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A61P 35/00 (2006.01)

Norwegian Industrial Property Office

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(54) Title **BENZAMIDE AND NICOTINAMIDE COMPOUNDS AND METHODS OF USING SAME**

(56) References Cited: US-A1- 2008 132 459
US-A1- 2011 212 969
US-A1- 2009 215 823
US-A1- 2011 053 975
US-A1- 2003 144 274
MATHENY CHRISTINA J ET AL: "Next-Generation NAMPT Inhibitors Identified by Sequential High-Throughput Phenotypic Chemical and Functional Genomic Screens", CHEMISTRY & BIOLOGY, vol. 20, no. 11, November 2013 (2013-11), pages 1352-1363, XP002769492, (CAMBRIDGE)
WEI MICHAEL C ET AL: "Next-Generation NAMPT Inhibitors For ALL Identified By Sequential High-Throughput Phenotypic Chemical and Functional Genomic Screens", BLOOD, vol. 122, no. 21, 171, November 2013 (2013-11), XP002769491, & 55TH ANNUAL MEETING OF THE AMERICAN-SOCIETY-OF-HEMATOLOGY; NEW ORLEANS, LA, USA; DECEMBER 07 -10, 2013

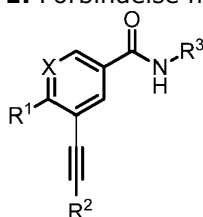
Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (<http://worldwide.espacenet.com>) or via the search engine on our website here: <https://search.patentstyret.no/>

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Patentkrav

1. Forbindelse med den følgende strukturen:



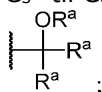
5 hvori X er et karbonatom eller nitrogenatom, R¹ er valgt fra gruppen bestående av en substituert eller usubstituert fem- til åtteleddet heterosyklisk ring, seksleddet arylring, fem- eller seksleddet heteroarylring, C₃- til C₈-sykloalkylgruppe, C₁- til C₆-alkylgruppe,



10 og



R² er valgt fra gruppen bestående av et hydrogenatom, en substituert eller usubstituert fem- eller seksleddet heteroarylring, en fem- eller seksleddet arylring, C₃- til C₆-sykloalkylgruppe, åtte- til tilledet heterosyklisk ringsystem, og



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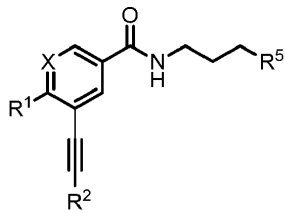
R³ er valgt fra gruppen bestående av en substituert eller usubstituert C₂- til C₈-alkylheteroarylgruppe, C₂- til C₈-alkylenheteroarylgruppe, C₆- til C₁₀-arylgruppe, C₂- til C₅-heteroarylgruppe, C₇- til C₁₃-alkylarylgruppe, C₇- til C₁₃-alkylenarylgruppe, C₂- til C₈-alkylheterosyklgruppe, C₂- til C₈-alkylenheterosyklgruppe, C₄- til C₈-alkylsykloalkylgruppe eller C₄- til C₈-alkylenesykloalkylgruppe; og R^a er en substituert eller usubstituert C₁- til C₆-alkylgruppe eller C₅- til C₆-arylgruppe.

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2. Forbindelsen ifølge krav 1, hvori forbindelsen har følgende struktur:

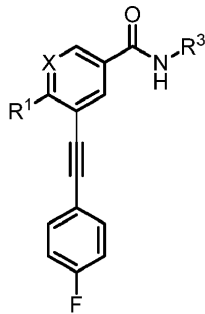
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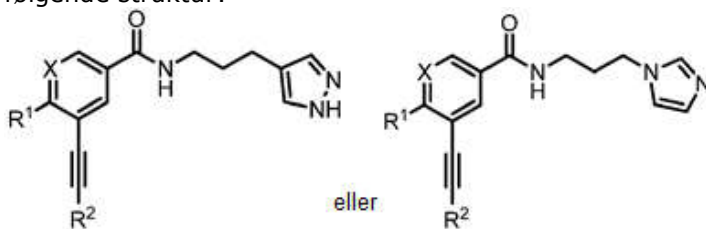
hvor R^5 er en C₂- til C₅-heteroarylgruppe.

3. Forbindelsen ifølge krav 1, hvori forbindelsen har følgende struktur:



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4. Forbindelsen ifølge hvilke som helst af kravene 1-2, hvori forbindelsen har følgende struktur:

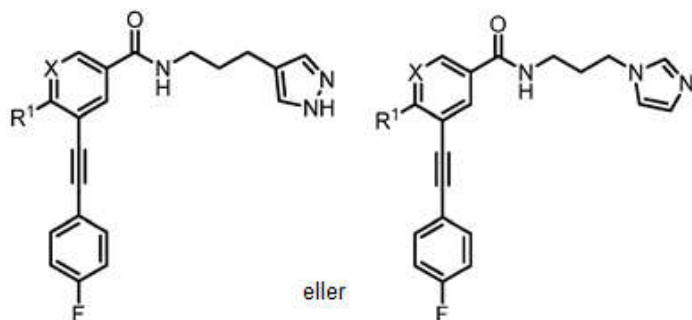


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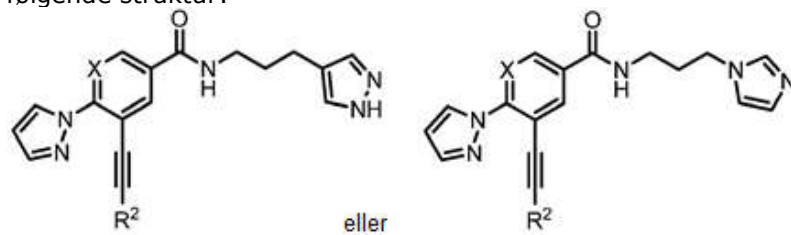
5. Forbindelsen ifølge hvilke som helst af kravene 1-3, hvori forbindelsen har følgende struktur:

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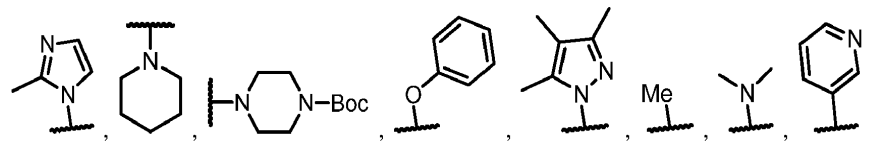
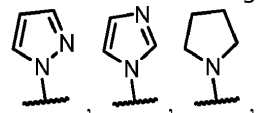


6. Forbindelsen ifølge hvilke som helst av kravene 1-2, hvori forbindelsen har følgende struktur:

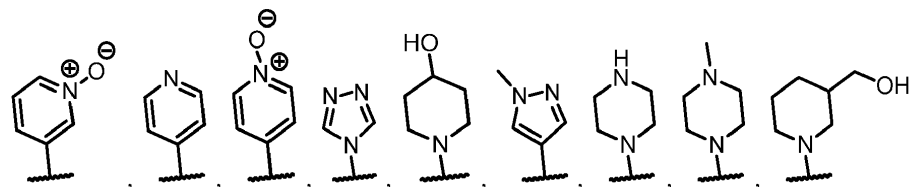


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7. Forbindelsen ifølge hvilke som helst av kravene 1-3, 4 eller 5, hvori R¹ er

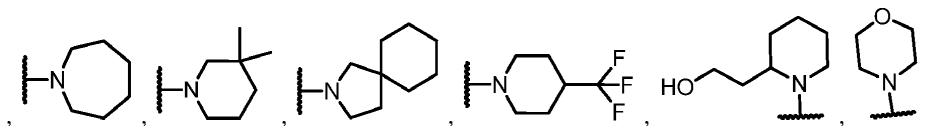
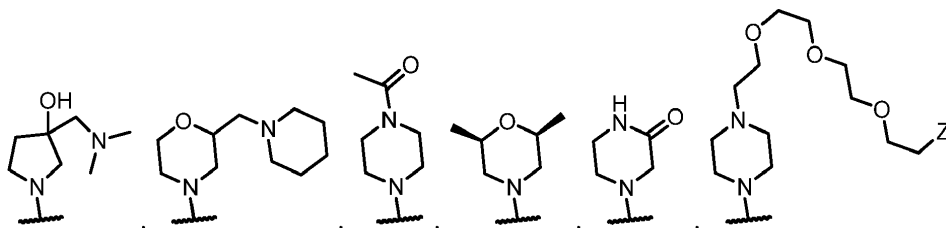


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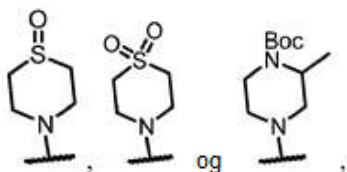
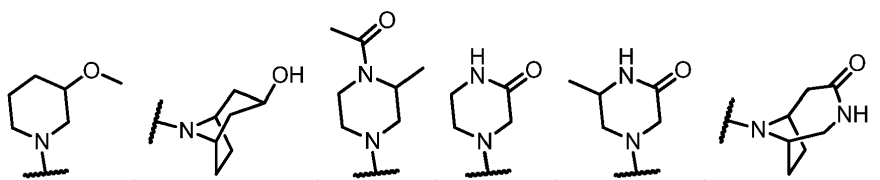
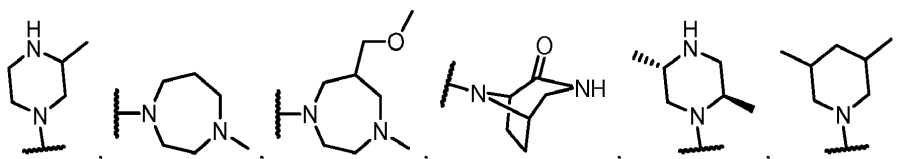


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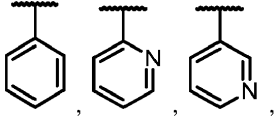
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hvor Z er $N(R^6)_2$ eller OR^6 , der hver R^6 uafhængig er et hydrogenatom eller substitueret eller usubstitueret C_1 - til C_6 -alkylgruppe.

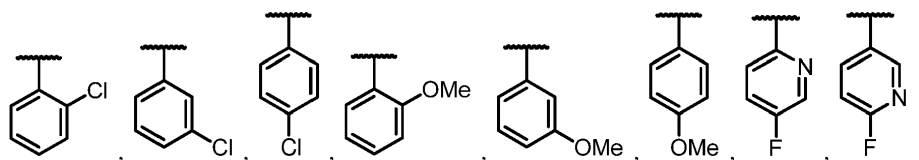
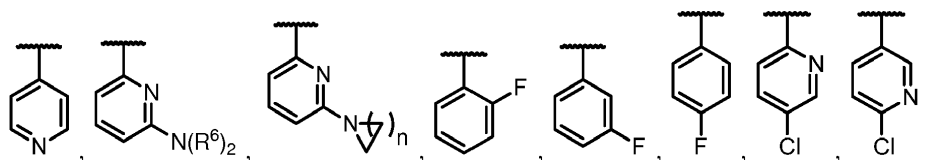
8. Forbindelsen ifølge hvilke som helst af kravene 1-2, 4, 6 eller 7, hvori R^2 er



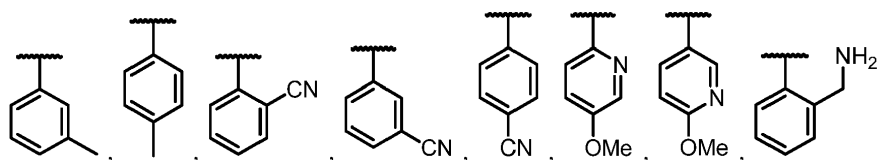
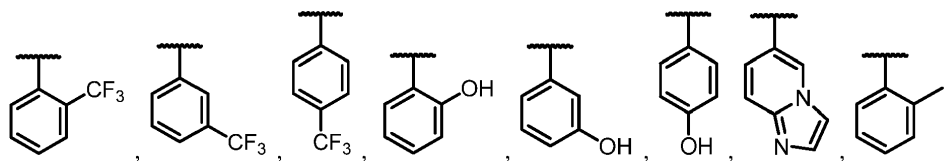
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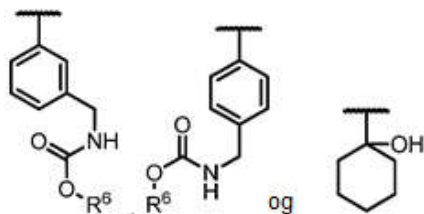
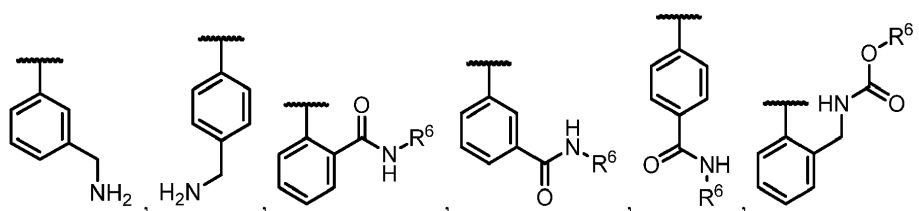
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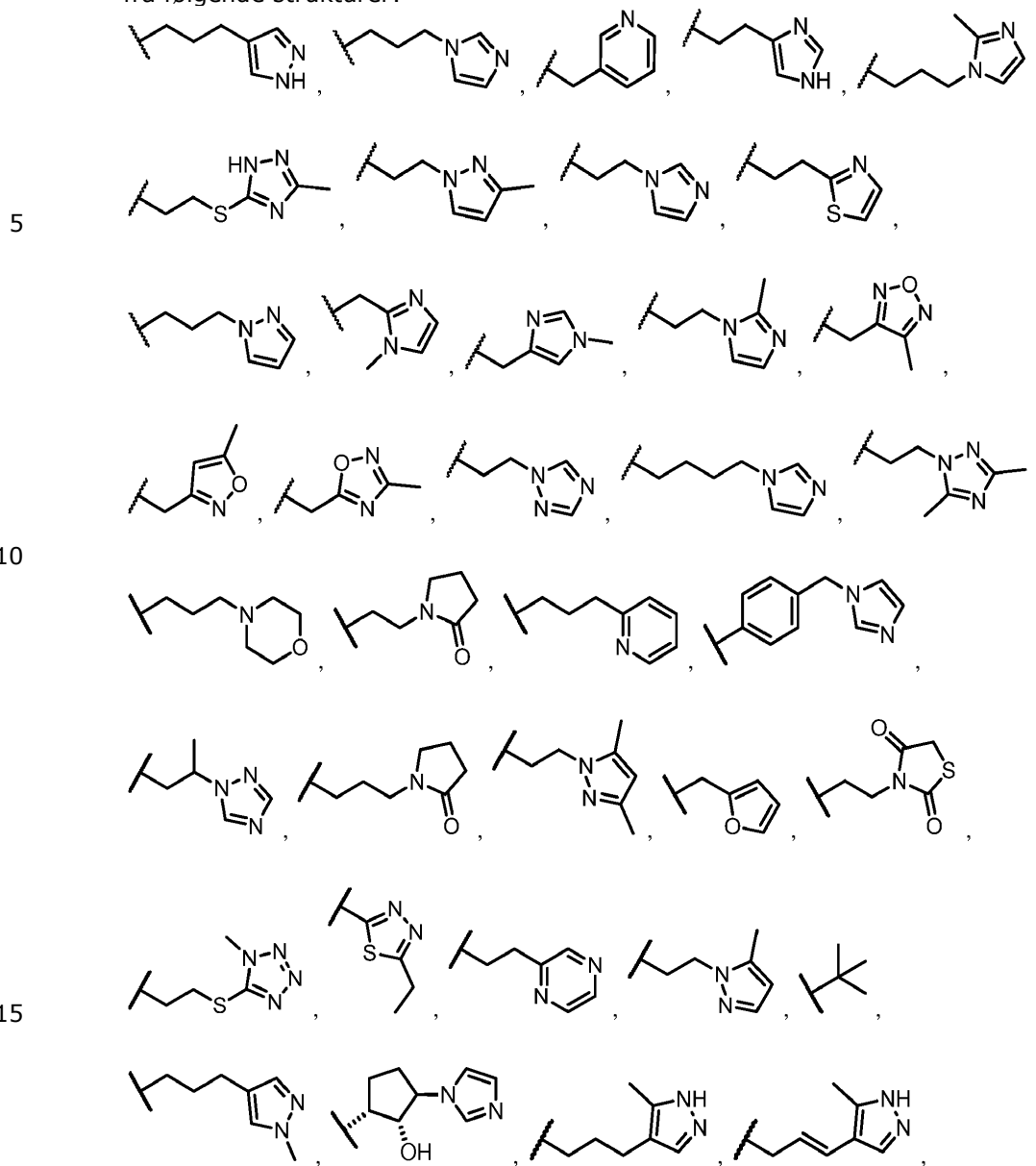


