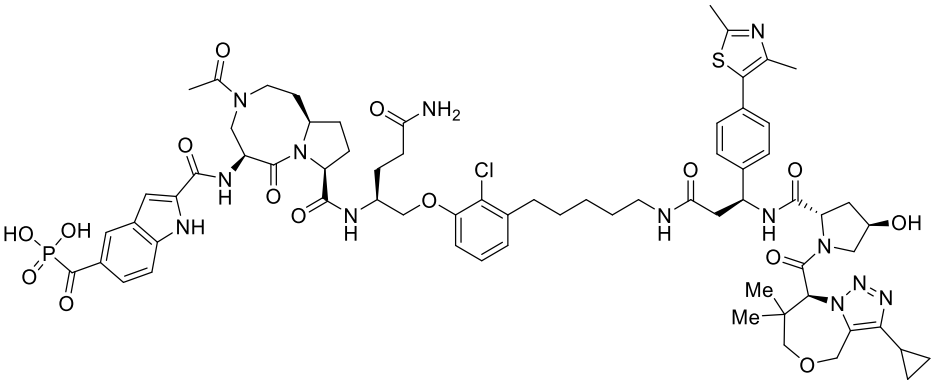
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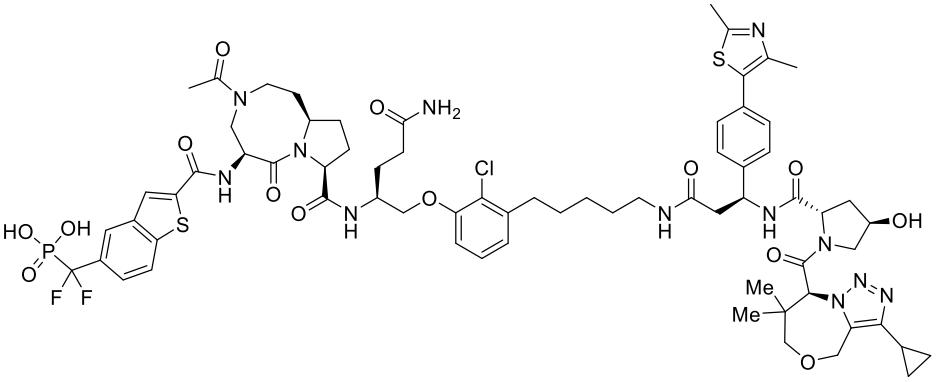
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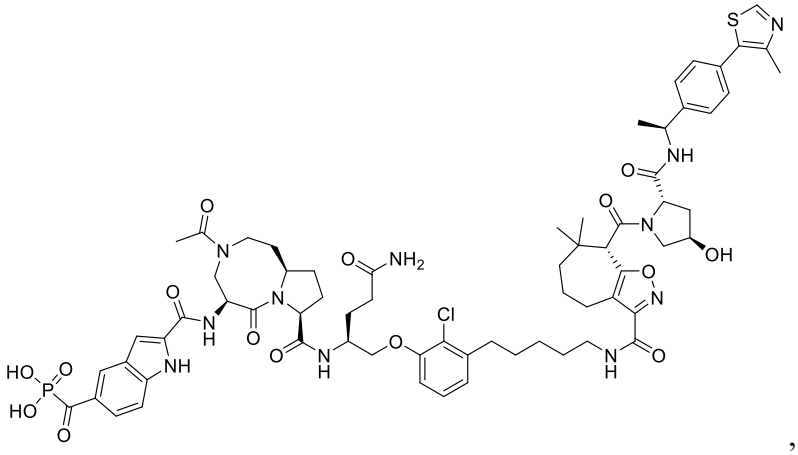
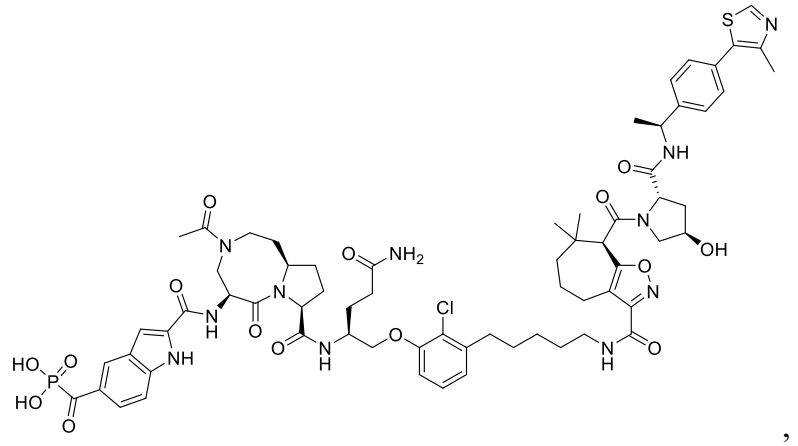
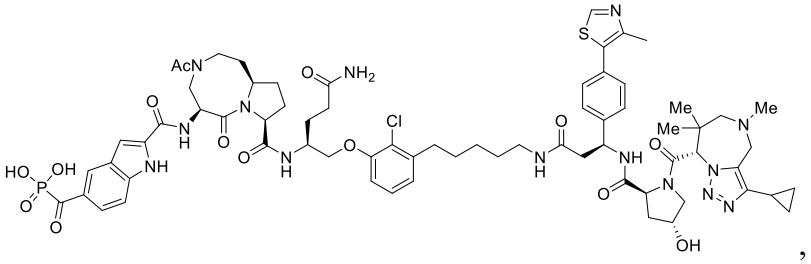
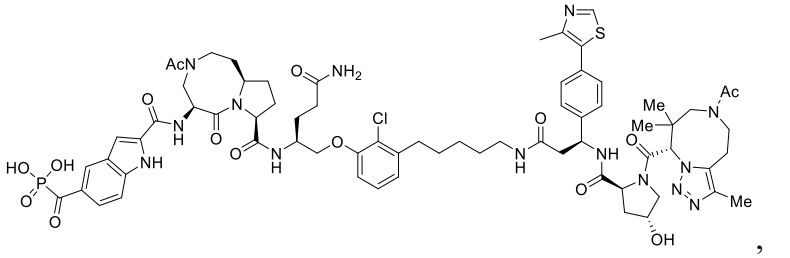
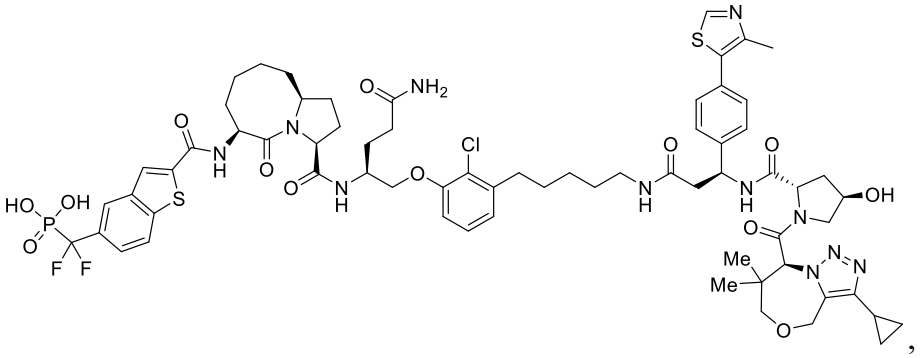
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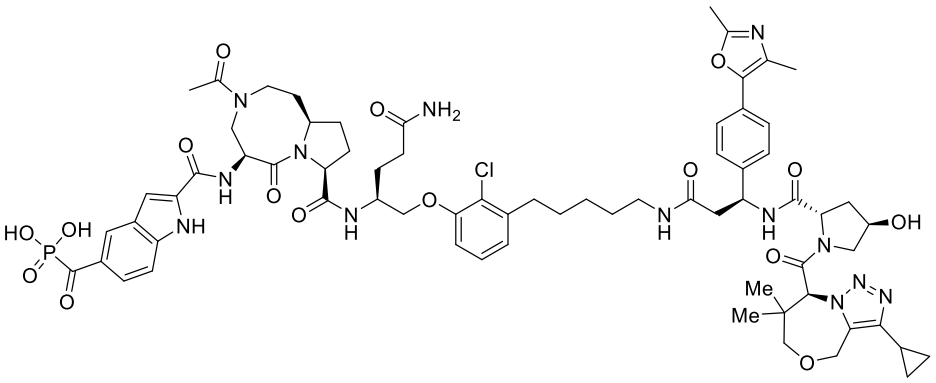


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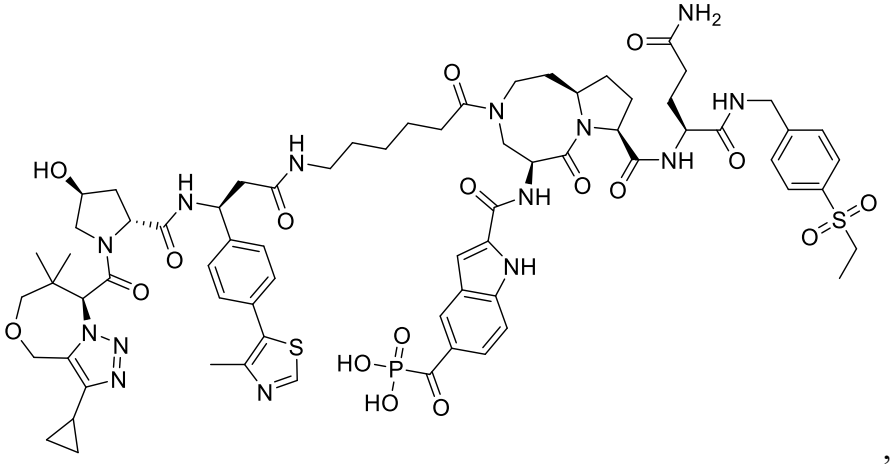


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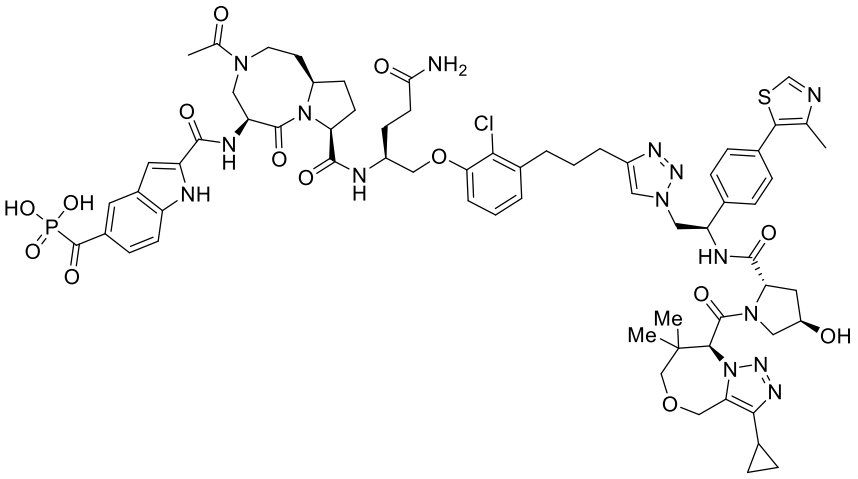

