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(54) Title **AMINE-SUBSTITUTED ARYL OR HETEROARYL COMPOUNDS AS EHMT1 AND EHMT2 INHIBITORS**

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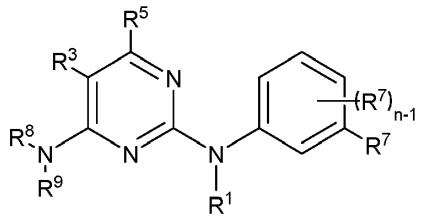
PATENTKRAV

1. Forbindelse av formel (IIa1) for anvendelse ved behandling eller forebygging av en blodlidelse:



(IIa1),

eller en tautomer derav, eller et farmasøytisk akseptabelt salt av forbindelsen eller tautomeren, hvori

R^1 er H eller C_1-C_4alkyl;

R^3 velges fra gruppen som består av H, halogen, cyano, C_1-C_6alkoksyl, C_6-C_{10}aryl, $NR^aC(O)R^b$, C_3-C_8sykloalkyl, 4- til 7-leddet heterosykloalkyl, 5- til 6-leddet heteroaryl, og C_1-C_6alkyl, hvori C_1-C_6alkoksyl og C_1-C_6alkyl er eventuelt substituert med ett eller flere av halogen, OR^a eller NR^aR^b, der hver av R^a og R^b uavhengig er H eller C_1-C_6alkyl, eller R^3 er $-Q^1$-T^1, der Q^1 er en binding eller C_1-C_6alkylen-, C_2-C_6alkenylen- eller C_2-C_6alkynylenbindeledd eventuelt substituert med ett eller flere av halogen, cyano, hydroksyl, okso eller C_1-C_6alkoksyl, og T^1 er H, halogen, cyano, NR^8R^9, $C(O)NR^8R^9$, OR^8, OR^9, eller R^{S1}, der R^{S1} er C_3-C_8sykloalkyl, fenyl, 4- til 12-leddet heterosykloalkyl som inneholder 1–4 heteroatomer valgt fra N, O, og S, eller et 5- eller 6-leddet heteroaryl og R^{S1} er eventuelt substituert med ett eller flere av halogen, C_1-C_6alkyl, hydroksyl, okso, $-C(O)R^9$, $-SO_2R^8$, $-SO_2N(R^8)_2$, $-NR^8C(O)R^9$, amino, mono- eller di-alkylamino eller C_1-C_6alkoksyl;

R^5 velges fra gruppen som består av F, Br, cyano, C_1-C_6alkoksyl, C_6-C_{10}aryl, NR^aR^b, $C(O)NR^aR^b$, $NR^aC(O)R^b$, C_3-C_8sykloalkyl, 4- til 12-leddet heterosykloalkyl som inneholder 1–4 heteroatomer valgt fra N, O og S, C_1-C_6alkyl eventuelt substituert med ett eller flere av halogen, OR^a eller NR^aR^b, og C_2-C_6alkynyl eventuelt substituert med 4- til 12-leddet heterosykloalkyl; hvori C_3-C_8sykloalkylet eller 4- til 12-leddet heterosykloalkyl er eventuelt substituert med ett eller flere av halogen, $C(O)R^a$, OR^a, NR^aR^b, 4- til 7-leddet heterosykloalkyl, $-C_1$-C_6alkylen-4- til 7-leddet heterosykloalkyl, eller C_1-C_4alkyl eventuelt substituert med ett eller flere av halogen, OR^a eller NR^aR^b, der hver av R^a og R^b uavhengig er H eller C_1-C_6alkyl; eller