hvori hver R^6 uavhengig er et hydrogenatom eller substituert eller usubstituert C_1 -til C_6 -alkylgruppe og n er 1, 2, 3 eller 4.

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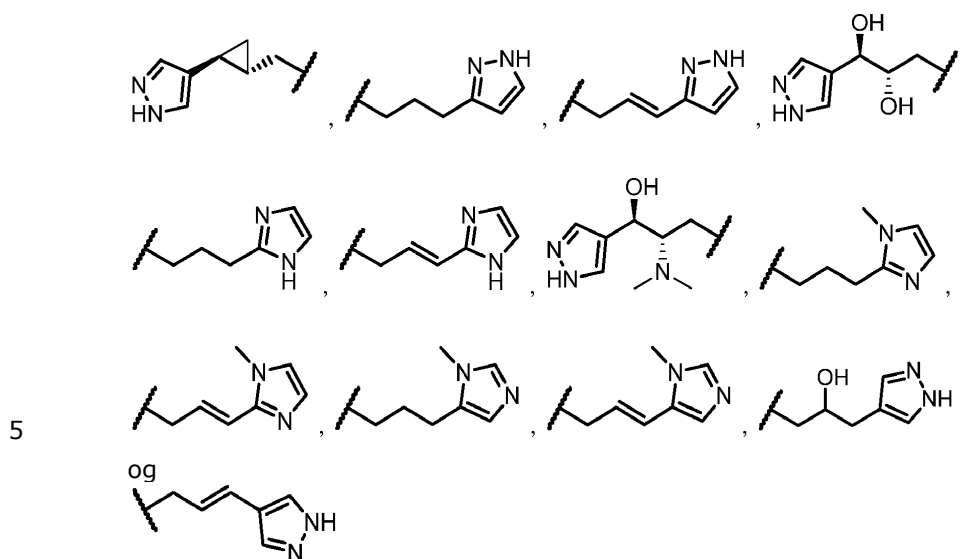
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9. Forbindelsen ifølge hvilke som helst av kravene 1, 3, 7 eller 8, hvori R³ er valgt fra følgende strukturer:



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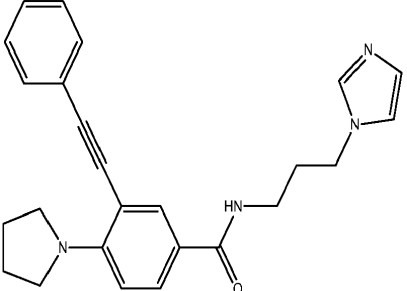
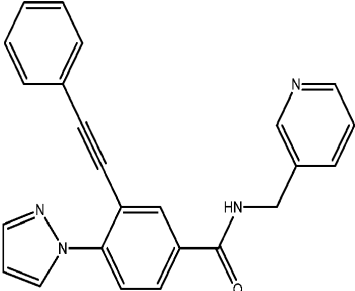
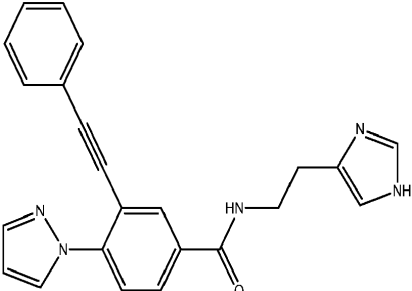
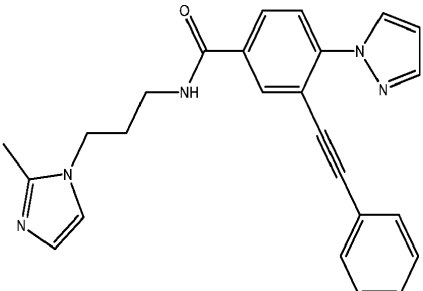
10 **10.** Forbindelsen ifølge hvilke som helst av kravene 1-5 eller 7-9, hvori R^1 er en substituert eller usubstituert fem- til åtteleddet heterosyklisk ring, eventuelt hvori den usubstituerte fem- til åtteleddede heterosykliske ringen omfatter minst ett nitrogenatom.

11. Forbindelsen ifølge krav 1, hvori forbindelsen er valgt fra følgende forbindelse:

Struktur	Struktur-ID
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	TT-02683

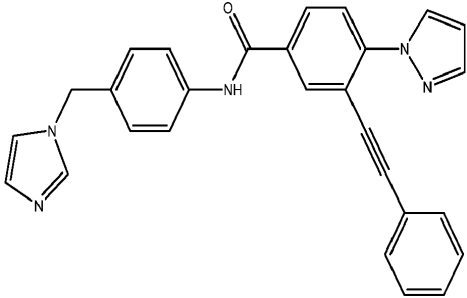
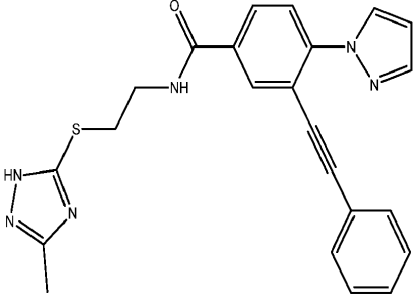
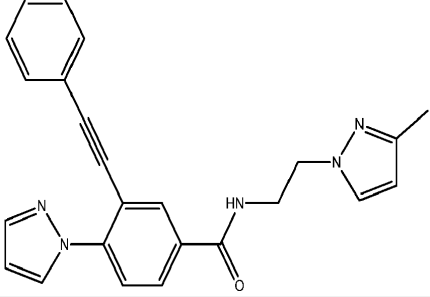
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Struktur	Struktur-ID
	
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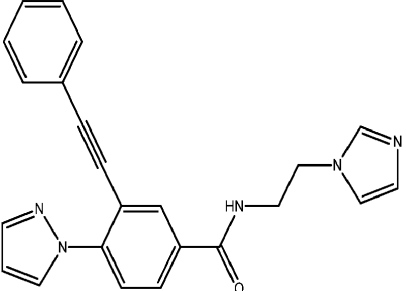
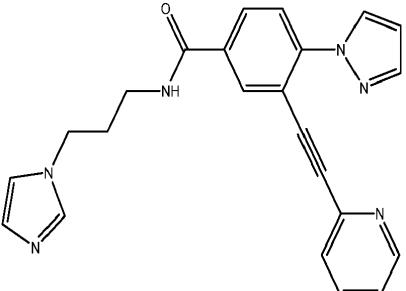
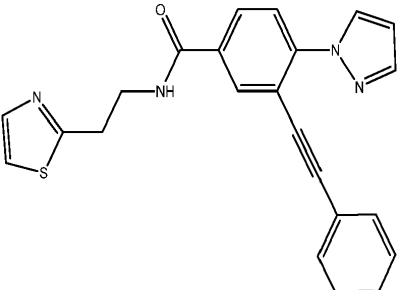
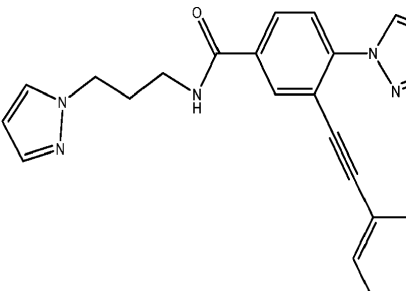
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Struktur	Struktur-ID
 <p>Chemical structure of compound TT-02690: A central benzene ring is substituted with a pyrazole ring at the 1-position, a propargyl group (ethynylbenzene) at the 2-position, and an amide group (-NH-) at the 4-position. The amide group is further substituted with a benzene ring, which is in turn substituted with a pyrazole ring at the 1-position.</p>	TT-02690
 <p>Chemical structure of compound TT-02691: A central benzene ring is substituted with a pyrazole ring at the 1-position, a propargyl group (ethynylbenzene) at the 2-position, and an amide group (-NH-) at the 4-position. The amide group is further substituted with a propyl chain, which is in turn substituted with a sulfur atom, which is further substituted with a 4-methyl-1H-imidazole ring.</p>	TT-02691
 <p>Chemical structure of compound TT-02692: A central benzene ring is substituted with a pyrazole ring at the 1-position, a propargyl group (ethynylbenzene) at the 2-position, and a carbonyl group (-C(=O)-) at the 4-position. The carbonyl group is further substituted with a propyl chain, which is in turn substituted with a 4-methyl-1H-imidazole ring.</p>	TT-02692
	TT-02694

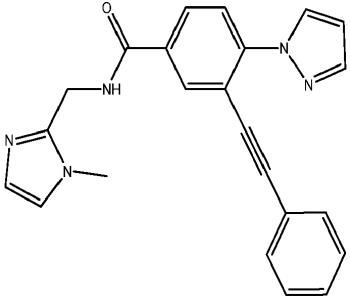
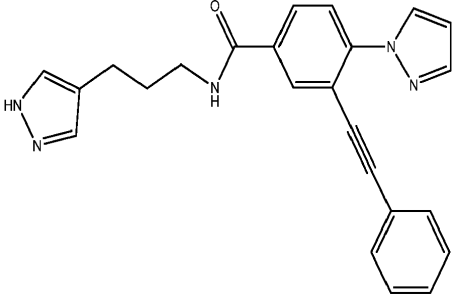
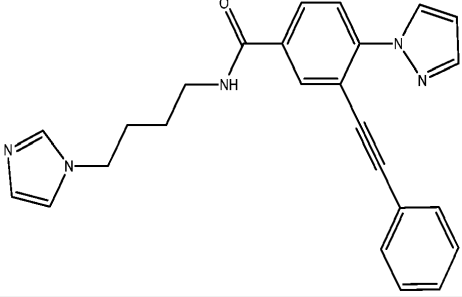
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Struktur	Struktur-ID
	