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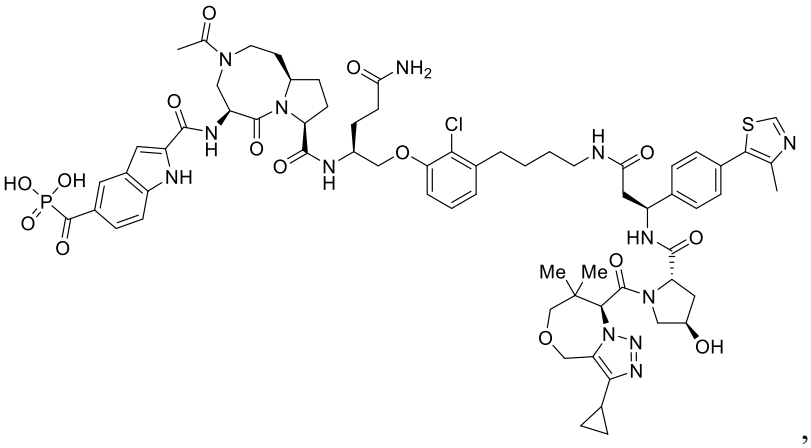
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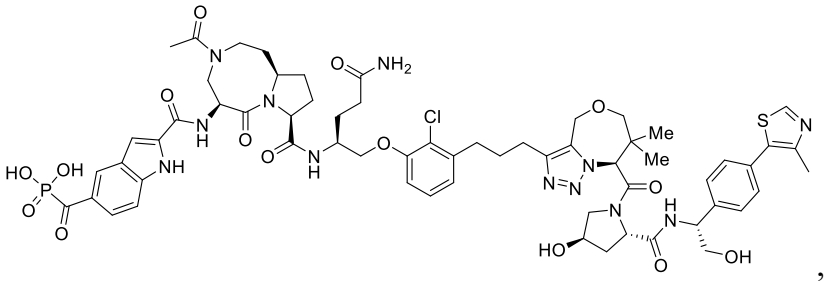
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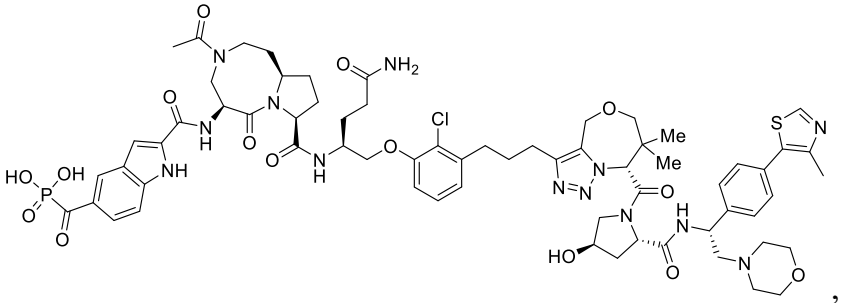
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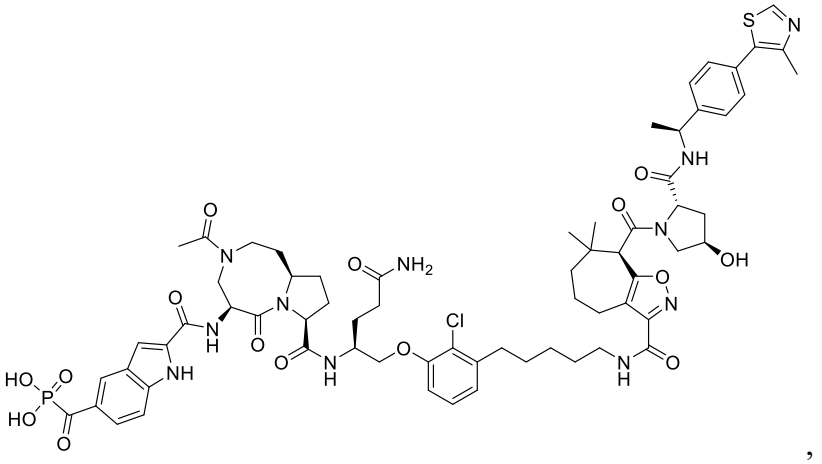
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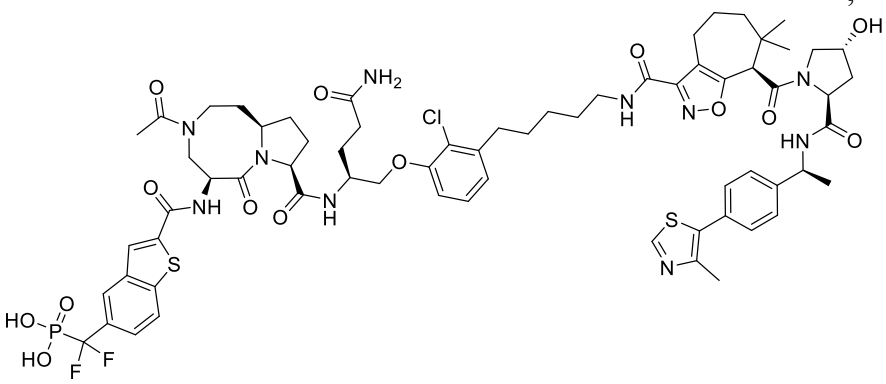
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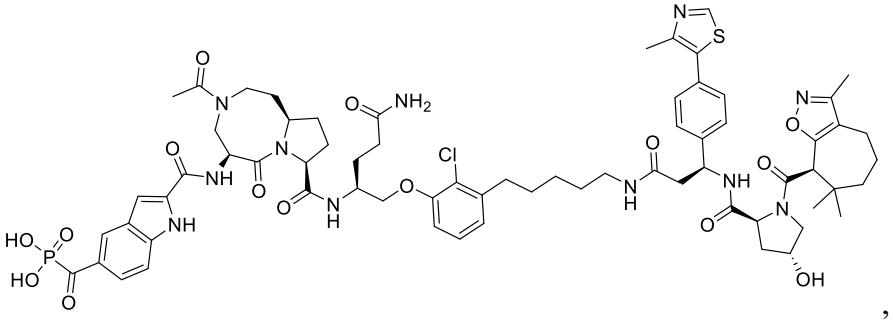
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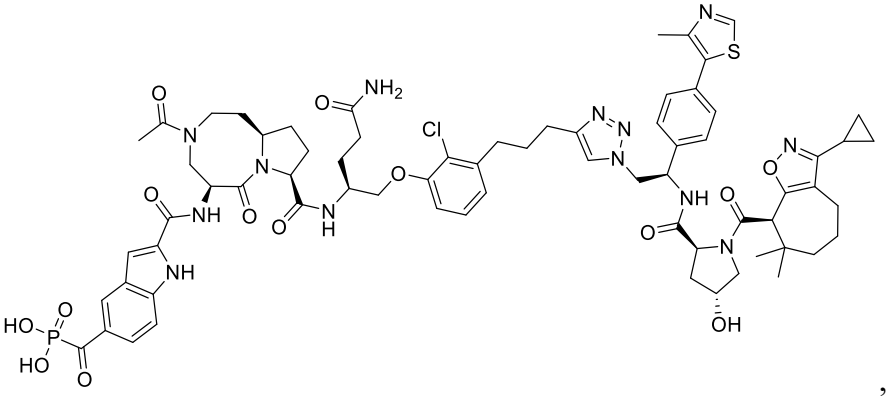
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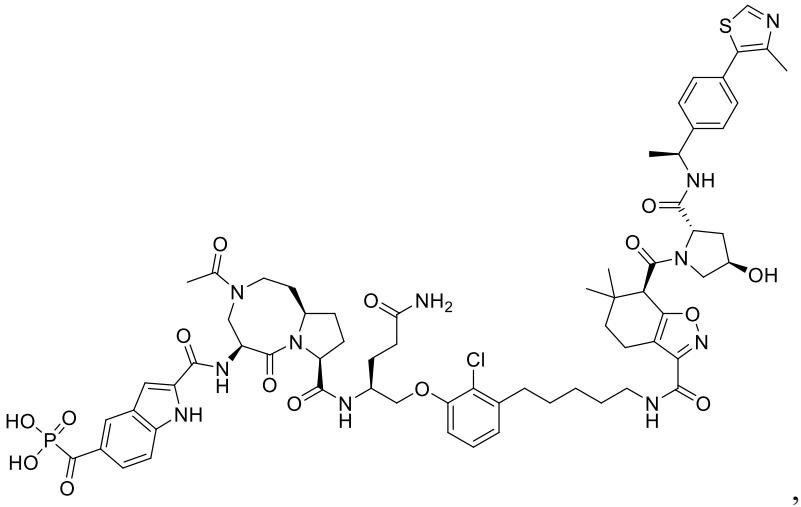
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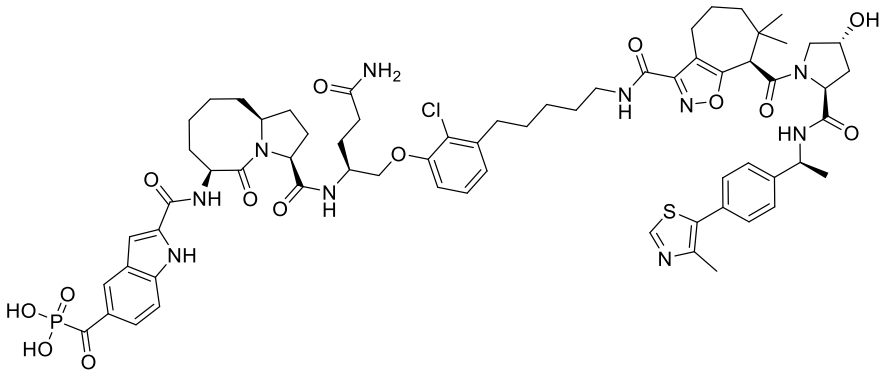
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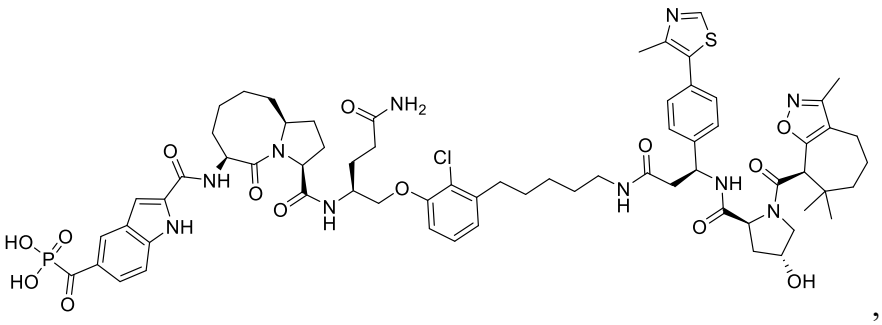
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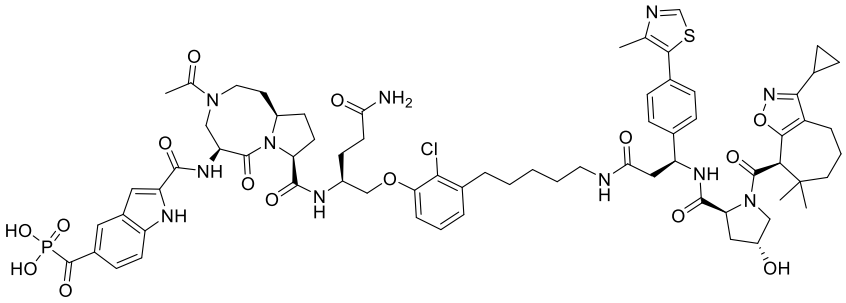
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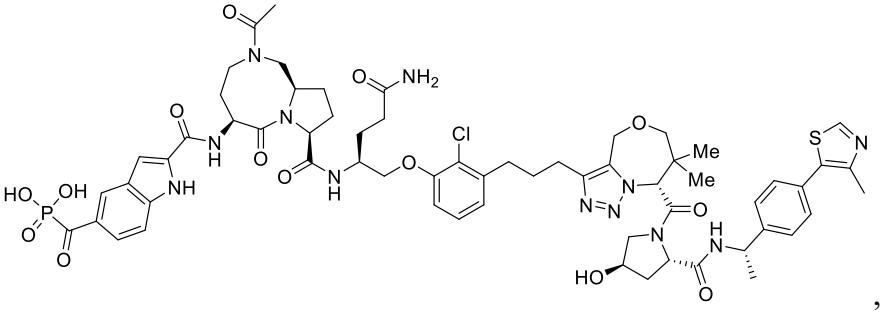
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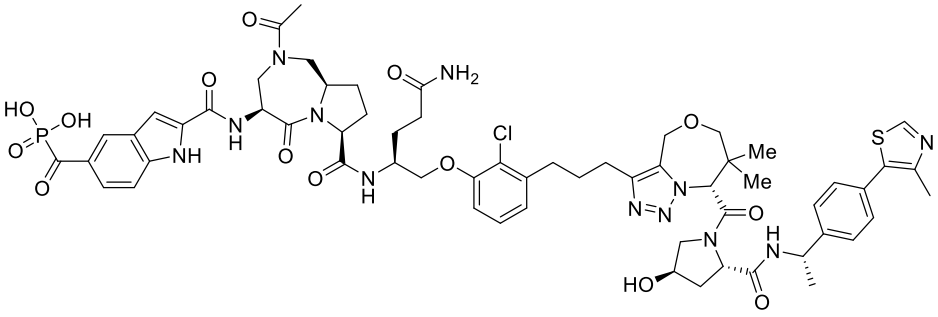
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or a pharmaceutically acceptable salt thereof.