R^5 og R^3 sammen med atomene som de festes til danner fenyl eller et 5- eller 6-leddet heteroaryl;

hver R^7 er uavhengig okso (=O) eller $-Q^2$-T^2, der hver Q^2 uavhengig er en binding eller C_1-C_6alkylen-, C_2-C_6alkenylen- eller C_2-C_6alkynylenbindeledd eventuelt substituert med ett eller flere av halogen, cyano, hydroksyl, amino, mono- eller di-alkylamino, eller C_1-C_6alkoksyl, og

hver T^2 uavhengig er H, halogen, cyano, OR^{10}, OR^{11}, $C(O)R^{11}$, $NR^{10}R^{11}$, $C(O)NR^{10}R^{11}$, $NR^{10}C(O)R^{11}$, 5- til 10-leddet heteroaryl, C_3-C_8sykloalkyl, eller 4- til 12-leddet heterosykloalkyl som inneholder 1–4 heteroatomer valgt fra N, O og S, og hvori det 5- til 10-leddede heteroarylet, C_3-C_8sykloalkylet eller det 4- til 12-leddede heterosykloalkylet er eventuelt substituert med ett eller flere av halogen, C_1-C_6alkyl eventuelt substituert med NR^xR^y, hydroksyl, okso, $N(R^8)_2$, cyano, C_1-C_6halogenalkyl, $-SO_2R^8$ eller C_1-C_6alkoksyl, hver av R^x og R^y er uavhengig H eller C_1-C_6alkyl; og R^7 er ikke H eller $C(O)OR^g$; eller eventuelt én R^7 og R^5 sammen danner et C_3-C_{10}alkylen-, C_2-C_{10}heteroalkylen-, C_4-C_{10}alkenylen-, C_2-C_{10}heteroalkenylen-, C_4-C_{10}alkynylen- eller C_2-C_{10}heteroalkynylenbindeledd eventuelt substituert med ett eller flere av halogen, cyano, hydroksyl eller C_1-C_6alkoksyl;

hver R^8 er uavhengig H eller C_1-C_6alkyl;

hver R^9 er uavhengig $-Q^3$-T^3, der Q^3 er en binding eller C_1-C_6alkylen, og T^3 er H;

hver R^{10} velges fra gruppen som består av H og C_1-C_6alkyl;

hver R^{11} er $-Q^6$-T^6, der hver Q^6 er en binding eller C_1-C_6alkylen-, C_2-C_6alkenylen- eller C_2-C_6alkynylenbindeledd eventuelt substituert med ett eller flere av halogen, cyano, hydroksyl, okso eller C_1-C_6alkoksyl, og T^6 er H, halogen, OR^g, NR^gR^h, $NR^gC(O)R^h$, $C(O)NR^gR^h$, $C(O)R^g$, $S(O)_2R^g$ eller R^{S3}, der hver av R^g og R^h uavhengig er H, fenyl, C_3-C_8sykloalkyl eller C_1-C_6alkyl eventuelt substituert med C_3-C_8sykloalkyl, eller R^g og R^h sammen med nitrogenatomet de festes til danner et 4- til 12-leddet heterosykloalkyl som inneholder 1–4 heteroatomer valgt fra N, O og S, og R^{S3} er C_3-C_8sykloalkyl, C_6-C_{10}aryl, 4- til 12-leddet heterosykloalkyl som inneholder 1–4 heteroatomer valgt fra N, O og S, eller et 5- til 10-leddet heteroaryl og R^{S3} er eventuelt substituert med ett eller flere $-Q^7$-T^7, hvori hver Q^7 uavhengig er en binding eller C_1-C_3alkylen-, C_2-C_3alkenylen- eller C_2-C_3alkynylenbindeledd hver eventuelt substituert med ett eller flere av halogen, cyano, hydroksyl eller C_1-C_6alkoksy, og hver T^7 uavhengig velges fra gruppen som består av H, halogen, cyano, C_1-C_6alkyl, C_3-C_8sykloalkyl, C_6-C_{10}aryl, 4- til 7-leddet heterosykloalkyl som inneholder 1–4 heteroatomer valgt fra N, O og S, 5- til 6-leddet heteroaryl, OR^j, $C(O)R^j$, NR^jR^k, $C(O)NR^jR^k$, $S(O)_2R^j$ og $NR^jC(O)R^k$, hver av R^j og R^k er uavhengig H eller C_1-C_6alkyl eventuelt substituert med ett eller flere halogen; eller $-Q^7$-T^7 er okso; eller

R^{10} og R^{11} tatt sammen med nitrogenatomet de festes til danner et 4- til 12-leddet heterosykloalkyl som inneholder 1–4 heteroatomer valgt fra N, O og S, som eventuelt er substituert med ett eller flere av halogen, C_1-C_6alkyl, hydroksyl eller C_1-C_6alkoksyl;

n er 0, 1, 2, 3 eller 4.