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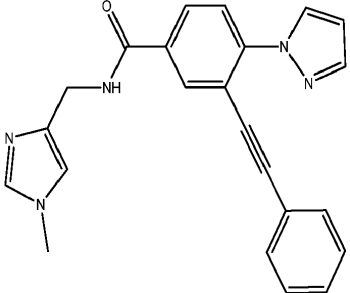
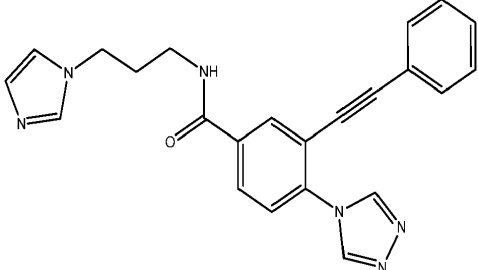
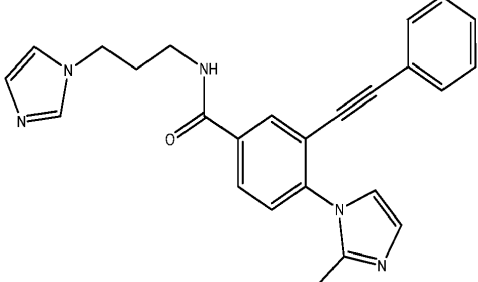
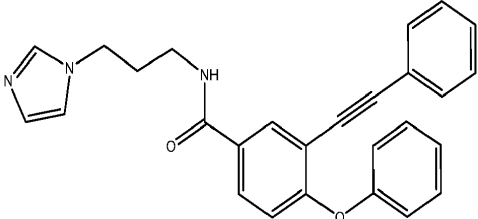
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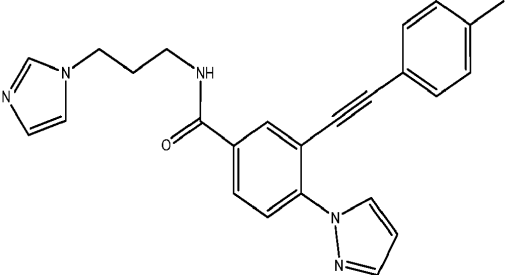
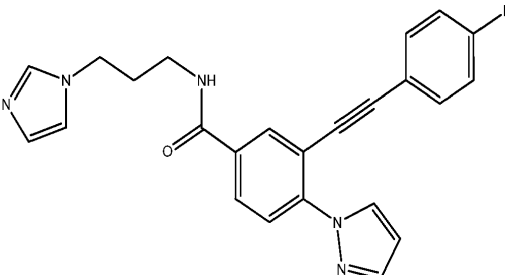
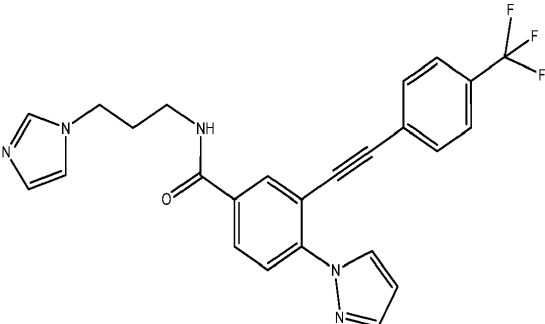
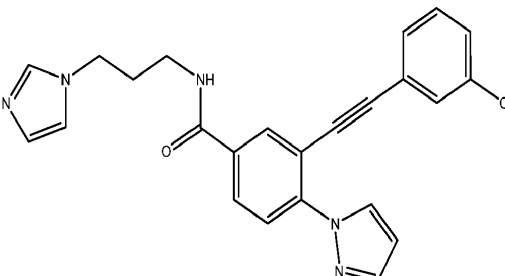
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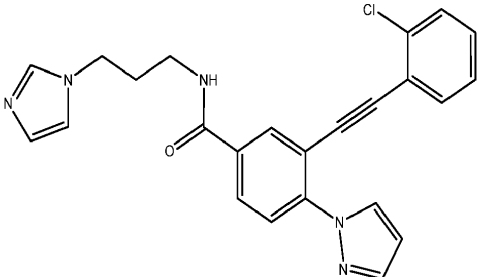
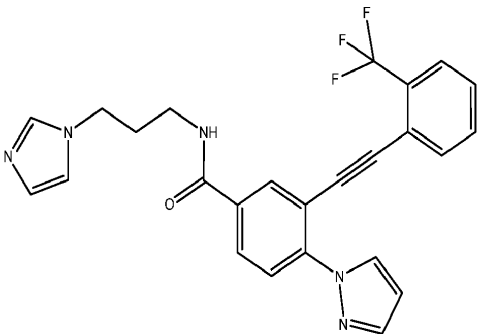
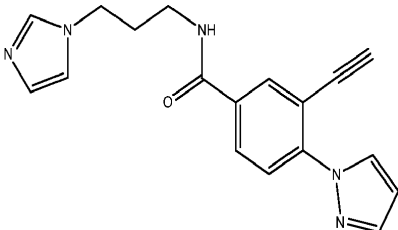
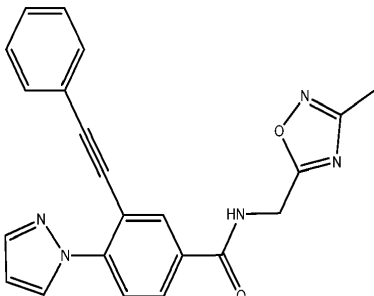
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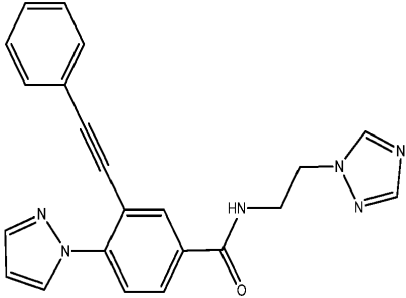
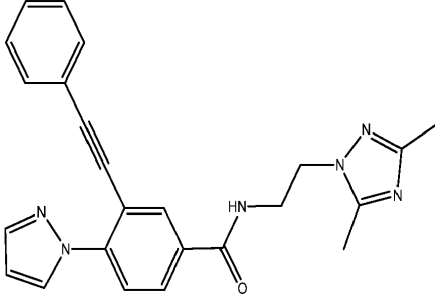
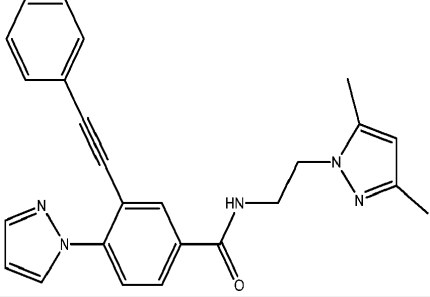
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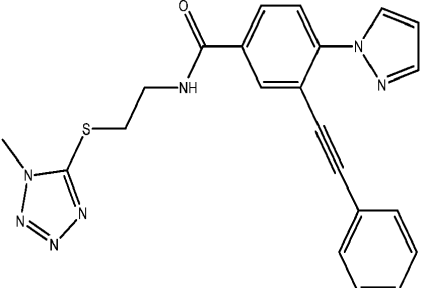
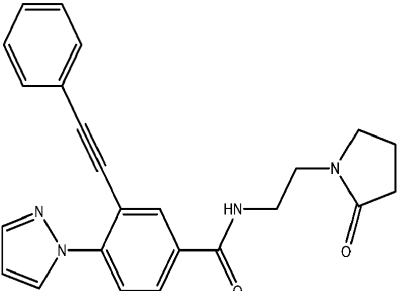
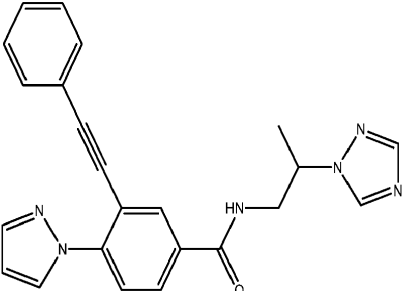
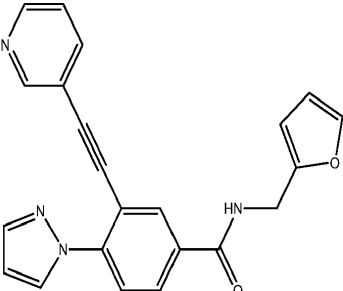
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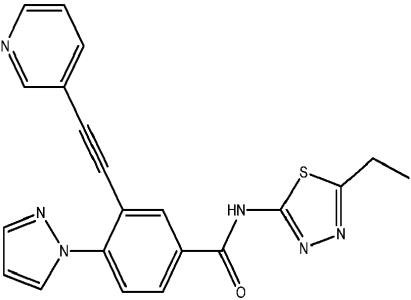
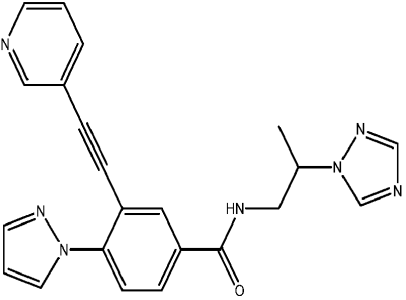
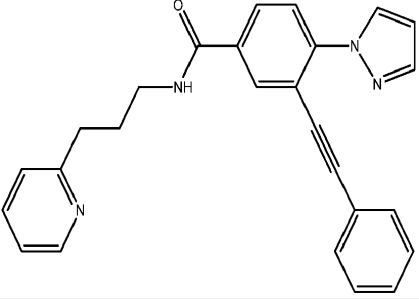
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	TT-02931

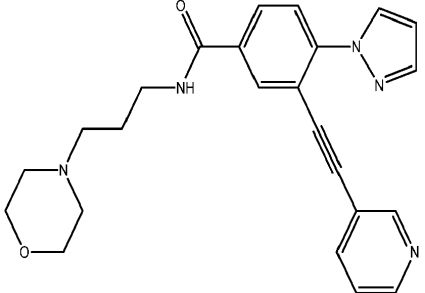
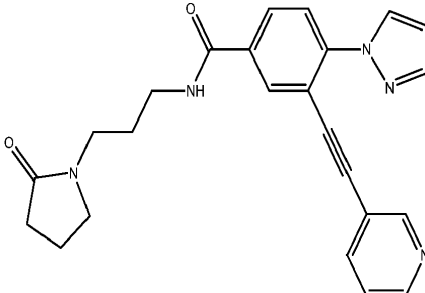
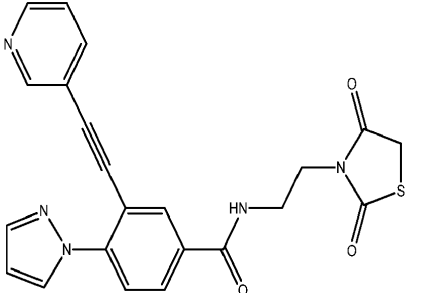
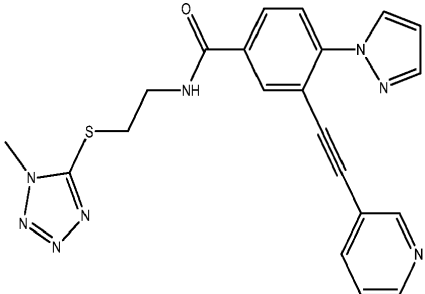
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Struktur	Struktur-ID
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	TT-02935
	TT-02936

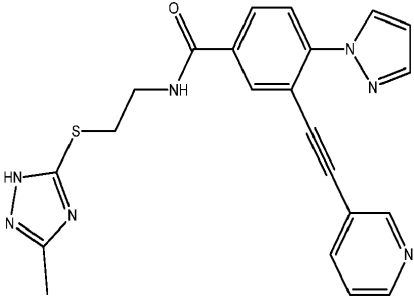
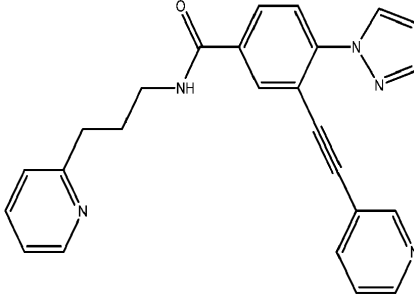
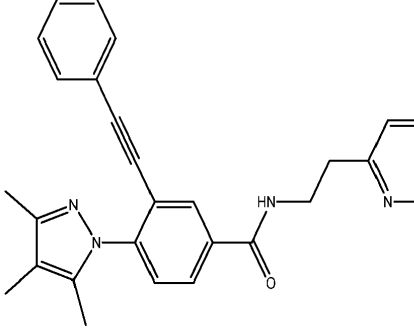
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Struktur	Struktur-ID
	
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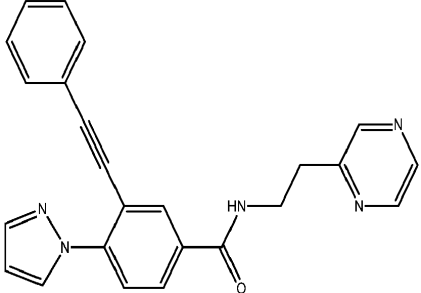
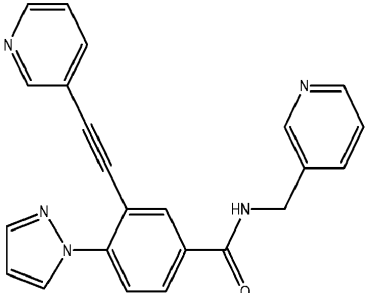
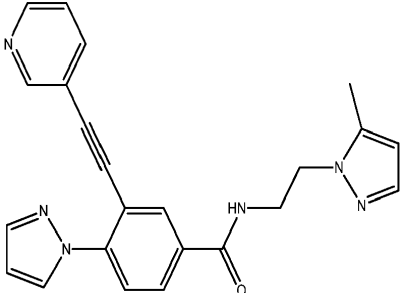
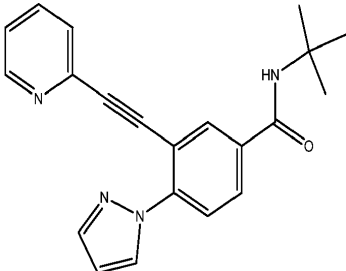
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Struktur	Struktur-ID
 <p>Chemical structure of compound TT-02940: A central benzene ring is substituted at the 1-position with a pyrazole ring, at the 2-position with a propyl chain ending in a secondary amide group (-NH-), and at the 4-position with a propargyl group (-C≡CH₂-) which is further substituted with a pyridine ring.</p>	TT-02940
 <p>Chemical structure of compound TT-02941: A central benzene ring is substituted at the 1-position with a pyrazole ring, at the 2-position with a pentyl chain ending in a secondary amide group (-NH-), and at the 4-position with a propargyl group (-C≡CH₂-) which is further substituted with a pyridine ring.</p>	TT-02941
 <p>Chemical structure of compound TT-02942: A central benzene ring is substituted at the 1-position with a 1,3,5-trimethyl-1H-imidazole ring, at the 2-position with a propargyl group (-C≡CH₂-) which is further substituted with a phenyl ring, and at the 4-position with a propyl chain ending in a secondary amide group (-NH-) which is further substituted with a pyridine ring.</p>	TT-02942
	TT-02943

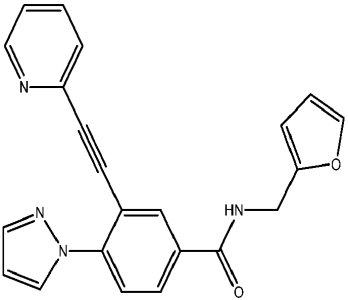
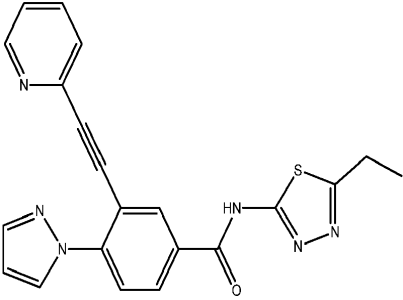
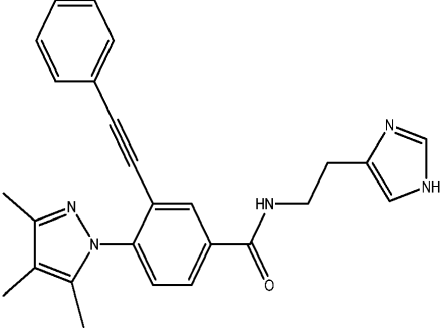
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Struktur	Struktur-ID
	