[0024] In certain examples, the present disclosure provides pharmaceutical compositions comprising a conjugate disclosed herein, and a pharmaceutically acceptable excipient.

[0024a] In another aspect, the present disclosure provides a pharmaceutical composition comprising the conjugate as disclosed herein, or a pharmaceutically acceptable salt thereof, and a pharmceutically acceptable excipient.

[0025] In certain examples, the present disclosure provides methods of degrading a protein (*e.g.*, STAT3) in a subject or biological sample comprising administering a conjugate disclosed herein to the subject or contacting the biological sample with the conjugates disclosed herein.

[0026] In certain examples, the present disclosure provides uses of a conjugate disclosed herein in the manufacture of a medicament for degrading a protein (*e.g.*, STAT3) in a subject or biological sample.

[0027] In certain examples, the present disclosure provides conjugates disclosed herein for use in degrading a protein (*e.g.*, STAT3) in a subject or biological sample.

[0028] In certain examples, the present disclosure provides methods of reducing a protein (*e.g.*, STAT3) in a subject or biological sample comprising administering a conjugate disclosed herein to the subject or contacting the biological sample with the conjugate disclosed herein.

[0029] In certain examples, the present disclosure provides uses of a conjugate disclosed herein in the manufacture of a medicament for reducing a protein (*e.g.*, STAT3) in a subject or biological sample.

[0030] In certain examples, the present disclosure provides conjugates disclosed herein for use in reducing a protein (*e.g.*, STAT3) in a subject or biological sample.

[0031] In certain examples, the present disclosure provides methods of treating or preventing a disease or disorder (*e.g.*, a STAT3-mediated disease or disorder) in a subject in need thereof, comprising administering to the subject a conjugate disclosed herein (e.g., in a therapeutically effective amount).

[0032] In certain examples, the present disclosure provides methods of treating a disease or disorder (*e.g.*, a STAT3-mediated disease or disorder) in a subject in need thereof, comprising administering to the subject a conjugate disclosed herein (e.g., in a therapeutically effective amount).

[0033] In certain examples, the present disclosure provides uses of a conjugate disclosed herein in the manufacture of a medicament for treating or preventing a disease or disorder (*e.g.*, a STAT3-mediated disease or disorder) in a subject in need thereof.

[0034] In certain examples, the present disclosure provides uses of a conjugate disclosed herein in the manufacture of a medicament for treating a disease or disorder (*e.g.*, a STAT3-mediated disease or disorder) in a subject in need thereof.

[0034a] In another aspect, the present disclosure provides use of a conjugate as disclosed herein in the manufacture of a medicament for treating a STAT3-mediated disease or disorder in a patient in need thereof, wherein the STAT3-mediated disease or disorder is cancer, an autoimmune disease, an inflammatory disorder, a neurodegenerative disease, a viral disease, a hereditary disorder, a hormone-related disease, a metabolic disorder, a condition associated

with organ transplantation, an immunodeficiency disorder, a destructive bone disorder, a proliferative disorder, an infectious disease, a condition associated with cell death, thrombin-induced platelet aggregation, liver disease, a pathologic immune condition involving T cell activation, a cardiovascular disorder, or a CNS disorder.

[0035] In certain examples, the present disclosure provides conjugates disclosed herein for use in treating or preventing a disease or disorder (*e.g.*, a STAT3-mediated disease or disorder) in a subject in need thereof.

[0036] In certain examples, the present disclosure provides conjugates disclosed herein for use in treating a disease or disorder (*e.g.*, a STAT3-mediated disease or disorder) in a subject in need thereof.

DESCRIPTION OF THE DRAWINGS

[0037] FIG. 1 is a graph showing antitumor activity (SUP-M2 tumor growth) of STAT3 degrader **B1** in SUP-M2 lymphoma xenograft models in SCID mice.

[0038] FIG. 2 is a graph showing antitumor activity (SUP-M2 body weight) of STAT3 degrader **B1** in SUP-M2 lymphoma xenograft models in SCID mice.

[0039] FIG. 3 is a graph showing antitumor activity (SU-DHL-1 tumor growth) of STAT3 degrader **B3** in SU-DHL-1 lymphoma xenograft models in SCID mice.

[0040] FIG. 4 is a graph showing antitumor activity (SU-DHL-1 body weight) of STAT3 degrader **B3** in SU-DHL-1 lymphoma xenograft models in SCID mice.

[0041] FIG. 5 is a graph showing antitumor activity (SUP-M2 tumor growth) of STAT3 degrader **B3** in SUP-M2 lymphoma xenograft models in SCID mice.

[0042] FIG. 6 is a graph showing antitumor activity (SUP-M2 body weight) of STAT3 degrader **B3** in SUP-M2 lymphoma xenograft models in SCID mice.

[0043] FIG. 7 is a graph showing antitumor activity (MDA-MB-468 tumor growth) of STAT3 degrader **B3** in the MDA-MB-468 triple-negative breast cancer model.

DETAILED DESCRIPTION

[0044] The present disclosure relates to compounds that show VHL E3 ubiquitin ligase protein complex-binding activity, bifunctional degraders comprising a VHL E3 ubiquitin ligase protein complex-binding moeity, and pharmaceutical compositions comprising such compounds or bifunctional degraders. The present disclosure further relates to methods of binding VHL E3 ubiquitin ligase protein complex in a subject or biological sample comprising administering a compound described herein to the subject or contacting the biological sample with a compound described herein. The present disclosure further relates to methods of degrading a protein in a subject or biological sample comprising administering a compound described herein to the subject or contacting the biological sample with a compound described herein. The present disclosure also relates to methods of treating or preventing a disease or disorder a subject in need thereof, comprising administering to the subject a compound described herein.

[0045] The present disclosure further relates to conjugates that may be useful as degraders for certain proteins (*e.g.*, STAT3). The present disclosure also relates to methods of degrading certain proteins (*e.g.*, STAT3) comprising contacting the STAT3 protein with a

CLAIMS

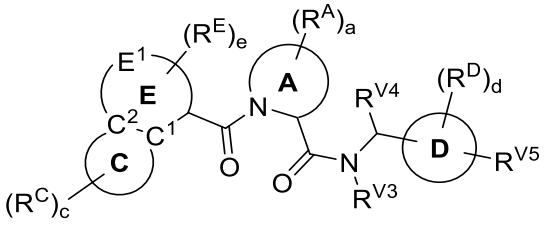
WHAT IS CLAIMED IS:

1. A conjugate of Formula **II**:

T-L-V (II),

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

V is of Formula **II-1**



(**II-1**),

wherein:

Ring A is 5- to 7-membered heterocycle;

each R^A is independently oxo, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

a is an integer selected from 0 to 10, as valency permits;

Ring C is C_6 aryl or 5- to 6-membered heteroaryl;

C^1 and C^2 are independently C or N;

each R^C is independently $-\S^{**}$, hydrogen, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

c is an integer selected from 0 to 5, as valency permits;

Ring D is C_6 aryl or 5- to 6-membered heteroaryl;

each R^D is independently $-\S^{**}$, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl,

C_{6-10} aryl, 5- to 10-membered heteroaryl, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)R^a$, $-NR^cS(=O)_2OR^b$, $-NR^cS(=O)_2NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, $-OS(=O)_2R^a$, $-OS(=O)_2OR^b$, $-OS(=O)_2NR^cR^d$, $-OC(=O)R^a$, $-OC(=O)OR^b$, $-OC(=O)NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

d is an integer selected from 0 to 4;

Ring E is C_{5-12} carbocycle or 5- to 12-membered heterocycle, wherein the carbocycle or heterocycle is optionally substituted with one or more R^E;

E^1 is $C(R^{E1'})_2$, $NR^{E1''}$, O, or S;

each $R^{E1'}$ is independently halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{3-6} carbocyclyl, or 3- to 6-membered heterocyclyl, wherein the alkyl, alkoxy, alkylamino, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

$R^{E1''}$ is an amino-protecting group, hydrogen, C_{1-6} alkyl, C_{3-6} carbocyclyl, 3- to 6-membered heterocyclyl, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$; wherein the alkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

each R^E is independently $-\S^{**}$, oxo, hydrogen, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u; or

two geminal R^E, together with the carbon atom to which they are bonded, form C_{3-6} carbocycle or 3- to 6-membered heterocycle, wherein the carbocycle or heterocycle is optionally substituted with one or more R^u;

e is an integer selected from 0 to 6;

R^{V3} is hydrogen, C_{1-6} alkyl, C_{3-6} carbocyclyl, 3- to 6-membered heterocyclyl, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$; wherein the alkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

R^{V4} is $-\S^{**}$, hydrogen, C_{1-6} alkyl, or C_{1-8} heteroalkyl, wherein the alkyl or heteroalkyl is optionally substituted with one or more R^u; and

R^{V5} is hydrogen, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to

10-membered heteroaryl, -C(=O)OR^b, or -C(=O)NR^{c}R^d, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u,

wherein one of R^C, R^D, R^E and R^{V4} is $-\!\!\!

R^{2a} and R^{2b}, together with the carbon atom to which they are attached, form C_{3-6} carbocycle or 3- to 6-membered heterocycle, wherein the carbocycle or heterocycle is optionally substituted with one or more R^u;

Ring A' is C_{6-10} aryl or 5- to 10-membered heteroaryl;

each $R^{A'}$ is independently halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)R^a$, $-NR^cS(=O)_2OR^b$, $-NR^cS(=O)_2NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, $-OS(=O)_2R^a$, $-OS(=O)_2OR^b$, $-OS(=O)_2NR^cR^d$, $-OC(=O)R^a$, $-OC(=O)OR^b$, $-OC(=O)NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

a' is an integer selected from 0 to 6, as valency permits;

R^3 is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

Ring B' is 3- to 12-membered heterocycle;

each $R^{B'}$ is independently $-\S^{*}_{\S}$, oxo, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)R^a$, $-NR^cS(=O)_2OR^b$, $-NR^cS(=O)_2NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, $-OS(=O)_2R^a$, $-OS(=O)_2OR^b$, $-OS(=O)_2NR^cR^d$, $-OC(=O)R^a$, $-OC(=O)OR^b$, $-OC(=O)NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

* denotes attachment to **L**;

b' is an integer selected from 0 to 6, as valency permits;

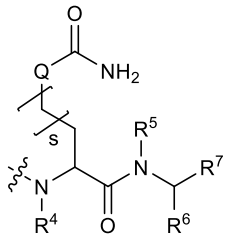
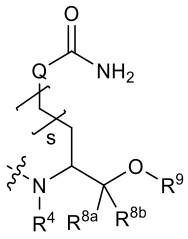
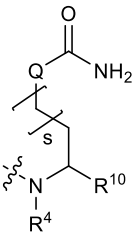
Ring C' is 3- to 8-membered heterocycle;

each $R^{C'}$ is independently oxo, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, -

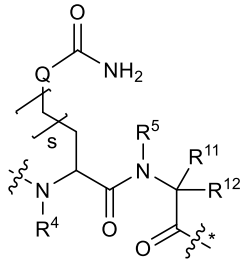
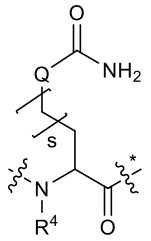
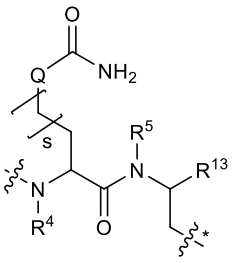
$S(=O)_2NR^cR^d$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)R^a$, $-NR^cS(=O)_2OR^b$, $-NR^cS(=O)_2NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, $-OS(=O)_2R^a$, $-OS(=O)_2OR^b$, $-OS(=O)_2NR^cR^d$, $-OC(=O)R^a$, $-OC(=O)OR^b$, $-OC(=O)NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

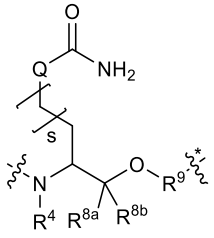
c' is an integer selected from 0 to 6, as valency permits;

W is


(W-1),

(W-2), or

(W-3), or

W is


(W-4)

(W-5),

(W-6), or


(W-7),

wherein:

* denotes attachment to **L**;

Q is absent; or

Q is $-C(R^Q)_2-$, -O-, and $-N(R^{Q'})-$;

each R^Q is independently hydrogen, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{3-6} carbocyclyl, or 3- to 6-membered heterocyclyl, wherein the alkyl, alkoxy, alkylamino, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u; or

two R^Q, together with the carbon atom to which they are attached, form C_{3-6} carbocyclyl or 3- to 6-membered heterocyclyl, wherein the carbocyclyl or heterocyclyl is optionally substituted with one or more R^u;

$R^{Q'}$ is hydrogen, C_{1-6} alkyl, C_{3-6} carbocyclyl, 3- to 6-membered heterocyclyl, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, carbocyclyl or heterocyclyl is optionally substituted with one or more R^u;

s is an integer selected from 0 to 4;

R^4 and R^5 are independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

R^6 and R^7 are independently C_{6-10} aryl or 5- to 10-membered heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more R^{6a} or R^{7a}, respectively;

each R^{6a} and each R^{7a} are independently halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)R^a$, $-NR^cS(=O)_2OR^b$, $-NR^cS(=O)_2NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, $-OS(=O)_2R^a$, $-OS(=O)_2OR^b$, $-OS(=O)_2NR^cR^d$, $-OC(=O)R^a$, $-OC(=O)OR^b$, $-OC(=O)NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

or

R^7 is hydrogen or C_{1-6} alkyl optionally substituted with one or more R^{7b};

each R^{7b} is independently halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

or

R^6 and R^7, together with the carbon atom to which they are attached, form C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

R^{8a} and R^{8b} are independently hydrogen, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkylamino, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

R^9 is C_{6-10} aryl or 5- to 10-membered heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more R^{9a};

each R^{9a} is independently halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

R^{10} is hydrogen, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkylamino, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

R^{11} is hydrogen or C_{1-6} alkyl optionally substituted with one or more R^u;

R^{12} is hydrogen, C_{1-6} alkyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -(C_{1-6} alkylene)-(C_{3-12} carbocyclyl), -(C_{1-6} alkylene)-(3- to 12-membered heterocyclyl), -(C_{1-6} alkylene)-(C_{6-10} aryl), or -(C_{1-6} alkylene)-(5- to 10-membered heteroaryl), wherein the alkyl, alkylene, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^{12a};

each R^{12a} is independently oxo, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

R^{11} and R^{12}, together with the carbon atom to which they are attached, form C_{3-6} carbocyclyl or 3- to 6-membered heterocyclyl, wherein carbocyclyl or heterocyclyl is optionally substituted with one or more R^u; or

R^{11} and R^5, together with the intervening atoms, form 4- to 8-membered heterocyclyl optionally substituted with one or more R^u; and

R^{13} is hydrogen, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u,

wherein:

each R^u is independently oxo, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$; wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more substituents selected from oxo, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} carbocyclyl, and 3- to 6-membered heterocyclyl;

each R^a is independently C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl;

each R^b is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl; and

each R^c and R^d is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl; or

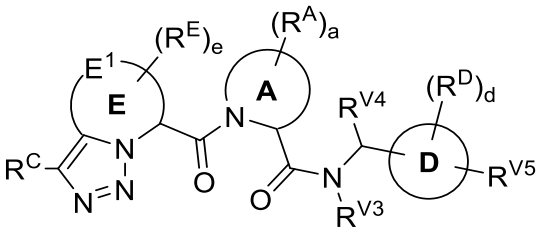
R^c and R^d, together with the nitrogen atom to which they are attached, form 3- to 12-membered heterocyclyl,

wherein each occurrence of R^a, R^b, R^c, and R^d is independently and optionally substituted with one or more R^z; and

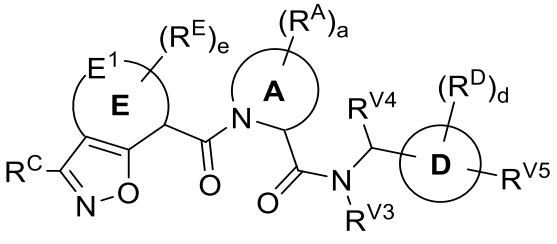
each R^z is independently oxo, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} carbocyclyl, or 3- to 6-membered heterocyclyl.

2. The conjugate of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

V is Formula **II-1-i** or Formula **II-1-ii:**

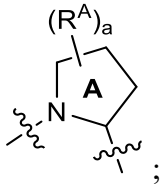


(**II-1-i**)



(**II-1-ii**),

Ring A is:



;

R^A is -OH;

a is 1 or 2;

R^C is $-\overset{**}{\S}$, hydrogen, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} carbocyclyl, or 3- to 6-membered heterocyclyl, wherein the alkyl, alkoxy, alkylamino, carbocyclyl, or heterocyclyl, is optionally substituted with one or more R^u; or

d is 0 or 1;

Ring E is C_{5-12} carbocycle or 5- to 12-membered heterocycle, wherein the carbocycle or heterocycle is optionally substituted with one or more R^E;

E^1 is $C(R^{E1'})_2$, $NR^{E1''}$, or O;

$R^{E1'}$ is hydrogen or C_{1-6} alkyl;

$R^{E1''}$ is hydrogen, C_{1-6} alkyl, or -C(=O)R^a;

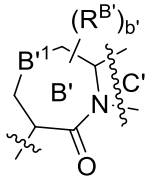
each R^E is independently $-\overset{**}{\S}$ hydrogen, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, or C_{1-6} alkoxy; or

two geminal R^E, together with the carbon atom to which they are bonded, form C_{3-6} carbocycle; or

e is an integer selected from 2 to 6;

R^{V3} is hydrogen or C_{1-6} alkyl, wherein the alkyl is optionally substituted with one or more R^u;

R^{V4} is $-\!\!\!



,

B'^1 is -$NHCH_2$-, -CH_2NH-, or -CH_2CH_2-.

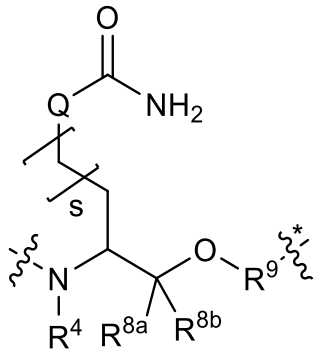
$R^{B'}$ is -C(=O)R^a,

b' is 0 or 1;

Ring C' is 4- to 7-membered heterocycle;

c' is 0;

W is:



(W-7);

wherein:

* denotes attachment to **L**;

Q is absent;

s is 1;

R^4 is hydrogen;

R^{8a} and R^{8b} are both hydrogen;

R^9 is C_{6-10} aryl or 5- to 10-membered heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more R^{9a};

each R^{9a} is independently halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl; and

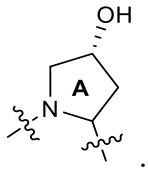
each R^u is independently halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more substituents selected from oxo, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} carbocyclyl, and 3- to 6-membered heterocyclyl.

3. The conjugate of claim 2, wherein each R^E is independently hydrogen or C_{1-6} alkyl, wherein the alkyl is optionally substituted with one or more R^u.

4. The conjugate of claim 2, wherein $R^{E1'}$ is hydrogen or C_{1-6} alkyl, and $R^{E1''}$ is hydrogen, C_{1-6} alkyl, or -C(=O)R^a.

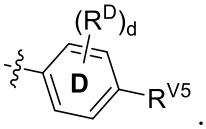
5. The conjugate of claim 2, wherein R^C is independently hydrogen, C_{1-6} alkyl, or C_{3-6} carbocyclyl.

6. The conjugate of claim 2, wherein Ring A is:



.

7. The conjugate of claim 2, wherein Ring D is:



.

8. The conjugate of claim 2, wherein R^{V3} is hydrogen.

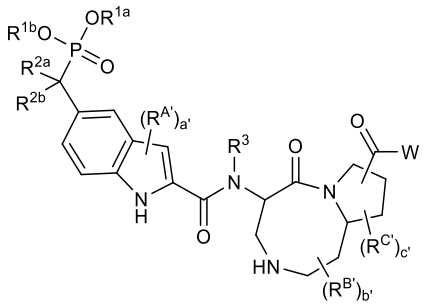
9. The conjugate of claim 2, wherein R^{V4} is hydrogen or methyl.

10. The conjugate of claim 7, wherein R^{V5} is thiazolyl optionally substituted with one or more R^u.

11. The conjugate of claim 2, wherein **L** is C_{1-6} alkylene, -(C_{1-6} alkylene)-(5- to 10-membered heteroarylene)-(C_{1-6} alkylene)-, -(C_{1-6} alkylene)-N($R^{L'}$)C(=O)-, -C(=O)-(C_{1-6} alkylene)-N($R^{L'}$)C(=O)-(C_{1-6} alkylene)-, or -(C_{1-6} alkylene)-N($R^{L'}$)C(=O)-(C_{1-6} alkylene)-, wherein the alkylene is optionally substituted with one or more R^u;

and $R^{L'}$ is hydrogen.

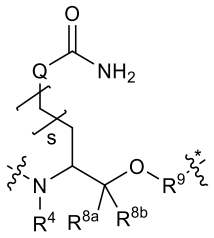
12. The conjugate of claim 2, wherein **T** is of Formula **II-3-ii-a:**



(**II-3-ii-a**).

13. The conjugate of claim 2, wherein R^{2a} and R^{2b} together form an oxo.

14. The conjugate of claim 2, wherein W is:



(W-7).

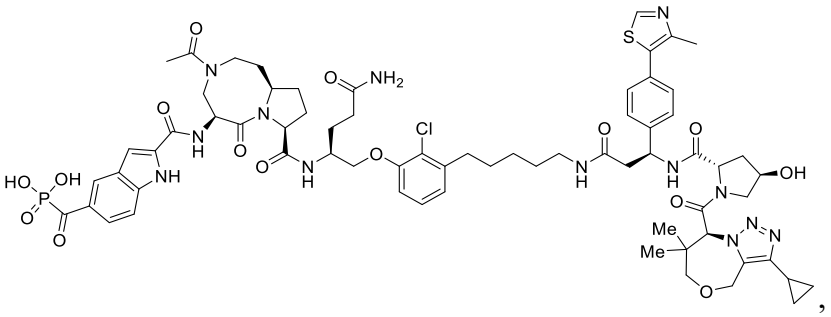
15. The conjugate of claim 14, wherein at least one R^{9a} is halogen.

16. The conjugate of claim 2, wherein B'^{1} is $-CH_2NH-$.

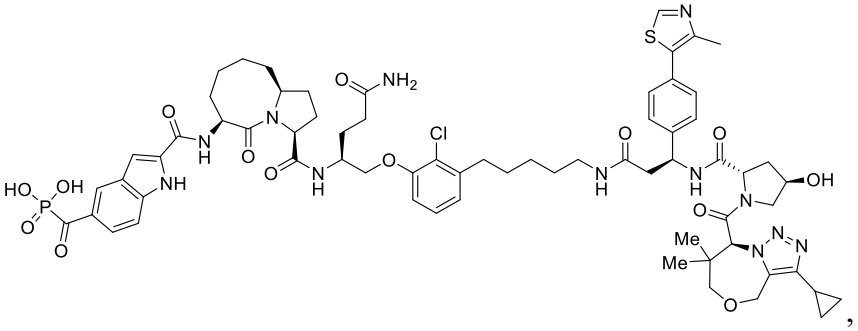
17. The conjugate of claim 2, wherein R^C is .