2. Forbindelse for anvendelse ifølge krav 1, hvori R^3 ikke er H.

3. Forbindelse for anvendelse ifølge et hvilket som helst av de foregående kravene, hvori n er 1 eller 2; og/eller

hvori R^1 er H eller CH_3; og/eller

hvori n er 1 eller 2, og minst én av R^7 er $-Q^2-OR^{11}$ der R^{11} er $-Q^6-R^{S3}$ og Q^6 er eventuelt substituert C_2-C_6alkylen-, C_2-C_6alkenylen-, eller C_2-C_6alkynylenbindeledd; og/eller

hvori n er 1 eller 2, og minst én av R^7 er $-Q^2-NR^{10}R^{11}$ der R^{11} er $-Q^6-R^{S3}$; og/eller

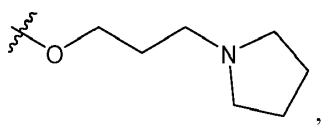
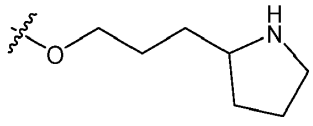
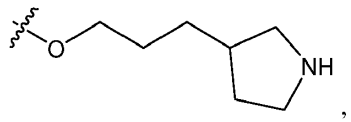
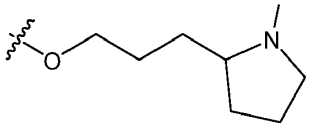
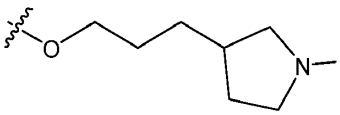
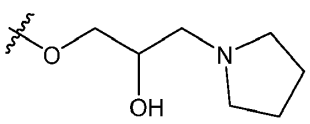
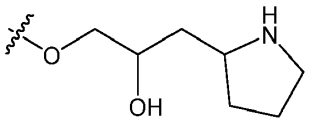
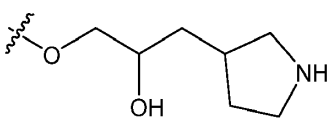
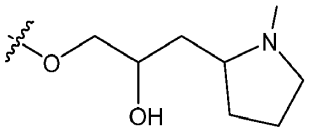
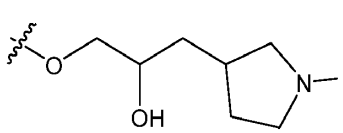
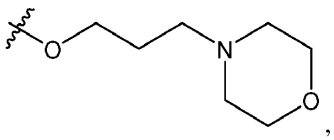
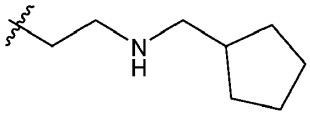
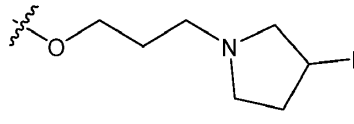
hvori Q^6 er C_2-C_6alkylen-, C_2-C_6alkenylen- eller C_2-C_6alkynylenbindeledd eventuelt substituert med et hydroksyl og R^{S3} er 4- til 7-leddet heterosykloalkyl eventuelt substituert med ett eller flere $-Q^7-T^7$; og/eller