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	TT-02946

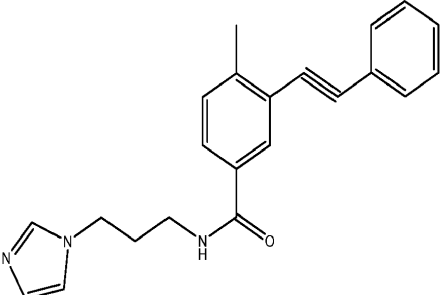
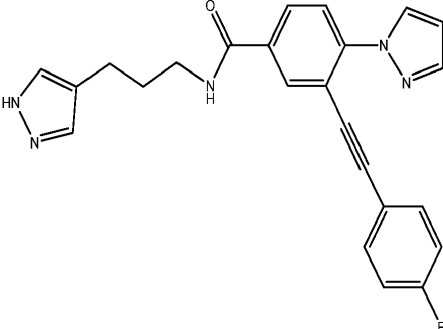
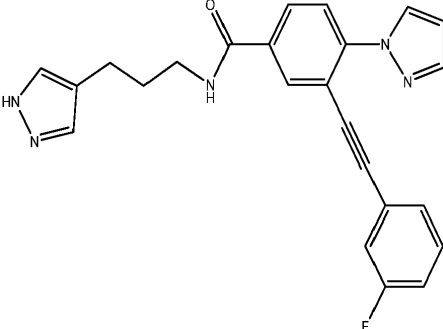
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Struktur	Struktur-ID
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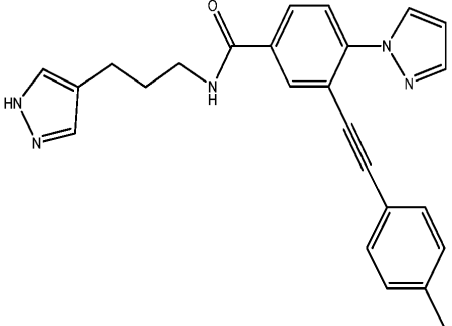
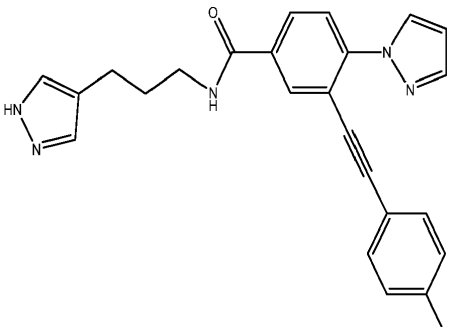
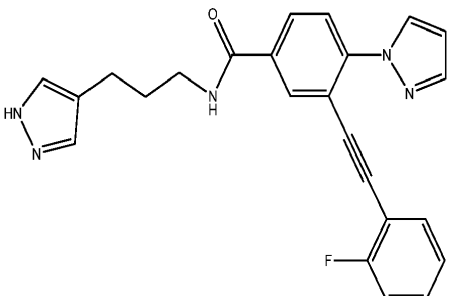
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Struktur	Struktur-ID
	
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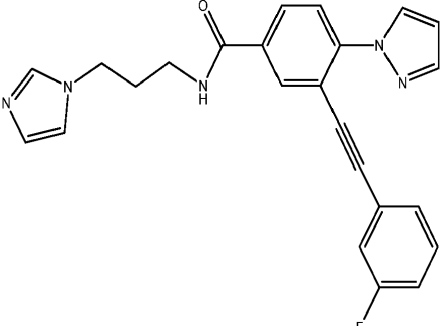
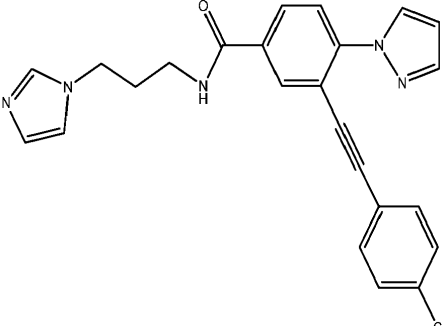
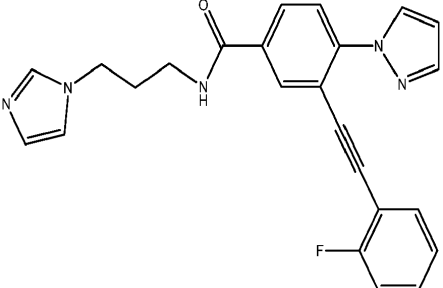
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Struktur	Struktur-ID
 <p>Chemical structure of a substituted benzamide derivative. The central benzene ring is substituted with a 4-methylphenyl group via a triple bond, a 1-imidazolyl group, and a 4-(4-imidazolylbutyl)amino group.</p>	
 <p>Chemical structure of a substituted benzamide derivative. The central benzene ring is substituted with a 4-chlorophenyl group via a triple bond, a 1-imidazolyl group, and a 4-(4-imidazolylbutyl)amino group.</p>	TT-03203
 <p>Chemical structure of a substituted benzamide derivative. The central benzene ring is substituted with a 3-fluorophenyl group via a triple bond, a 1-imidazolyl group, and a 4-(4-imidazolylbutyl)amino group.</p>	TT-03211
	TT-03217

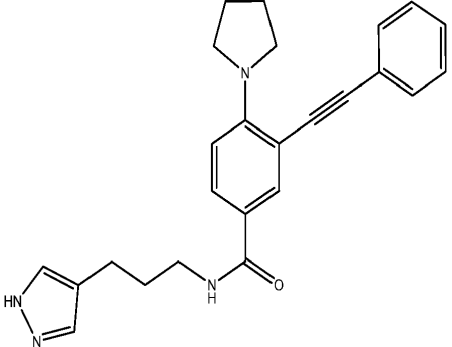
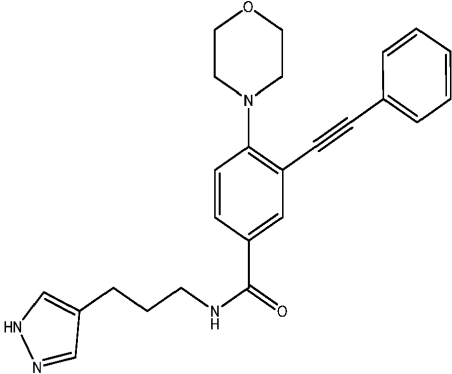
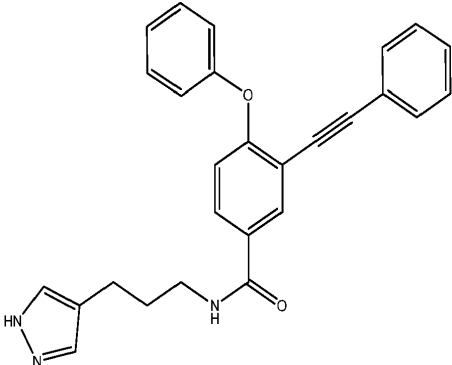
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Struktur	Struktur-ID
	
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	TT-03230

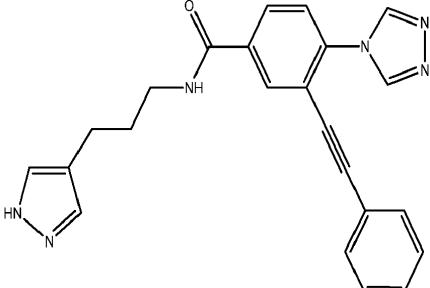
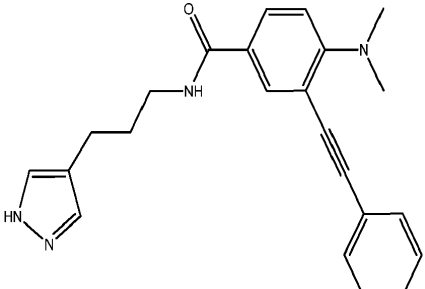
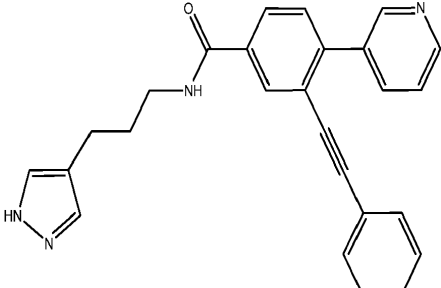
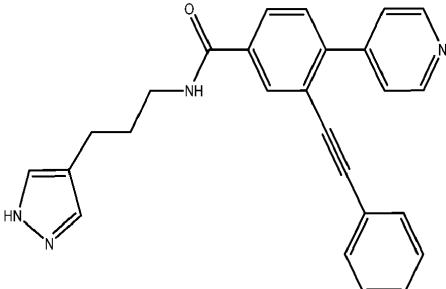
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Struktur	Struktur-ID
	
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	TT-03237

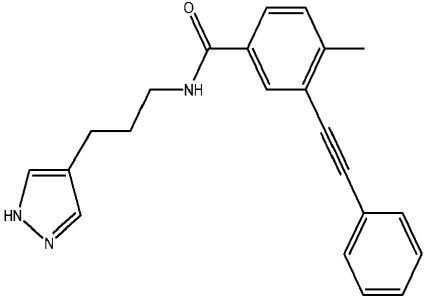
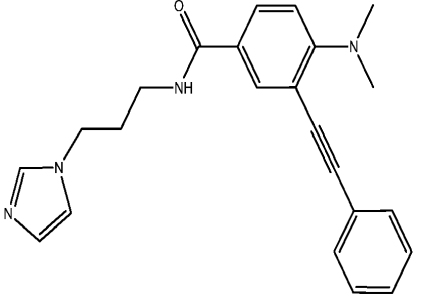
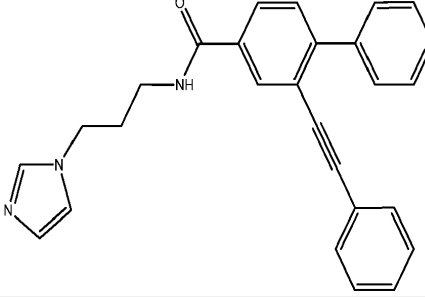
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Struktur	Struktur-ID
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 <chem>CC1=CC=C(C=C1)C#CC2=CC=C(C=C2)C(=O)NCCC3=CNC=C3N(C)C</chem>	TT-03242
 <chem>CC1=CC=C(C=C1)C#CC2=CC=C(C=C2)C(=O)NCCC3=CNC=C3c4ccncc4</chem>	TT-03245
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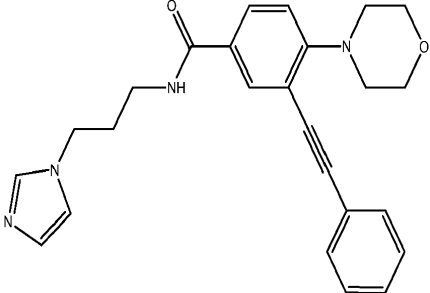
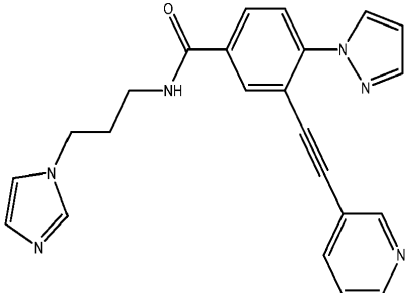
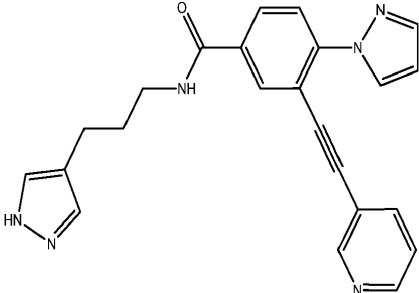
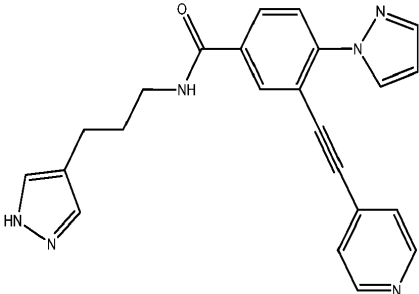
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Struktur	Struktur-ID
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	TT-03256
	TT-03261

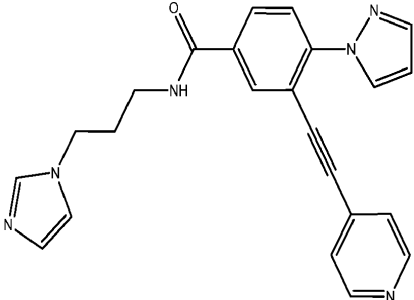
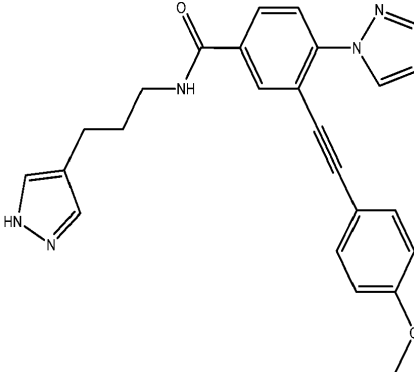
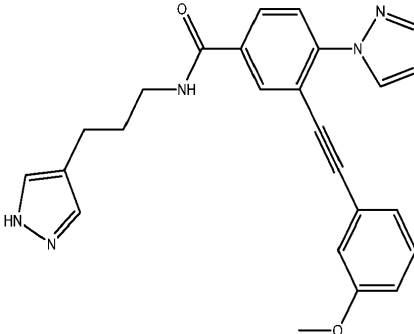
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Struktur	Struktur-ID
	