18. The conjugate of claim 2, R^{V4} is .

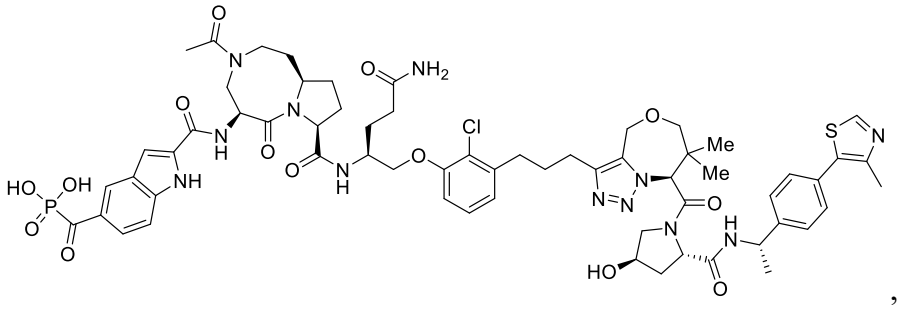
19. A conjugate selected from the group consisting of:



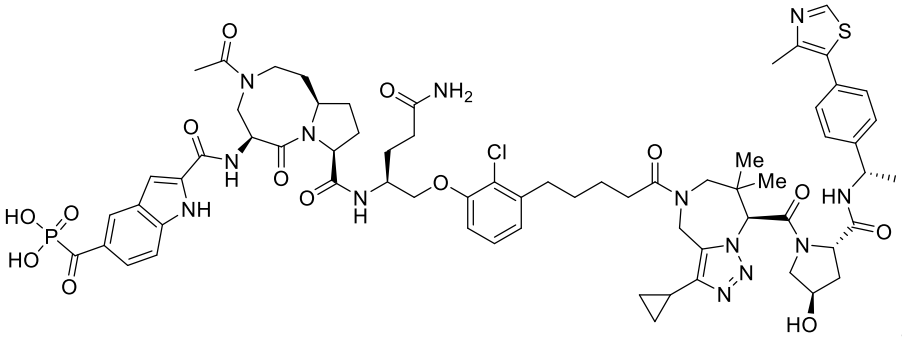
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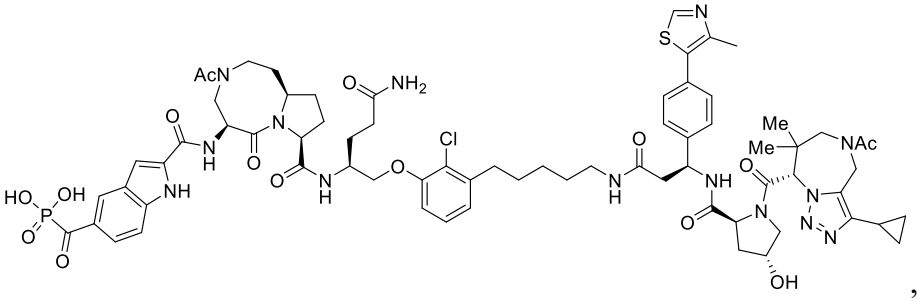
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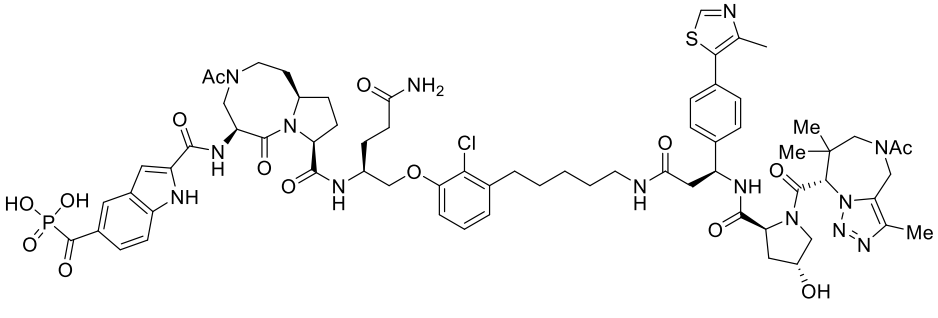
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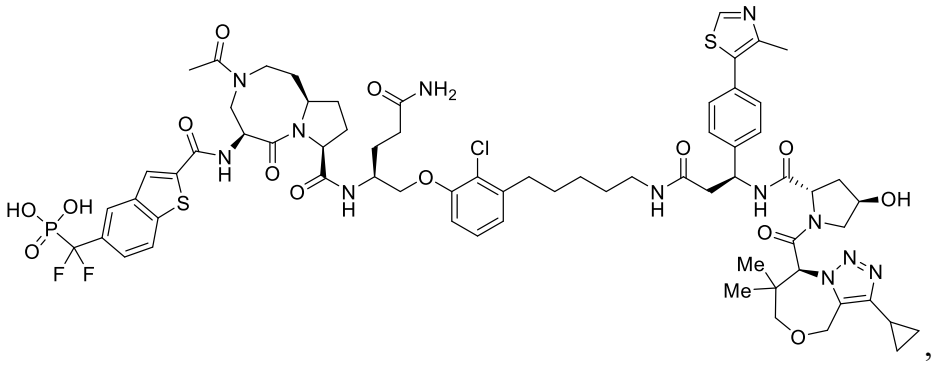
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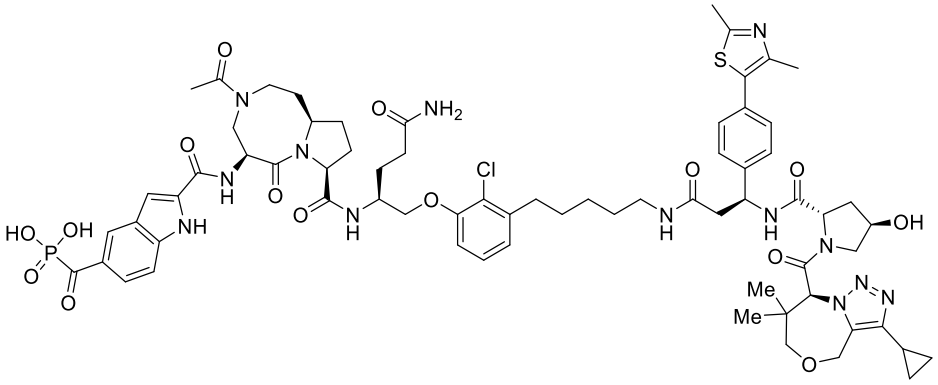
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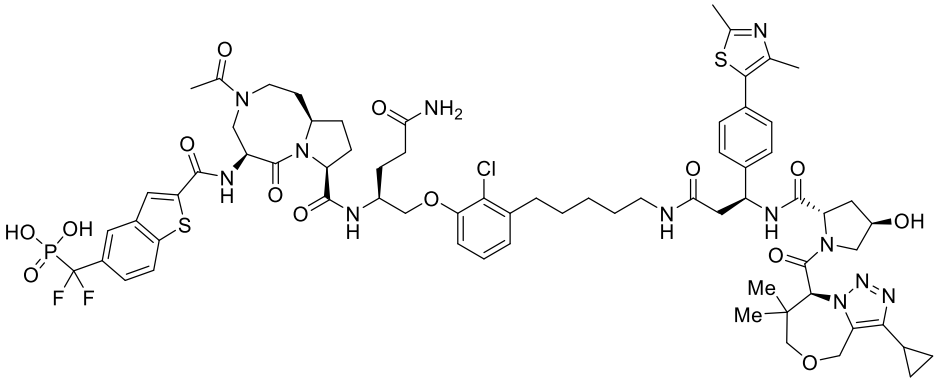
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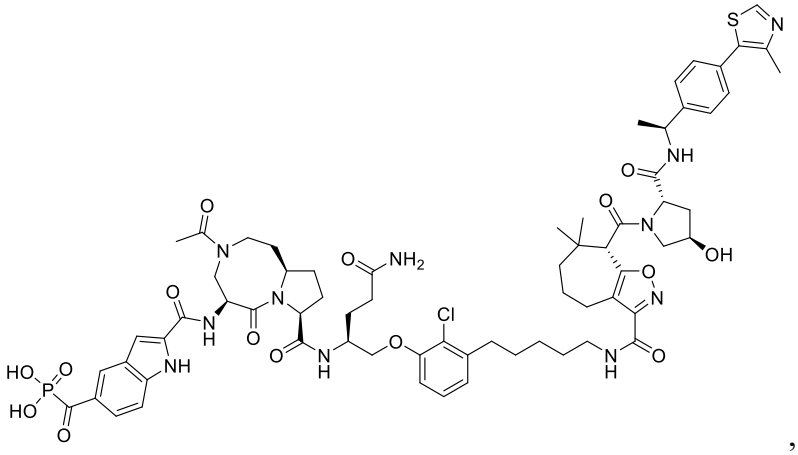
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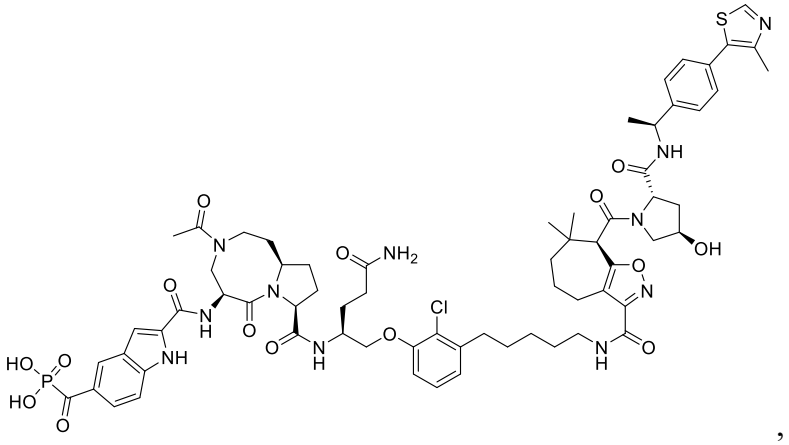
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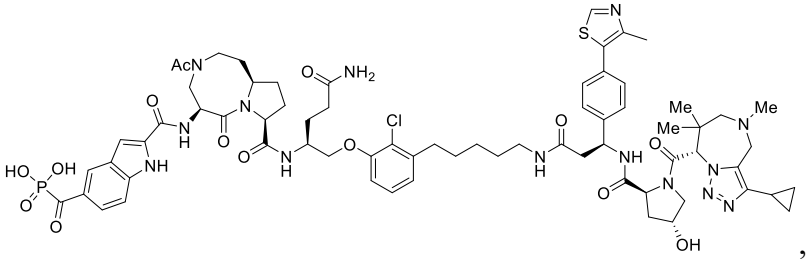
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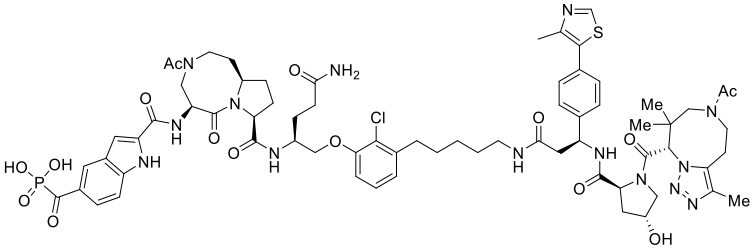
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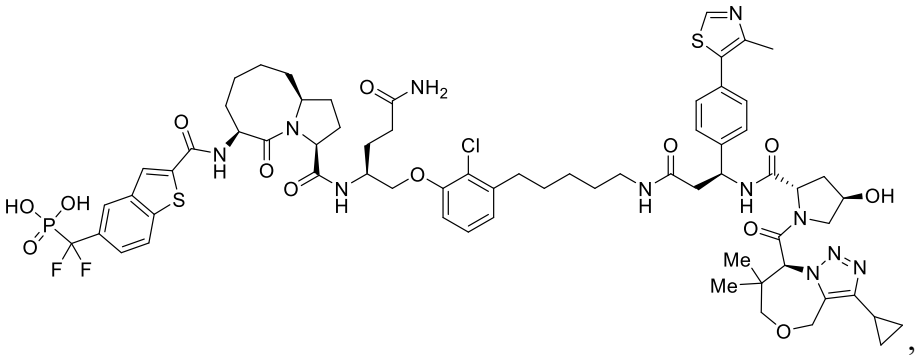
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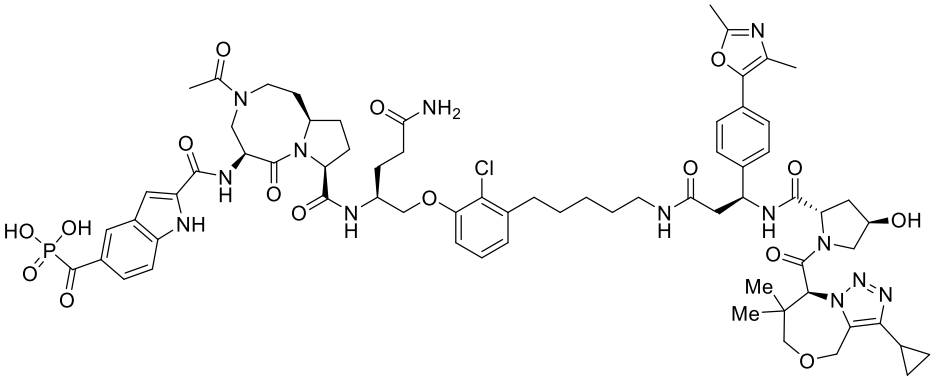
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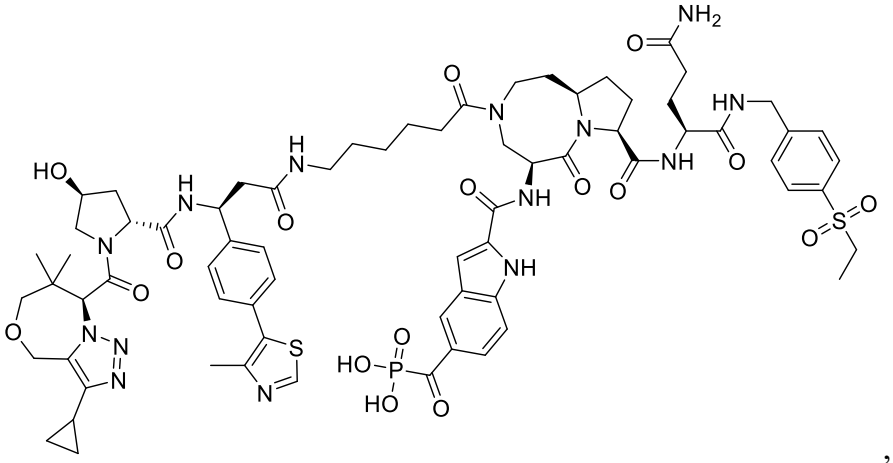
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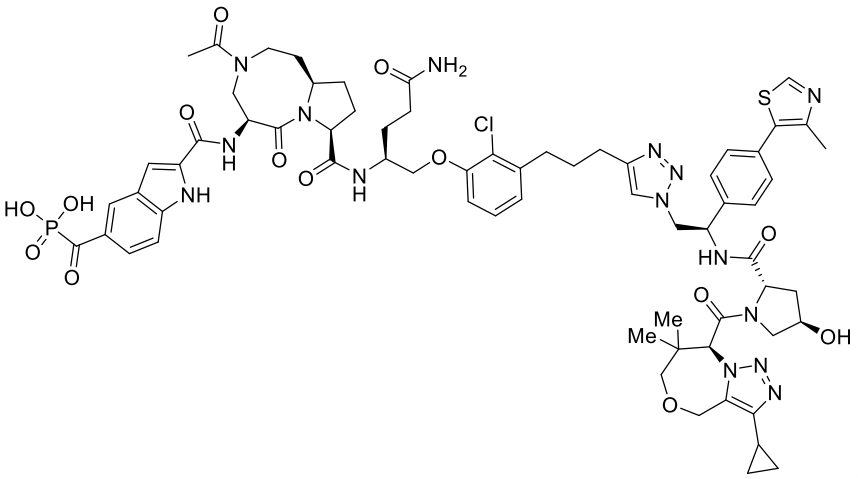