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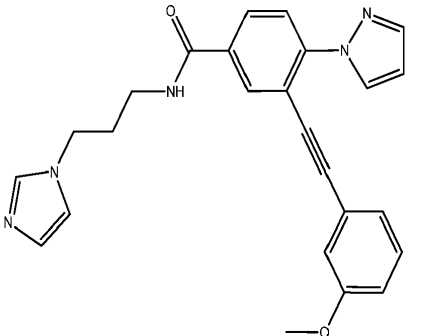
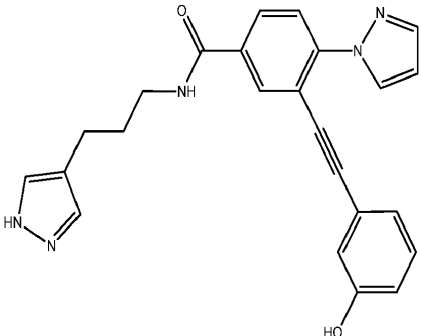
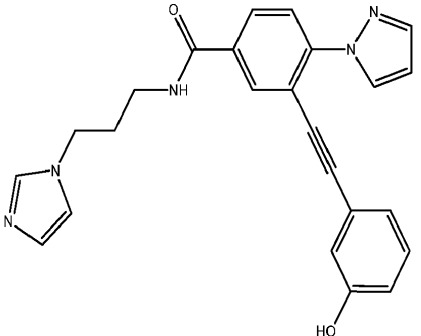
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Struktur	Struktur-ID
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	TT-03309

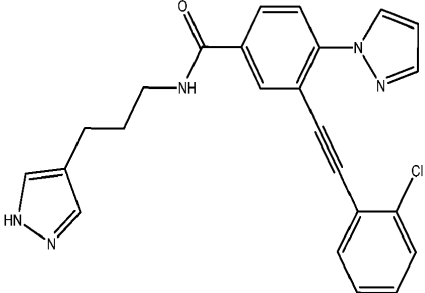
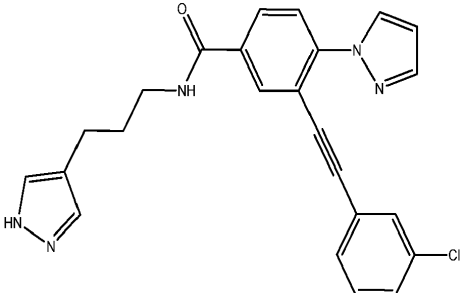
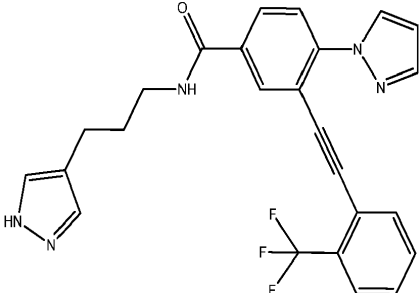
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Struktur	Struktur-ID
 <p>Chemical structure showing a central benzamide core. The benzamide ring is substituted with an imidazole ring at the 2-position and a 4-methoxyphenylethynyl group at the 4-position. The amide group is attached to a 4-(1H-imidazol-2-yl)butan-1-yl chain.</p>	
 <p>Chemical structure showing a central benzamide core. The benzamide ring is substituted with an imidazole ring at the 2-position and a 4-hydroxyphenylethynyl group at the 4-position. The amide group is attached to a 4-(1H-imidazol-2-yl)butan-1-yl chain.</p>	TT-03311
 <p>Chemical structure showing a central benzamide core. The benzamide ring is substituted with an imidazole ring at the 2-position and a 4-hydroxyphenylethynyl group at the 4-position. The amide group is attached to a 4-(1H-imidazol-2-yl)butan-1-yl chain.</p>	TT-03312
	TT-03321

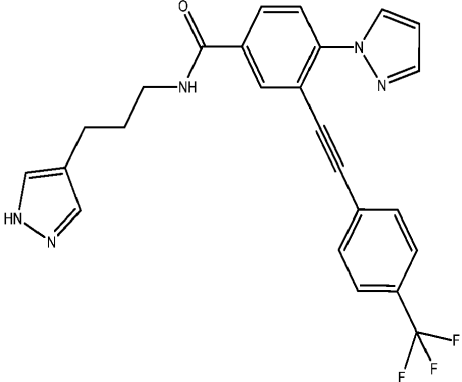
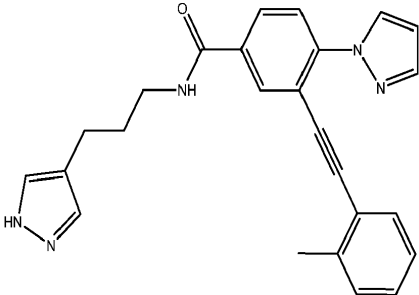
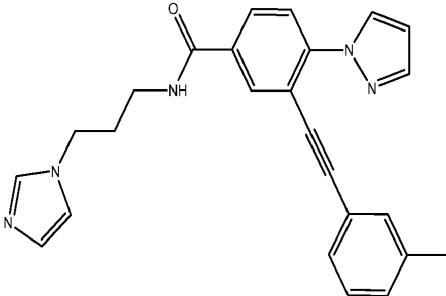
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Struktur	Struktur-ID
	
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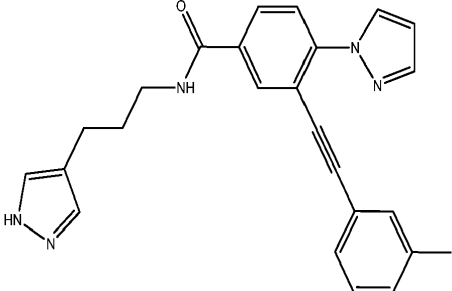
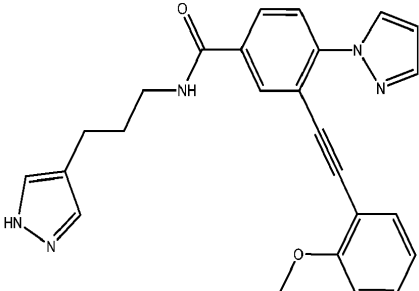
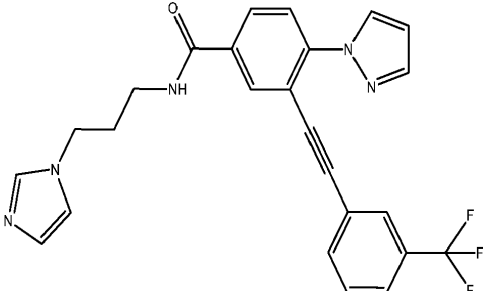
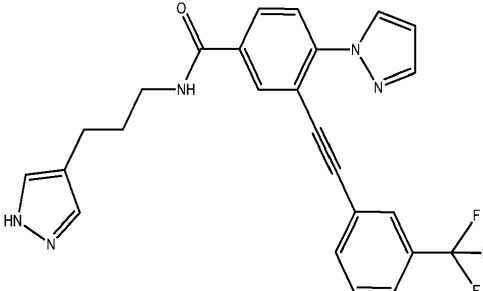
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Struktur	Struktur-ID
	
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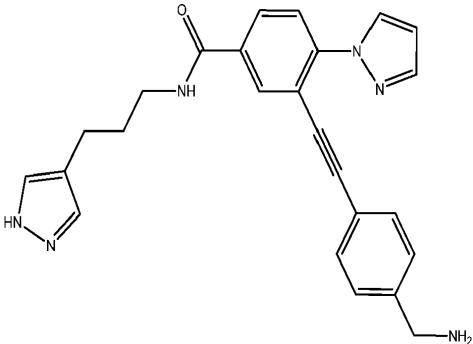
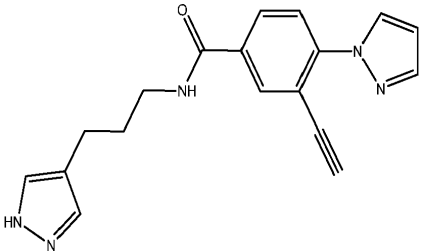
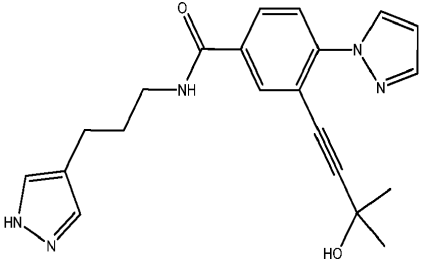
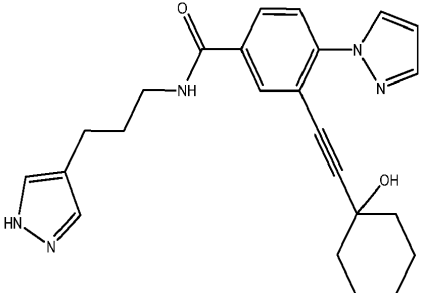
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Struktur	Struktur-ID
	
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	TT-03331
	TT-03332

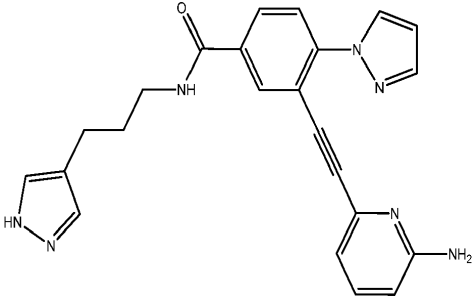
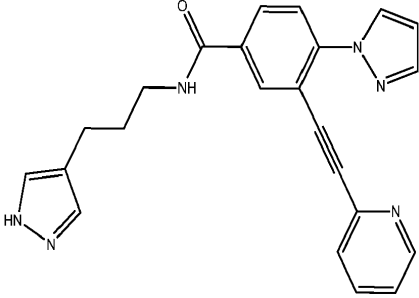
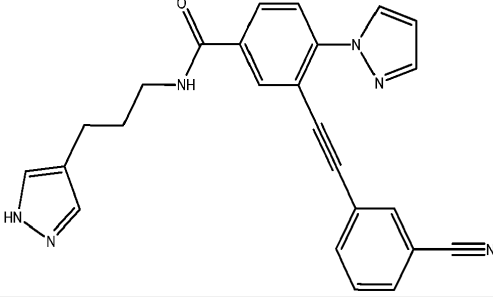
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Struktur	Struktur-ID
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	TT-03337
	TT-03346
	TT-03351

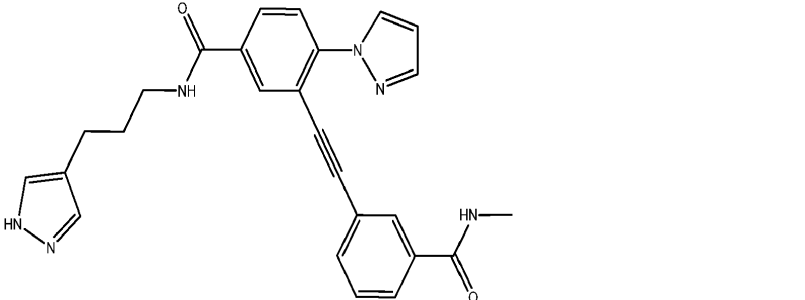
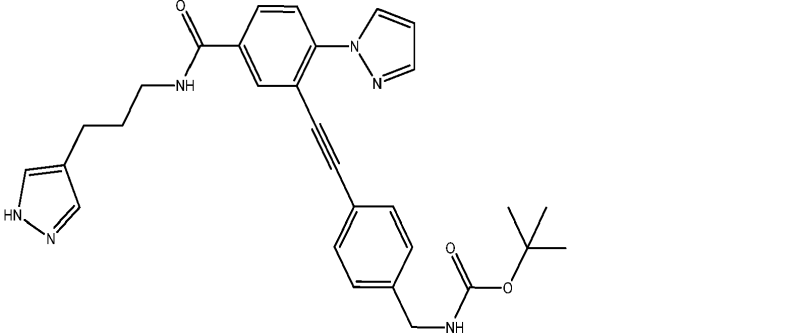
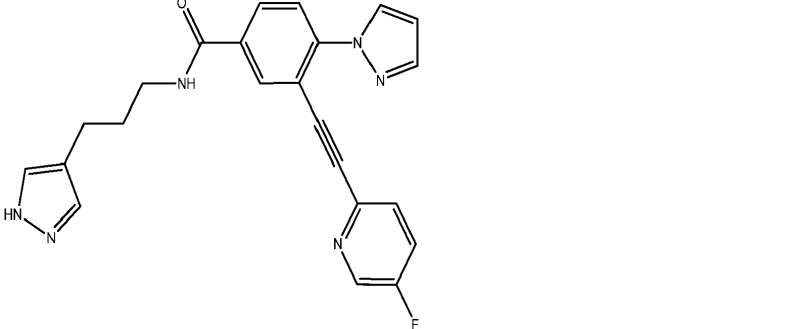
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Struktur	Struktur-ID
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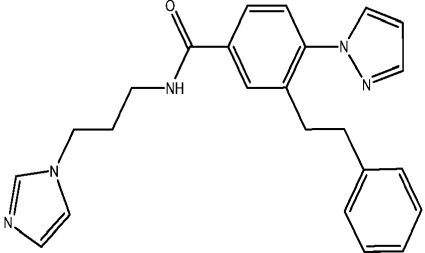
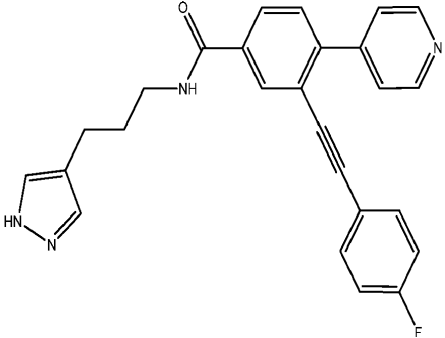
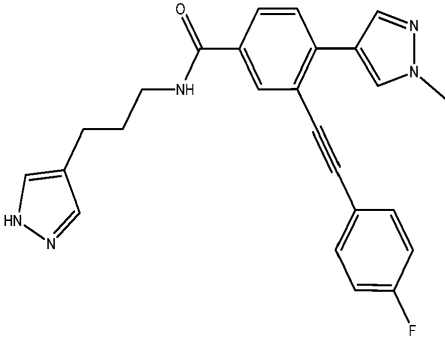
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Struktur	Struktur-ID
	
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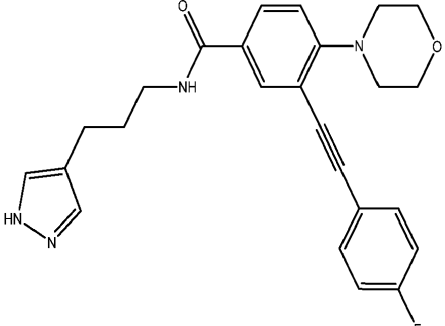
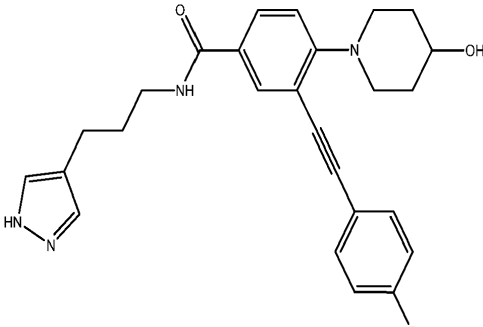
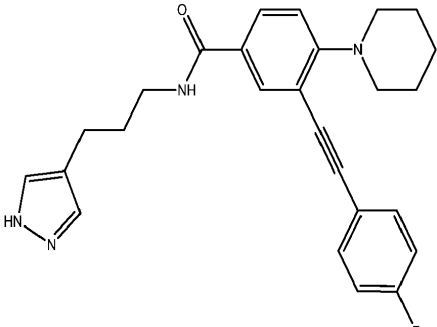
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Struktur	Struktur-ID
	
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	TT-03586

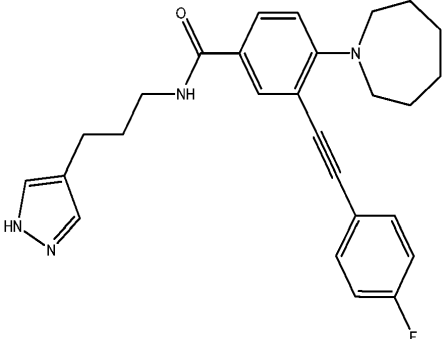
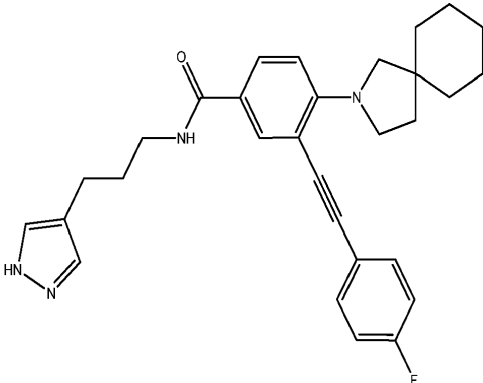
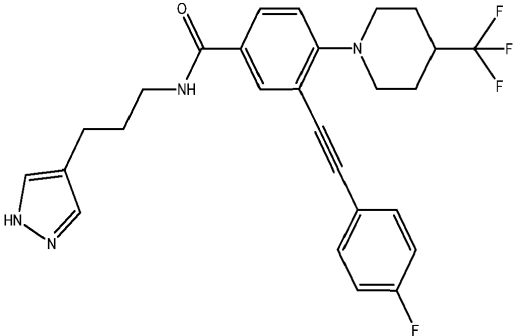
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Struktur	Struktur-ID
	
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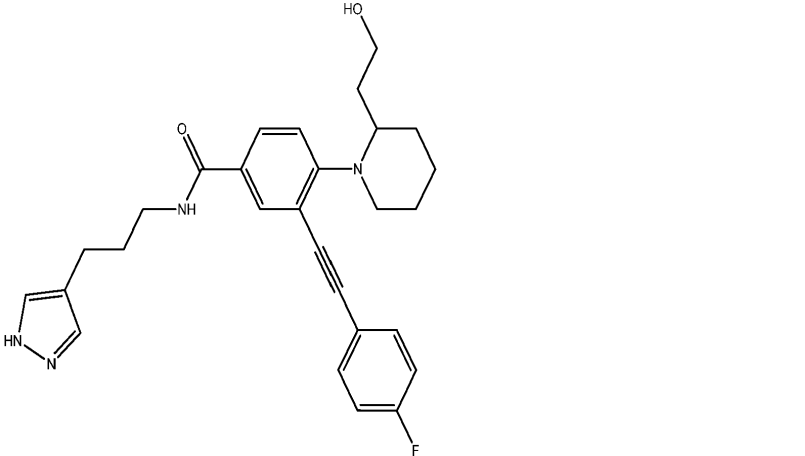
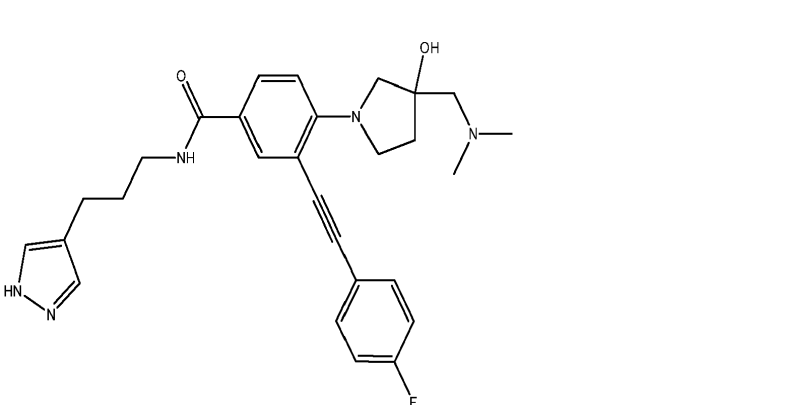
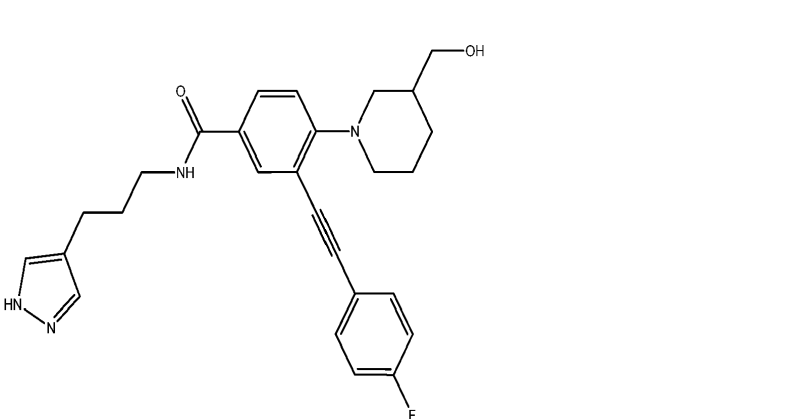
EP 3087051

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Struktur	Struktur-ID
	
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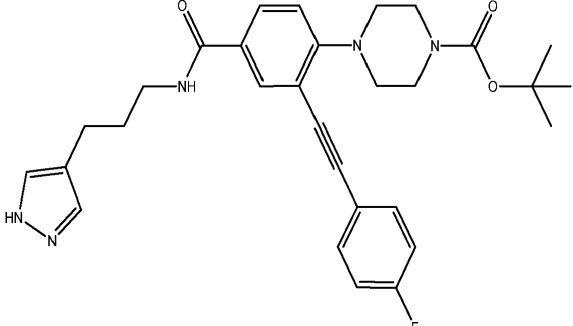
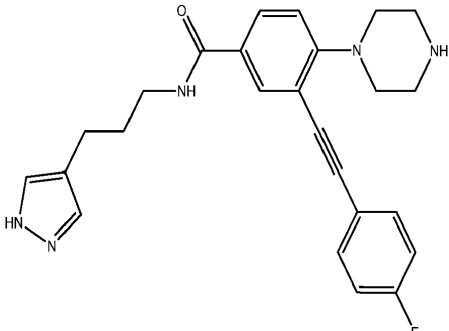
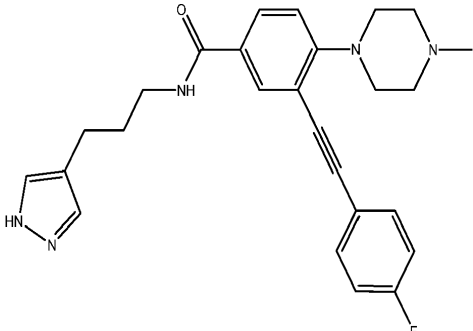
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Struktur	Struktur-ID
 <p>The structure shows a central benzene ring substituted at the 1 and 4 positions. At the 1-position, there is a piperidine ring with a hydroxyethyl group (-CH₂CH₂OH) attached to its 2-position. At the 4-position, there is a propyl chain (-CH₂CH₂CH₂-) attached to its 2-position, which is further connected to an imidazole ring. A triple bond (-C≡C-) connects the 1 and 4 positions of the benzene ring to a 4-fluorophenyl ring.</p>	
 <p>The structure is similar to the first one, but the piperidine ring is replaced by a pyrrolidine ring. The hydroxyethyl group is attached to the 2-position of the pyrrolidine ring, and the propyl chain is attached to its 1-position. The rest of the molecule (benzene ring, triple bond, and 4-fluorophenyl group) remains the same.</p>	TT-03594
 <p>The structure is similar to the first one, but the hydroxyethyl group is replaced by a hydroxymethyl group (-CH₂OH) attached to the 2-position of the piperidine ring. The rest of the molecule remains the same.</p>	TT-03595
	TT-03596

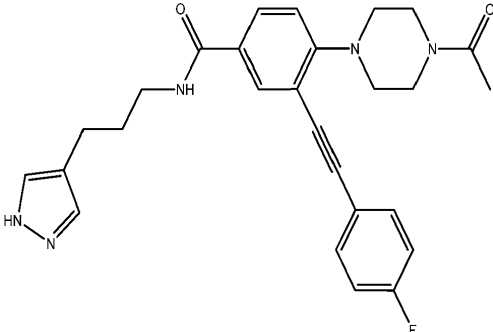
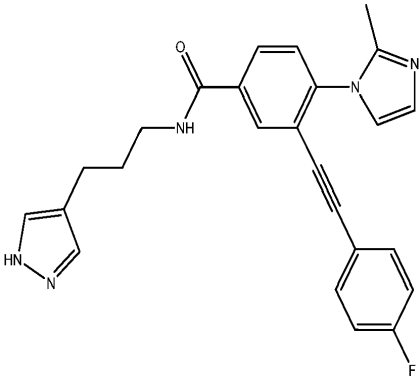
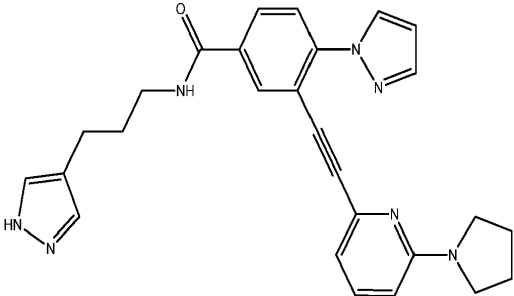
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Struktur	Struktur-ID
 <p>Chemical structure showing a central benzene ring substituted with a 4-(4-fluorophenyl)but-1-yn-1-yl group, a 4-(4-fluorophenyl)but-1-yn-1-yl group, a 4-(4-fluorophenyl)but-1-yn-1-yl group, and a 4-(4-fluorophenyl)but-1-yn-1-yl group. The benzamide part is substituted with a 4-(4-fluorophenyl)but-1-yn-1-yl group and a 4-(4-fluorophenyl)but-1-yn-1-yl group. The piperazine ring is substituted with a tert-butyl ester group.</p>	
 <p>Chemical structure showing a central benzene ring substituted with a 4-(4-fluorophenyl)but-1-yn-1-yl group, a 4-(4-fluorophenyl)but-1-yn-1-yl group, a 4-(4-fluorophenyl)but-1-yn-1-yl group, and a 4-(4-fluorophenyl)but-1-yn-1-yl group. The benzamide part is substituted with a 4-(4-fluorophenyl)but-1-yn-1-yl group and a 4-(4-fluorophenyl)but-1-yn-1-yl group. The piperazine ring is substituted with a hydrogen atom.</p>	TT-03597
 <p>Chemical structure showing a central benzene ring substituted with a 4-(4-fluorophenyl)but-1-yn-1-yl group, a 4-(4-fluorophenyl)but-1-yn-1-yl group, a 4-(4-fluorophenyl)but-1-yn-1-yl group, and a 4-(4-fluorophenyl)but-1-yn-1-yl group. The benzamide part is substituted with a 4-(4-fluorophenyl)but-1-yn-1-yl group and a 4-(4-fluorophenyl)but-1-yn-1-yl group. The piperazine ring is substituted with a methyl group.</p>	TT-03598
	TT-03599

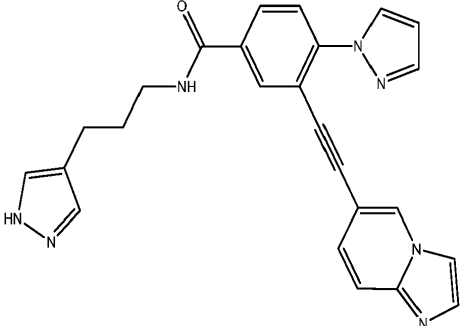
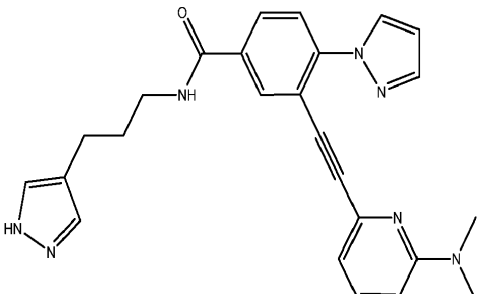
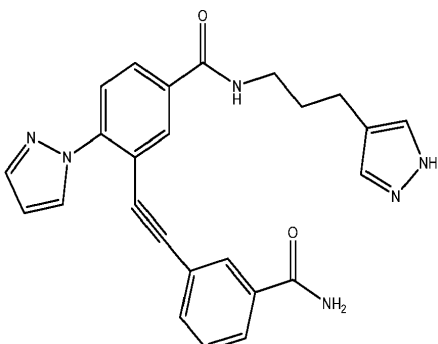
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Struktur	Struktur-ID
	