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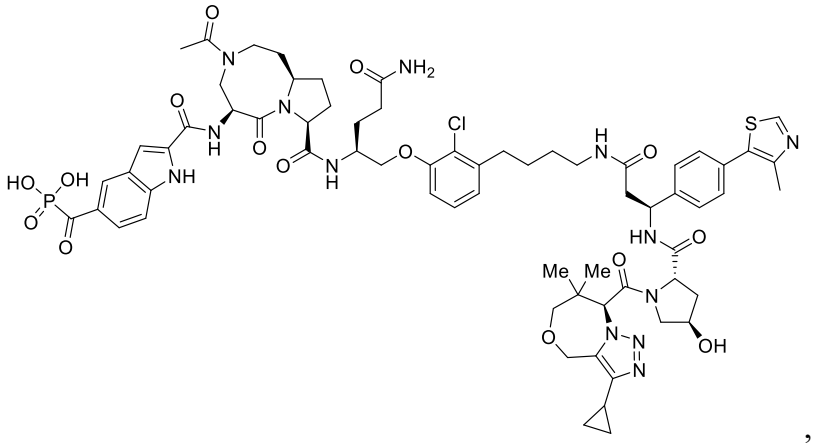
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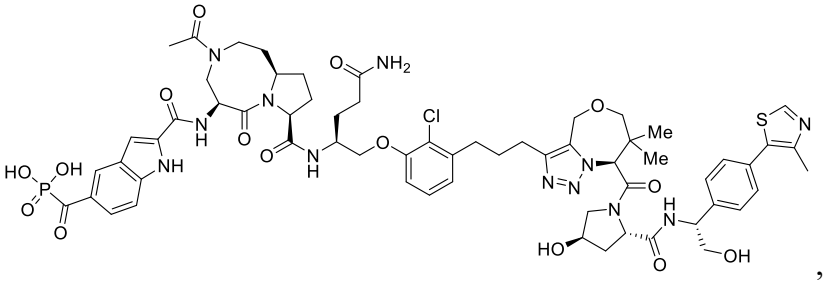
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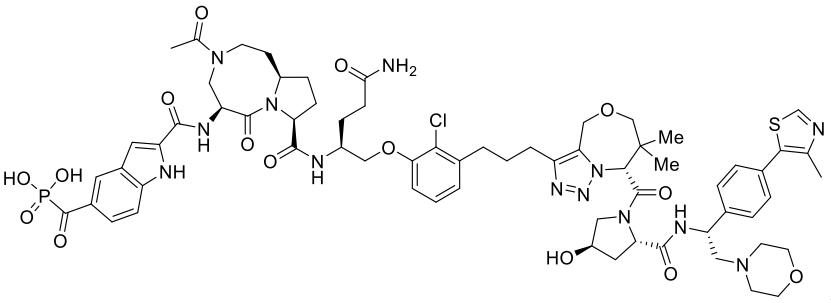
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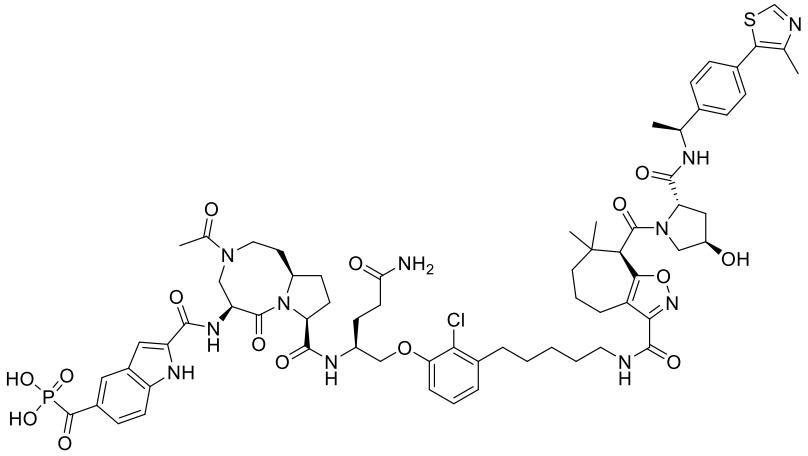
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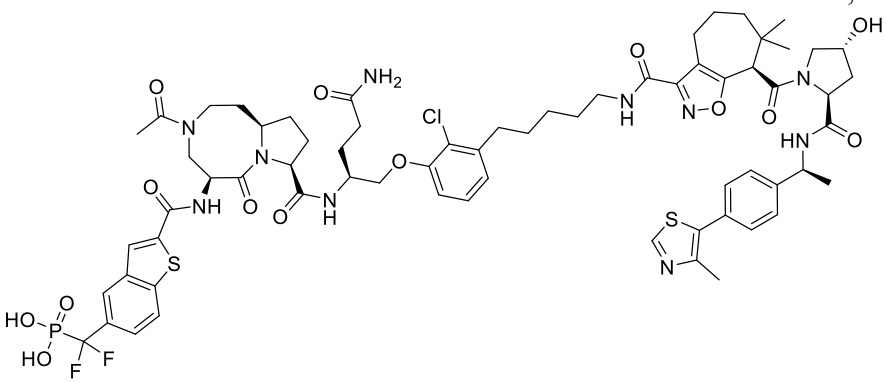
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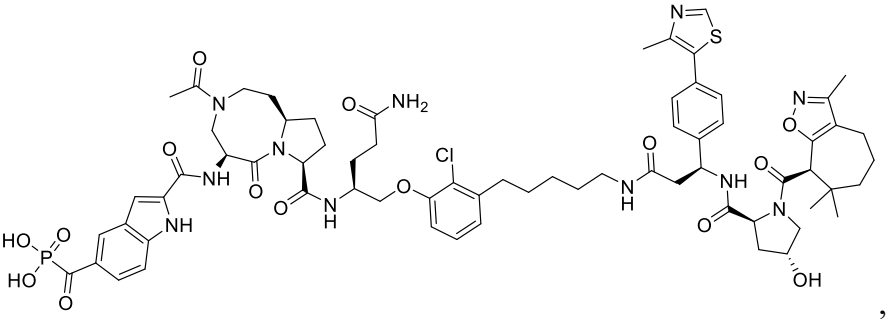
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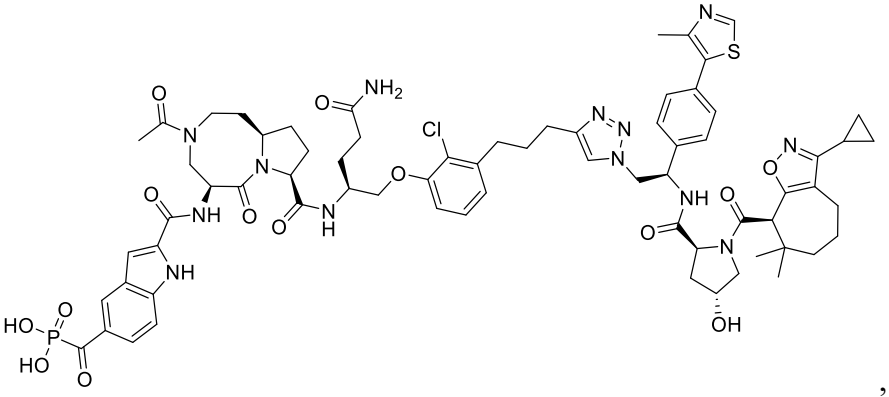
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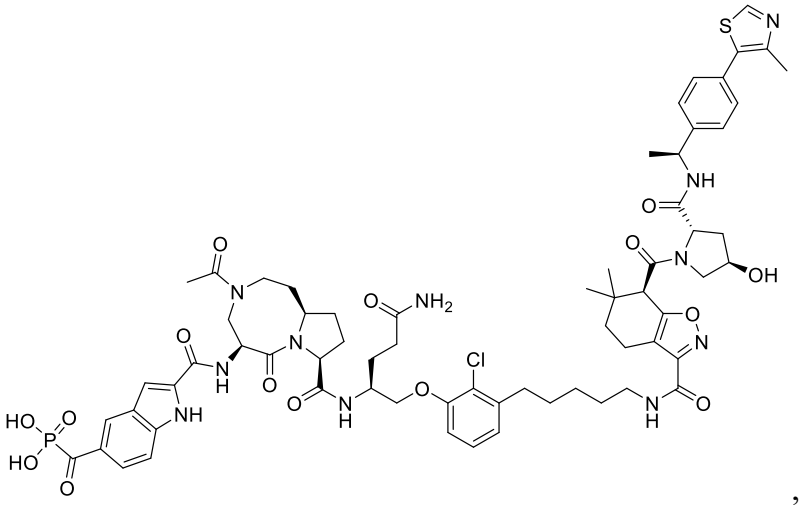
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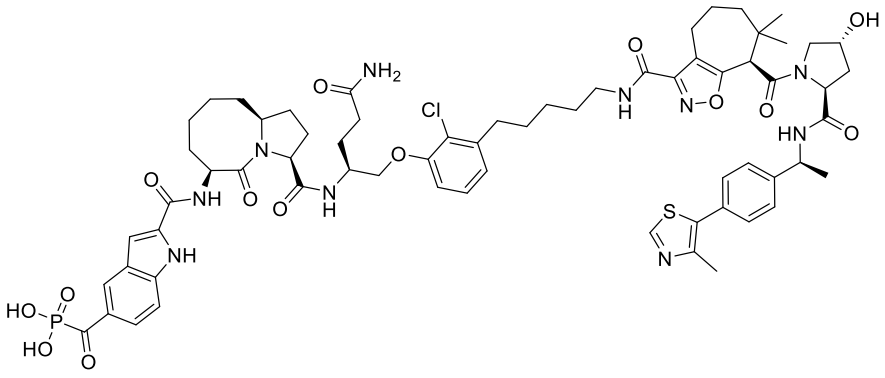
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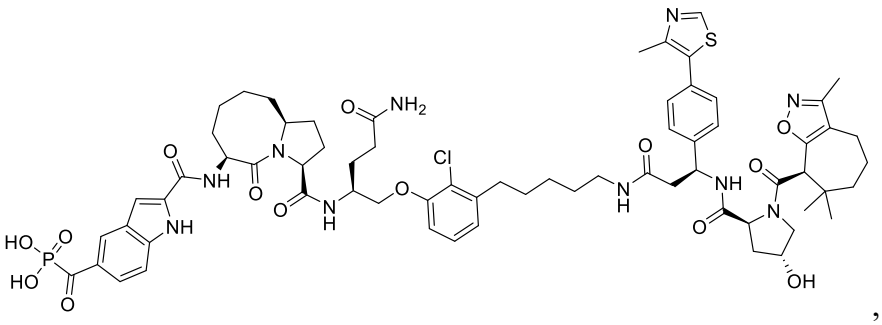
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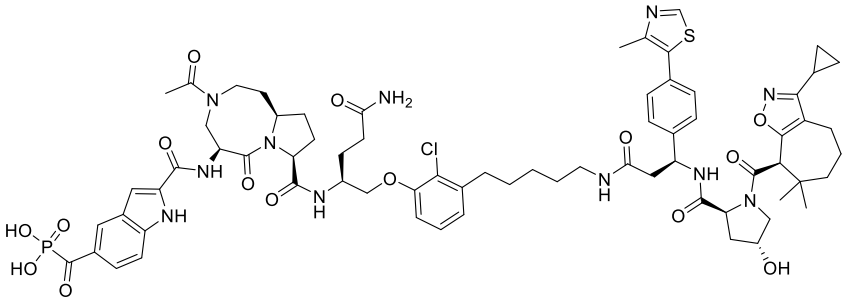
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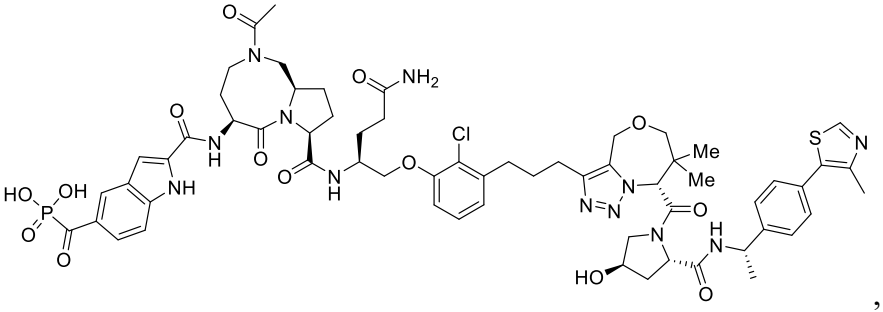
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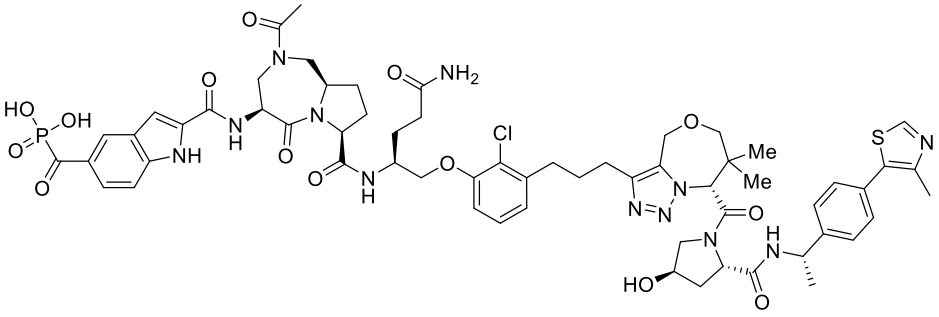
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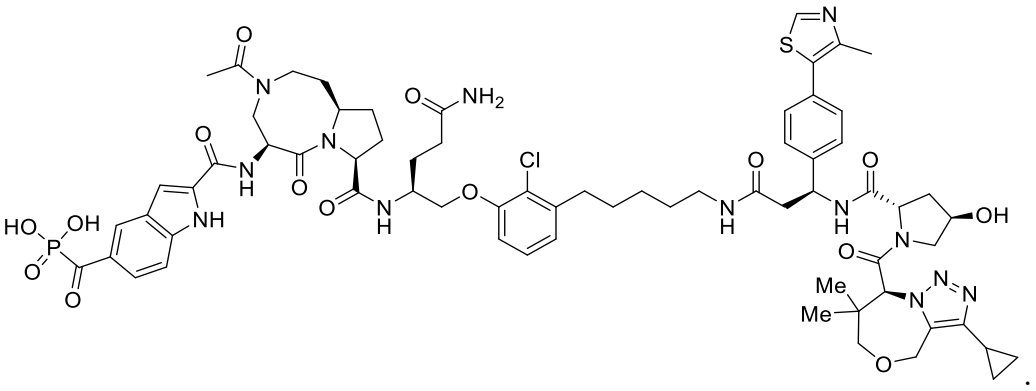
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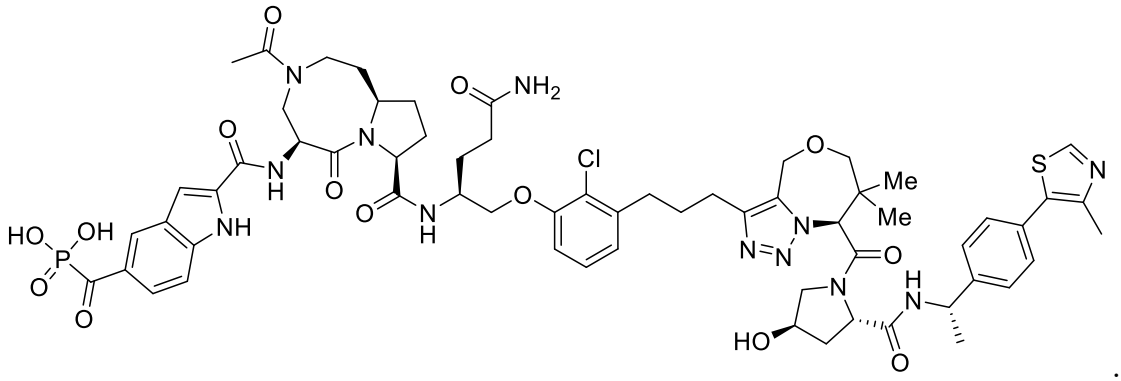
or a pharmaceutically acceptable salt thereof.

20. The conjugate of claim 19, or a pharmaceutically acceptable salt thereof, that is:

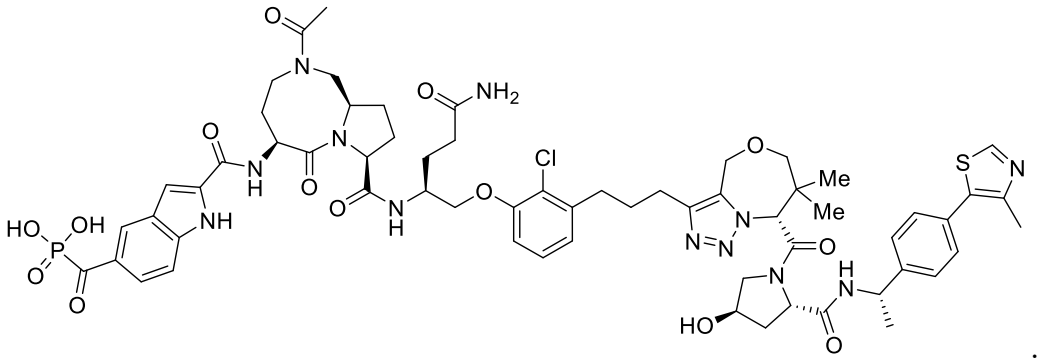


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21. The conjugate of claim 19, or a pharmaceutically acceptable salt thereof, that is:



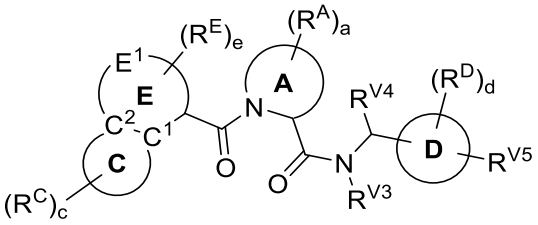
22. The conjugate of claim 19, or a pharmaceutically acceptable salt thereof, that is:



23. A pharmaceutical composition comprising the conjugate of any one of claims 1-22, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

24. Use of a conjugate of any one of claims 1-22 in the manufacture of a medicament for treating a STAT3-mediated disease or disorder in a patient in need thereof, wherein the STAT3-mediated disease or disorder is cancer, an autoimmune disease, an inflammatory disorder, a neurodegenerative disease, a viral disease, a hereditary disorder, a hormone-related disease, a metabolic disorder, a condition associated with organ transplantation, an immunodeficiency disorder, a destructive bone disorder, a proliferative disorder, an infectious disease, a condition associated with cell death, thrombin-induced platelet aggregation, liver disease, a pathologic immune condition involving T cell activation, a cardiovascular disorder, or a CNS disorder.

25. A compound of Formula **I**:



(**I**),

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

Ring A is 5- to 7-membered heterocycle;

each R^A is independently oxo, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

a is an integer selected from 0 to 10, as valency permits;

Ring C is C_6 aryl or 5- to 6-membered heteroaryl;

C^1 and C^2 are independently C or N;

each R^C is independently hydrogen, halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

c is an integer selected from 0 to 5, as valency permits;

Ring D is C_6 aryl or 5- to 6-membered heteroaryl;

each R^D is independently halogen, -CN, -NO_2, -OH, -NH_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2NR^cR^d$, -$NR^cS(=O)_2R^a$, -$NR^cS(=O)R^a$, -$NR^cS(=O)_2OR^b$, -$NR^cS(=O)_2NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, -$OS(=O)_2R^a$, -$OS(=O)_2OR^b$, -$OS(=O)_2NR^cR^d$, -$OC(=O)R^a$, -$OC(=O)OR^b$, -$OC(=O)NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, or -$C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

d is an integer selected from 0 to 4;

Ring E is C_{5-12} carbocycle or 5- to 12-membered heterocycle, wherein the carbocycle or heterocycle is optionally substituted with one or more R^E;

E^1 is $C(R^{E1'})_2$, $NR^{E1''}$, O, or S;

each $R^{E1'}$ is independently halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{3-6} carbocyclyl, or 3- to 6-membered heterocyclyl, wherein the alkyl, alkoxy, alkylamino, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

$R^{E1''}$ is an amino-protecting group, hydrogen, C_{1-6} alkyl, C_{3-6} carbocyclyl, 3- to 6-membered heterocyclyl, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$; wherein the alkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

each R^E is independently oxo, hydrogen, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u; or

two geminal R^E, together with the carbon atom to which they are bonded, form C_{3-6} carbocycle or 3- to 6-membered heterocycle, wherein the carbocycle or heterocycle is optionally substituted with one or more R^u;

e is an integer selected from 0 to 6;

R^{V3} is hydrogen, C_{1-6} alkyl, C_{3-6} carbocyclyl, 3- to 6-membered heterocyclyl, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$; wherein the alkyl, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

R^{V4} is hydrogen, C_{1-6} alkyl, or C_{1-8} heteroalkyl, wherein the alkyl or heteroalkyl is optionally substituted with one or more R^u; and

R^{V5} is hydrogen, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u,

wherein:

each R^u is independently oxo, halogen, $-N_3$, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, -