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	TT-03620

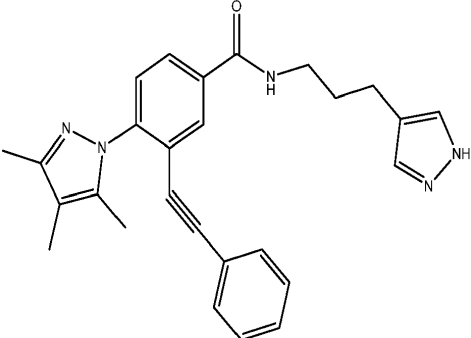
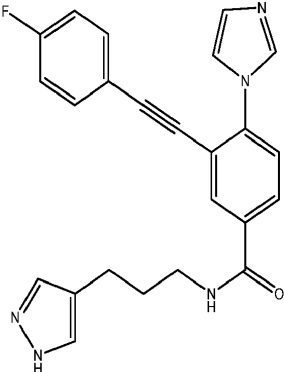
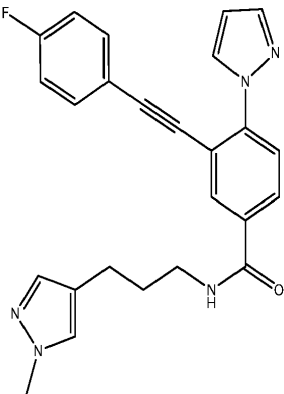
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Struktur	Struktur-ID
	
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	TT-03626

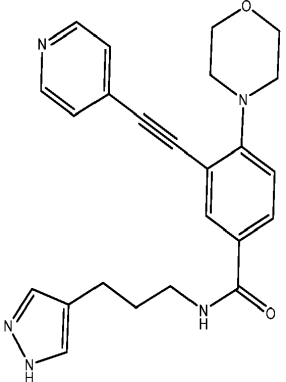
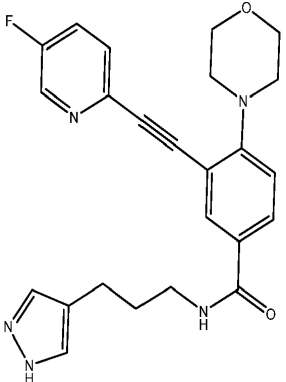
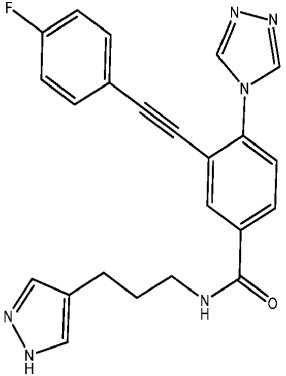
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Struktur	Struktur-ID
	
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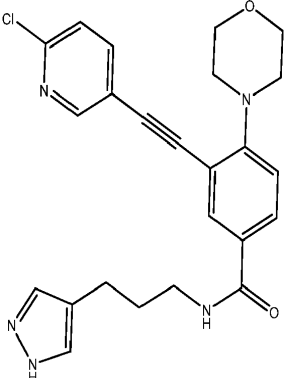
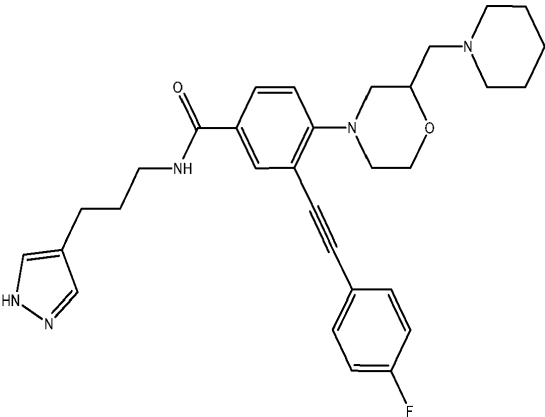
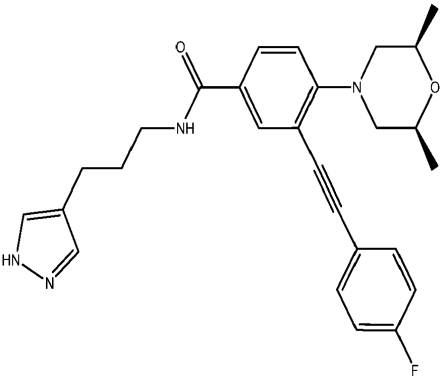
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Struktur	Struktur-ID
 <p>Chemical structure showing a pyridine ring connected via a triple bond to a benzene ring. The benzene ring is also connected to a morpholine ring and a 4-ethyl-5H-imidazole ring.</p>	
 <p>Chemical structure showing a 4-fluoropyridine ring connected via a triple bond to a benzene ring. The benzene ring is also connected to a morpholine ring and a 4-ethyl-5H-imidazole ring.</p>	TT-03633
 <p>Chemical structure showing a 4-fluorophenyl ring connected via a triple bond to a benzene ring. The benzene ring is also connected to a 1H-imidazole ring and a 4-ethyl-5H-imidazole ring.</p>	TT-03634
	TT-03655

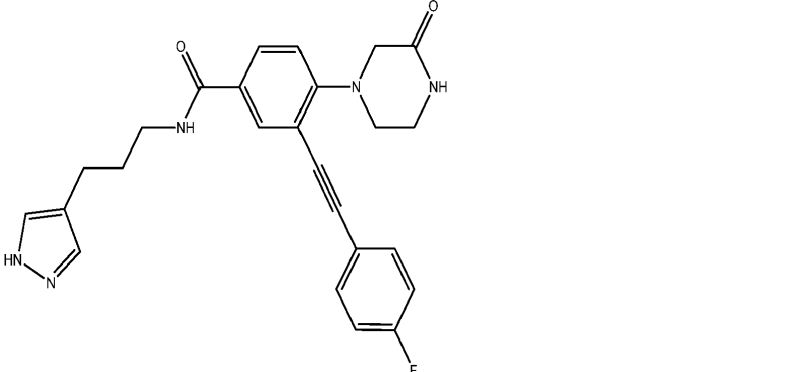
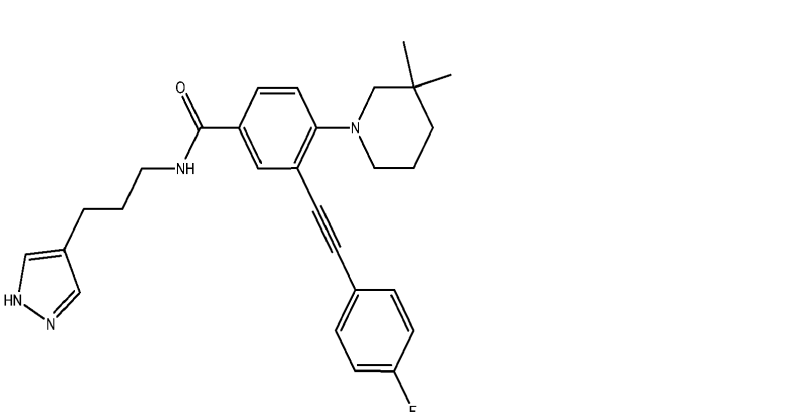
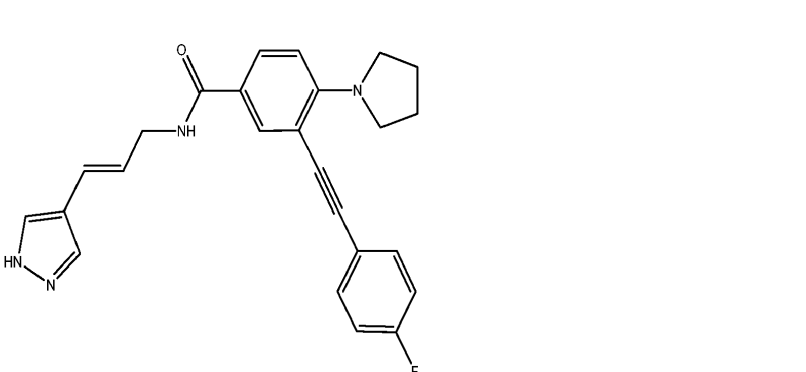
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Struktur	Struktur-ID
	
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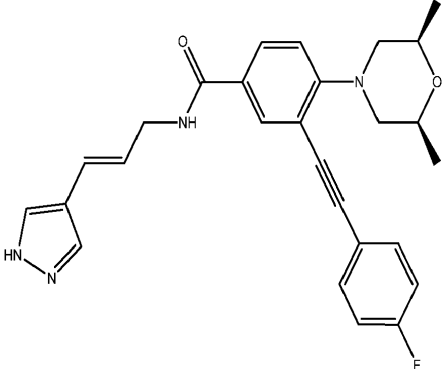
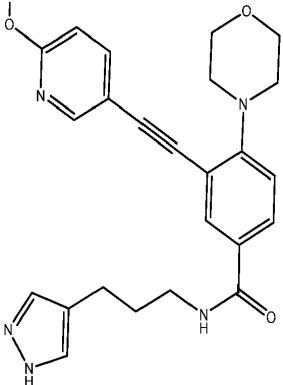
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Struktur	Struktur-ID
	
	TT-03676
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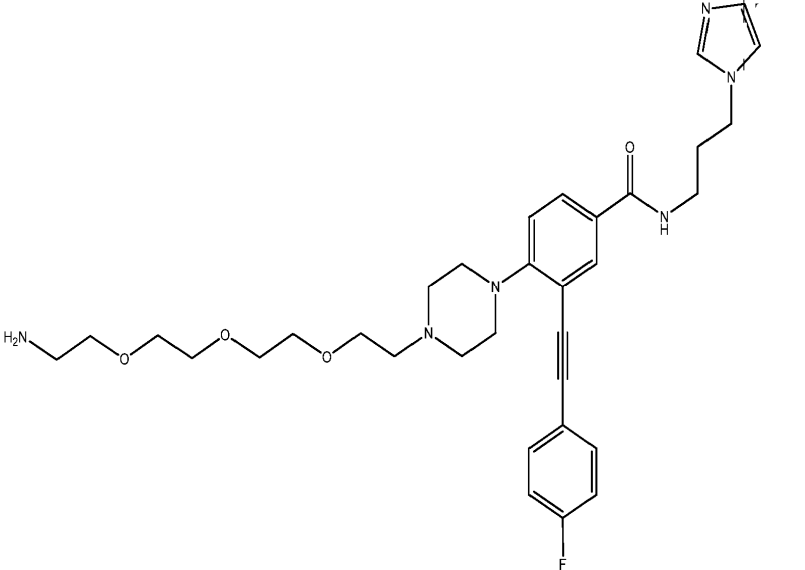
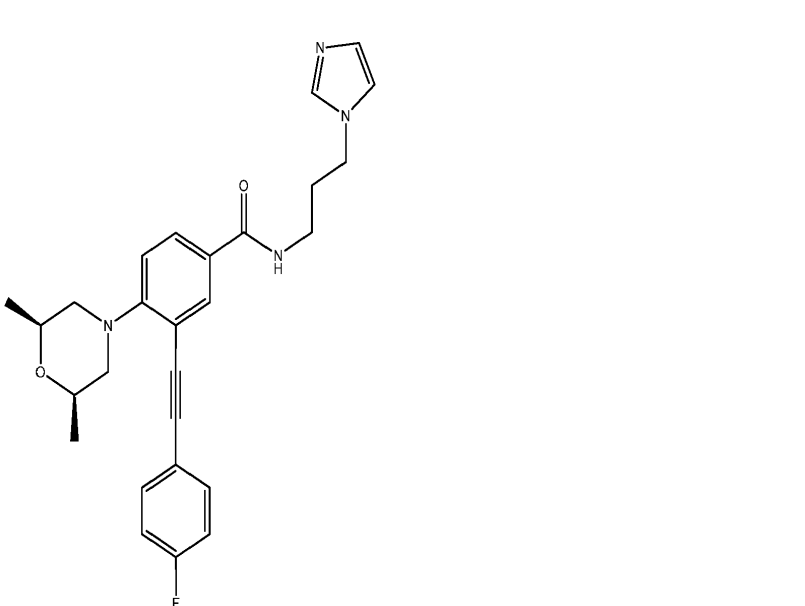
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Struktur	Struktur-ID
	
	TT-03720
	TT-03725

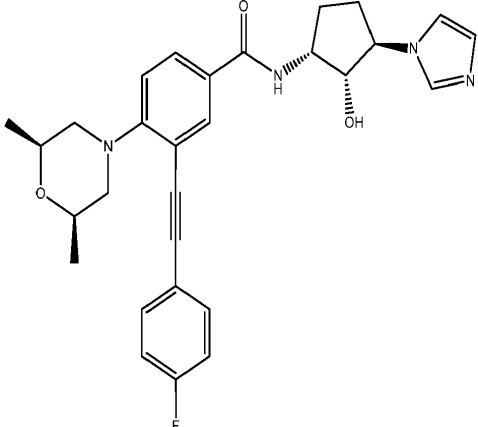
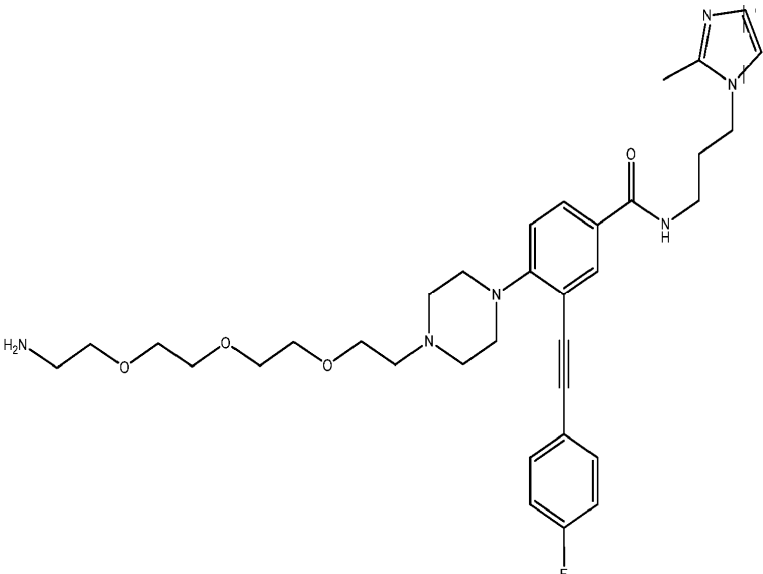
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Struktur	Struktur-ID
 <p>Chemical structure showing a long-chain molecule. It features a primary amine group (H₂N) at the left end, followed by a polyether chain (three ether linkages). This is connected to a piperazine ring. The piperazine ring is further substituted with a 4-(4-fluorophenyl)but-1-yn-1-yl group (a triple bond connecting to a para-fluorophenyl ring) and a 3-(4-methyl-1H-imidazol-1-yl)propanamide group (a propanamide chain connected to an imidazole ring).</p>	
 <p>Chemical structure showing a molecule with a morpholine ring substituted with a methyl group. It is further substituted with a 4-(4-fluorophenyl)but-1-yn-1-yl group (a triple bond connecting to a para-fluorophenyl ring) and a 3-(4-methyl-1H-imidazol-1-yl)propanamide group (a propanamide chain connected to an imidazole ring).</p>	TT-03727
	TT-03733

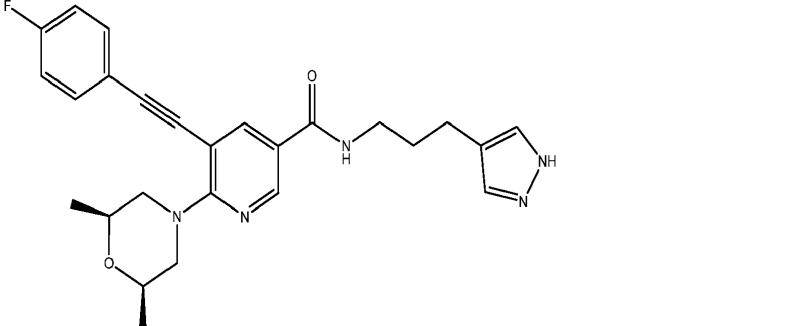
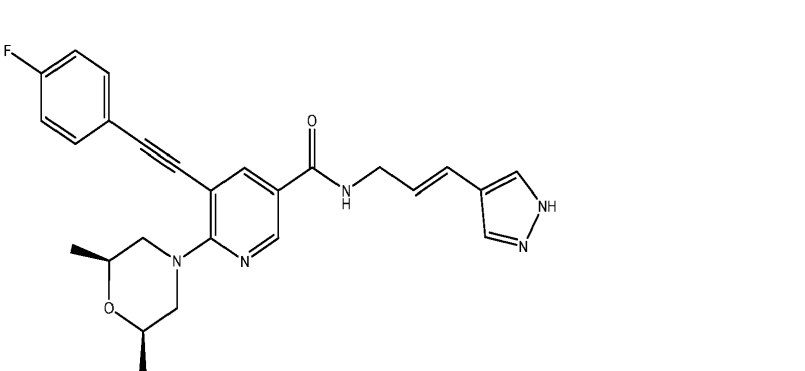
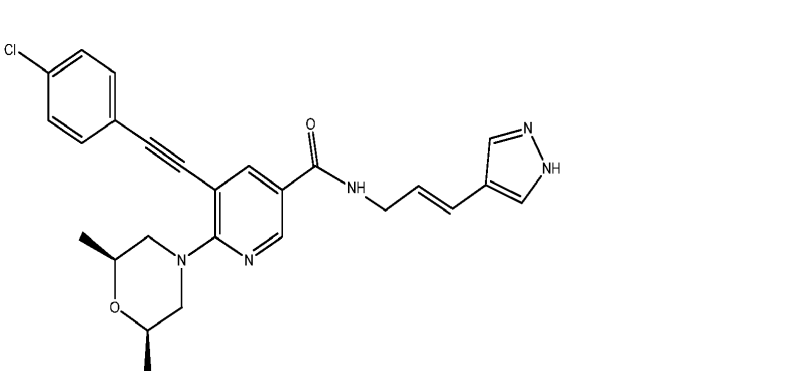
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Struktur	Struktur-ID
	
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	TT-03750

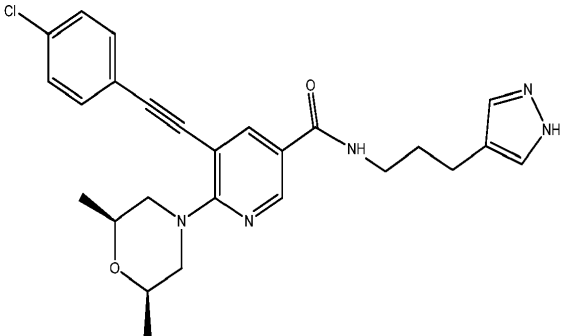
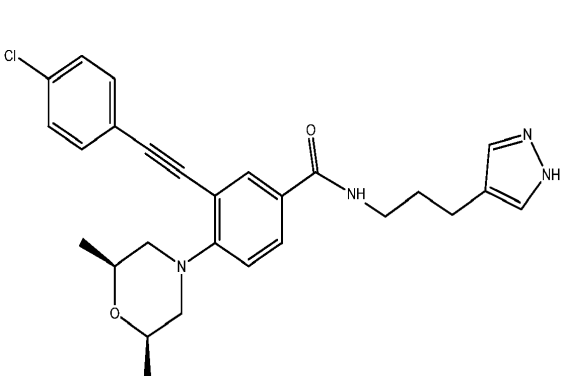
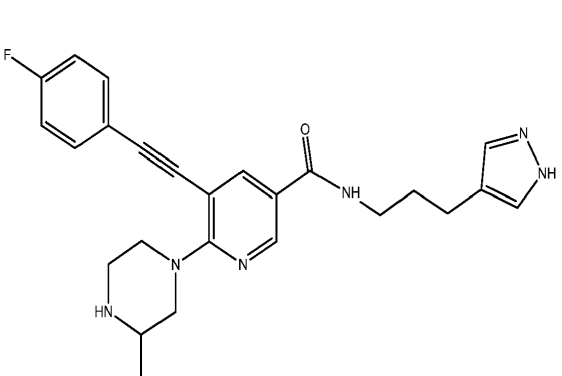
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Struktur	Struktur-ID
	
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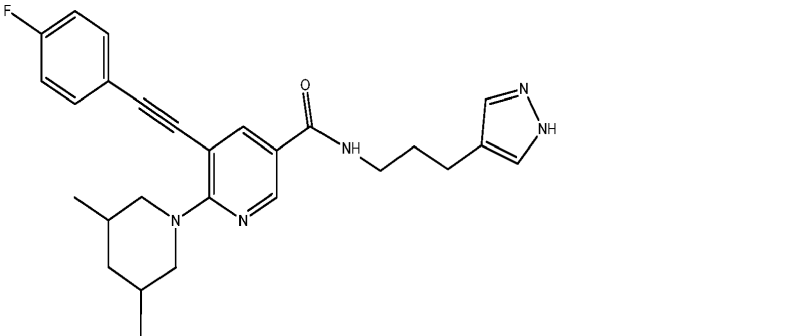
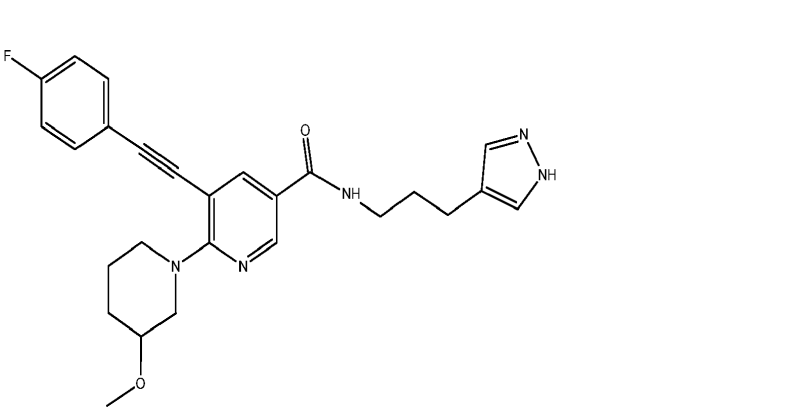
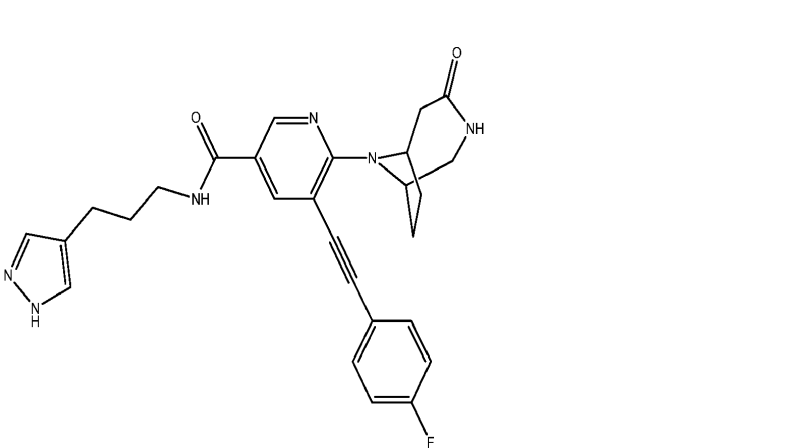
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Struktur	Struktur-ID
	
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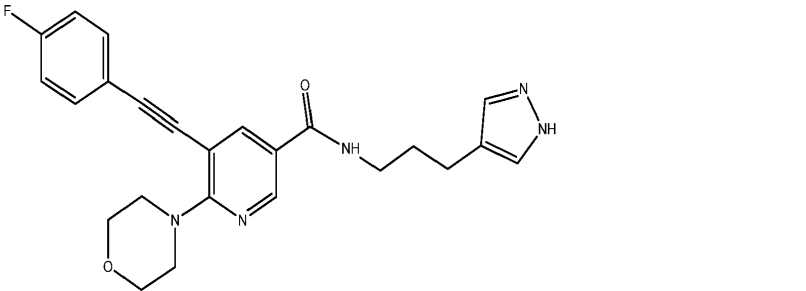
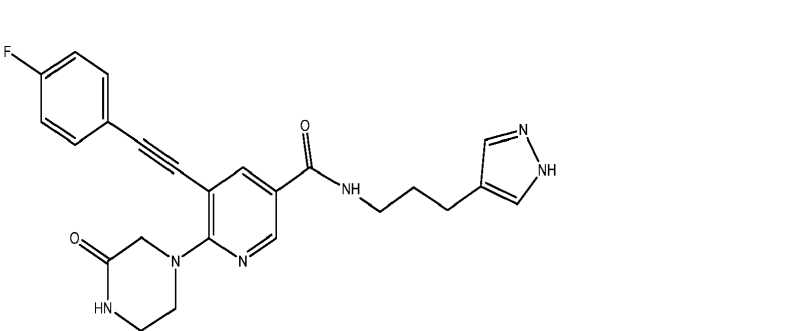
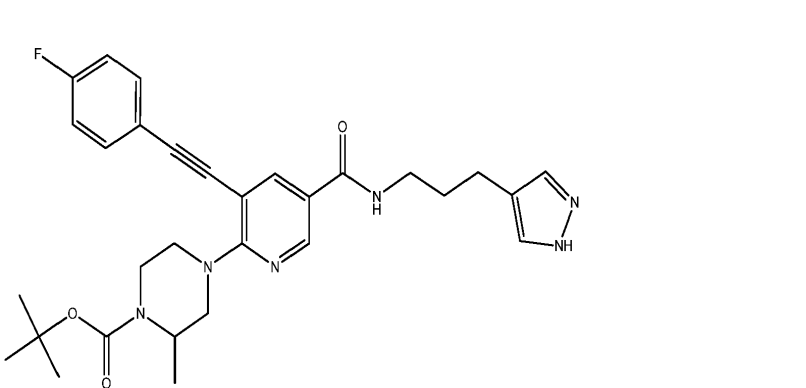
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Struktur	Struktur-ID
	
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	TT-03767

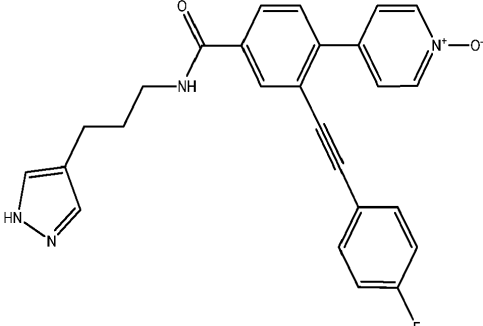
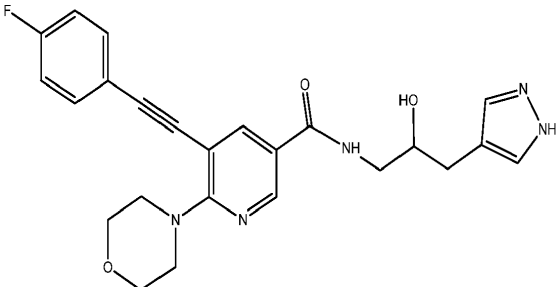
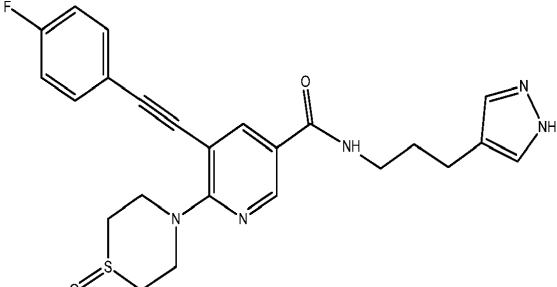
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Struktur	Struktur-ID
	
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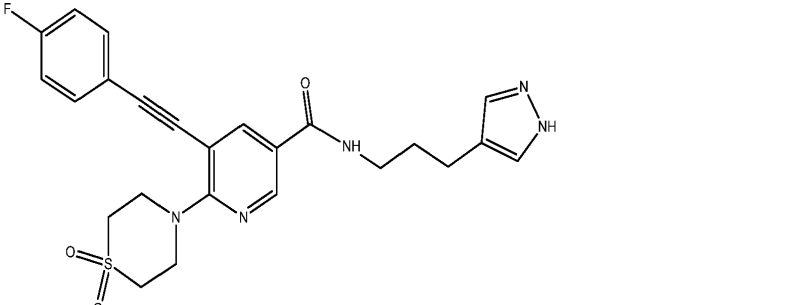
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Struktur	Struktur-ID
	
	TT-03774
	TT-03782
	TT-03783

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Struktur	Struktur-ID
	

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12. Forbindelse ifølge et hvilket som helst av kravene 1-11, for anvendelse i en fremgangsmåte for behandling av kreft i et individ diagnostisert med eller mistenkt for å ha kreft.

13. Forbindelsen for anvendelse ifølge krav 12, hvori kreften er hematopoietisk kreft, eventuelt hvori den hematopoietiske kreften er leukemi.