$S(=O)_2NR^cR^d$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)R^a$, $-NR^cS(=O)_2OR^b$, $-NR^cS(=O)_2NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, $-OS(=O)_2R^a$, $-OS(=O)_2OR^b$, $-OS(=O)_2NR^cR^d$, $-OC(=O)R^a$, $-OC(=O)OR^b$, $-OC(=O)NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$; wherein the alkyl, alkoxy, alkylamino, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more substituents selected from oxo, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} carbocyclyl, and 3- to 6-membered heterocyclyl; or

two R^u, together with the one or more intervening atoms, form C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl;

each R^a is independently C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl;

each R^b is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl; and

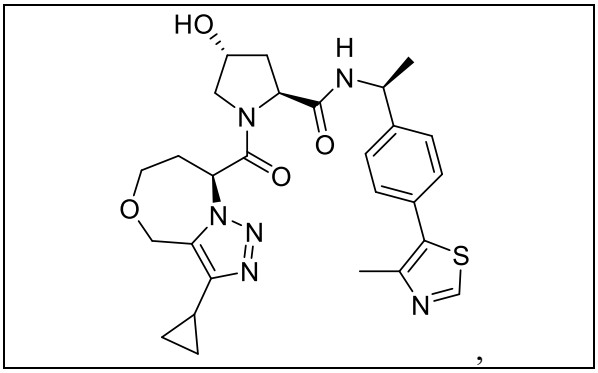
each R^c and R^d is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-12} carbocyclyl, 3- to 12-membered heterocyclyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl; or

R^c and R^d, together with the nitrogen atom to which they are attached, form 3- to 12-membered heterocyclyl,

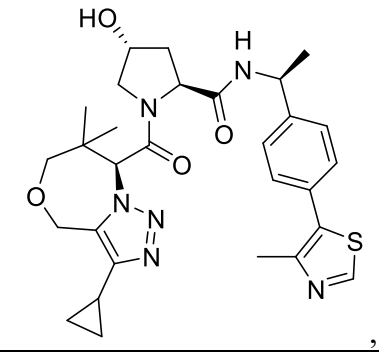
wherein each occurrence of R^a, R^b, R^c, and R^d is independently and optionally substituted with one or more R^z; and

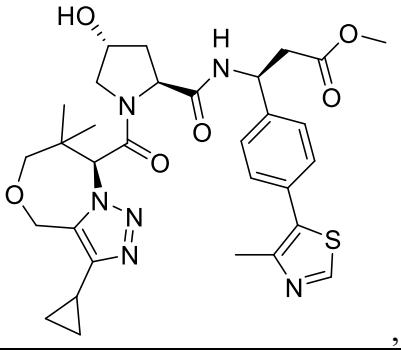
each R^z is independently oxo, halogen, -CN, $-NO_2$, -OH, $-NH_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} carbocyclyl, or 3- to 6-membered heterocyclyl.

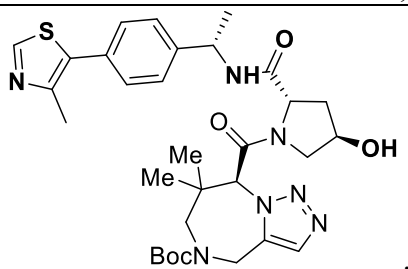
26. The compound of claim 25, wherein the compound is selected from the group consisting of:

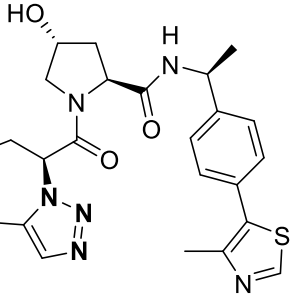


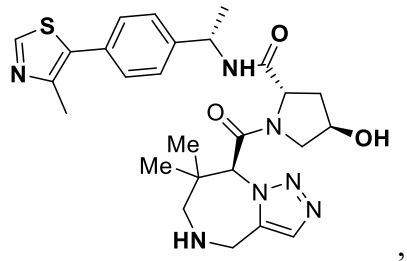
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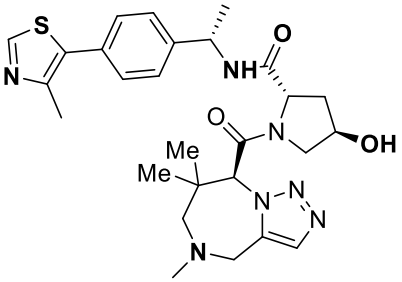

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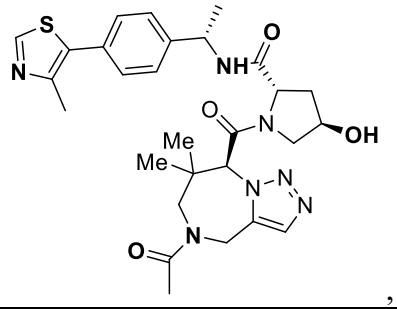

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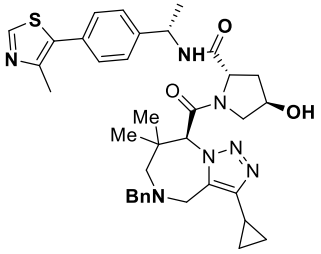

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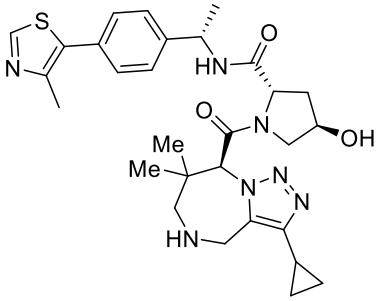

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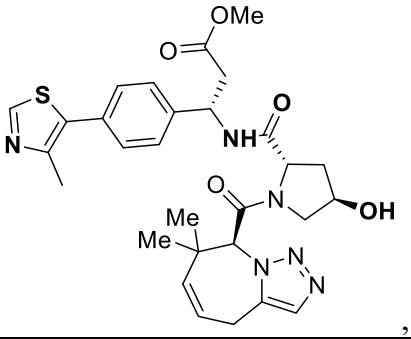

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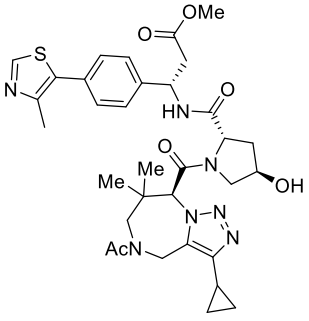

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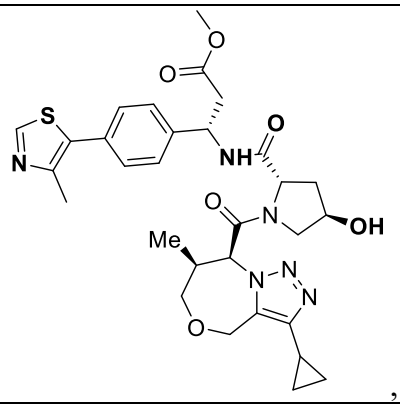

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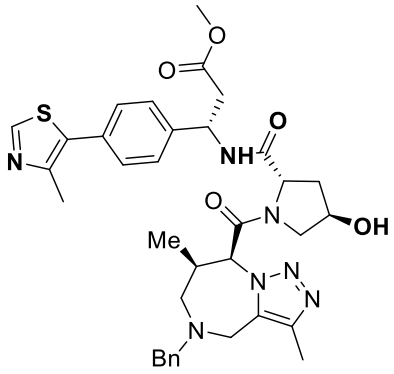

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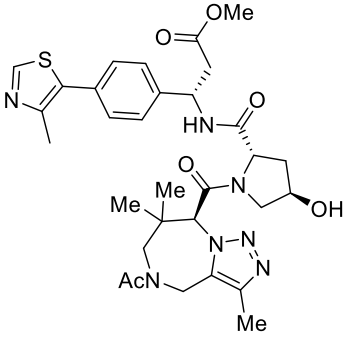

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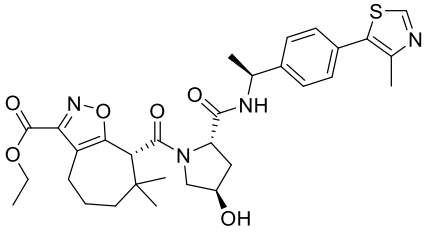

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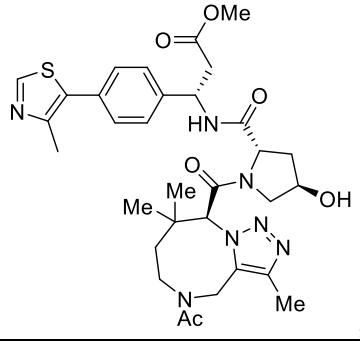

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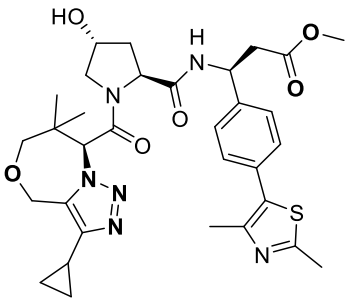

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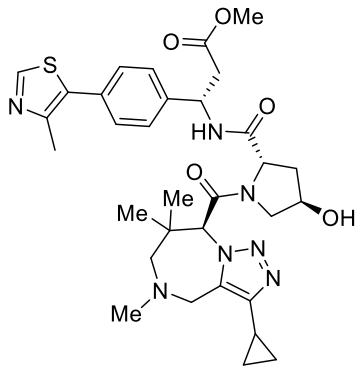

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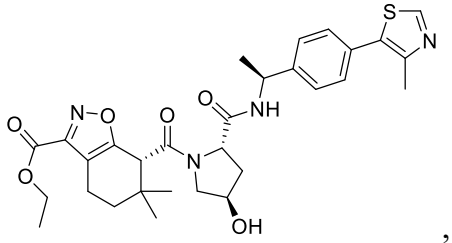

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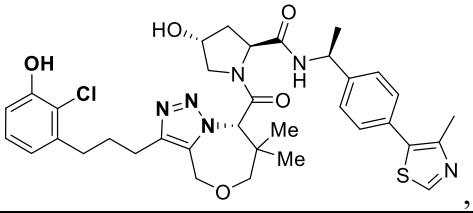

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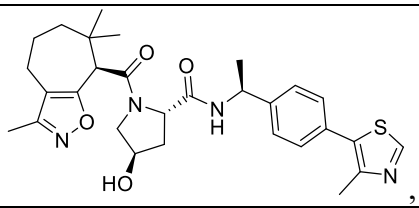

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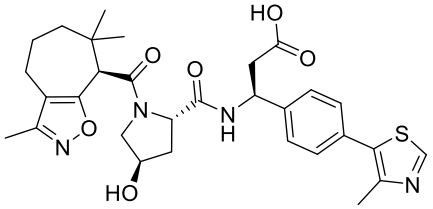

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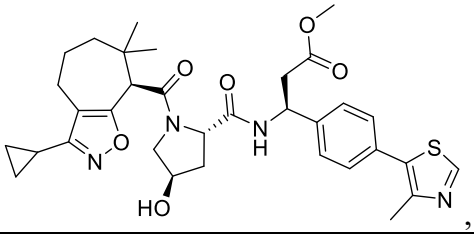

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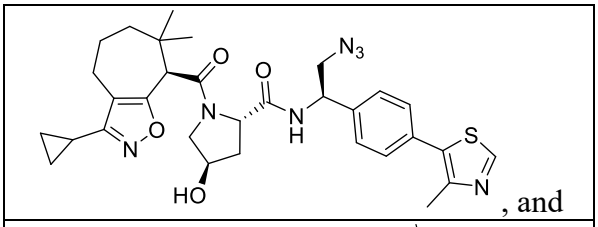

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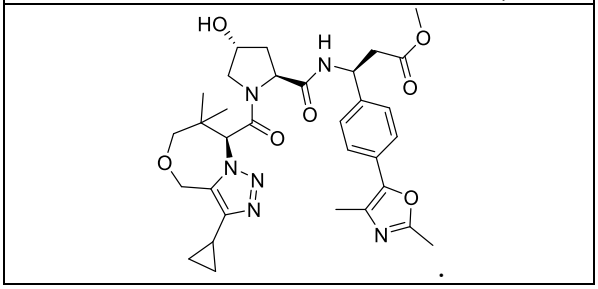

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