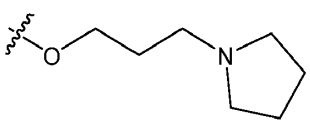
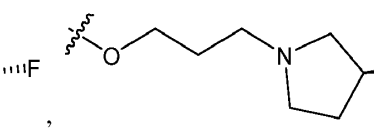
hvori Q^6 er C_1-C_6alkylen-, C_2-C_6alkenylen- eller C_2-C_6alkynylenbindeledd eventuelt substituert med et hydroksyl og R^{S3} er C_3-C_6sykloalkyl eventuelt substituert med ett eller flere $-Q^7-T^7$; og/eller

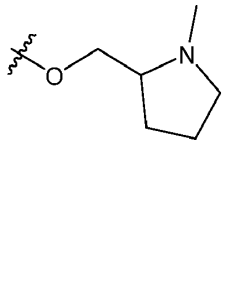
hvori hver Q^7 er uavhengig en binding eller et C_1-C_3alkylen-, C_2-C_3alkenylen- eller C_2-C_3alkynylenbindeledd og hver T^7 er uavhengig H, halogen, C_1-C_6alkyl eller fenyl; og/eller

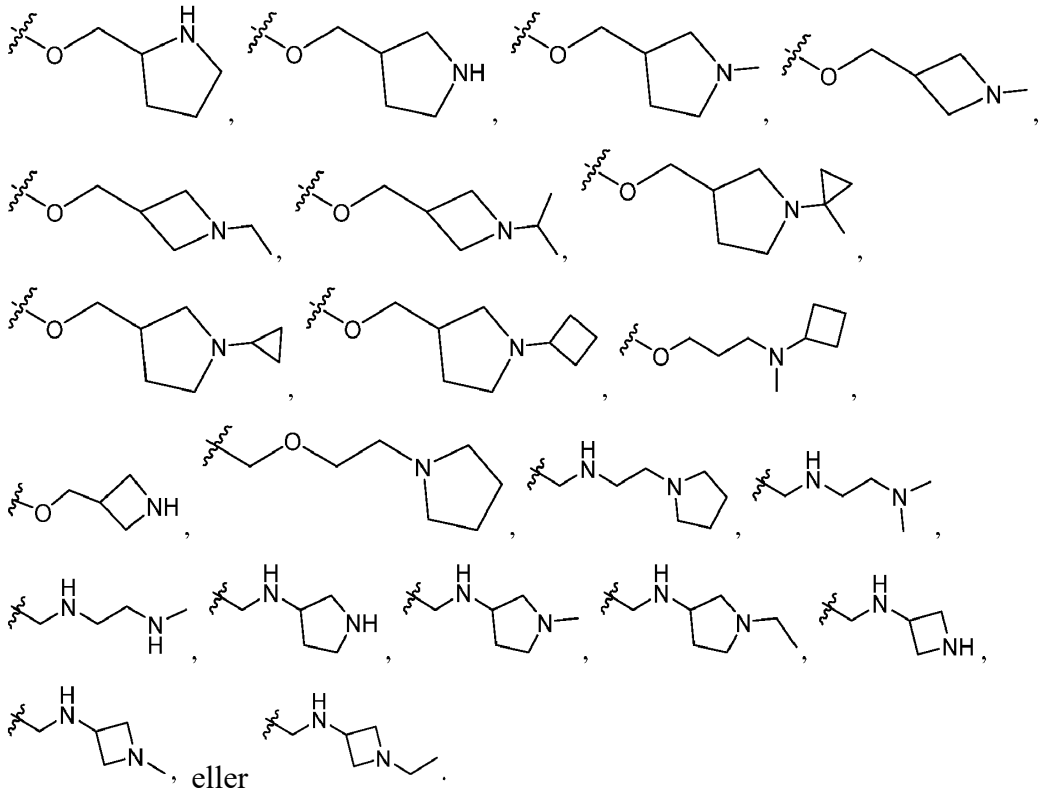
hvori Q^2 er en binding eller et C_1-C_4alkylen-, C_2-C_4alkenylen- eller C_2-C_4alkynylenbindeledd; og/eller

hvori minst én av R_7 er

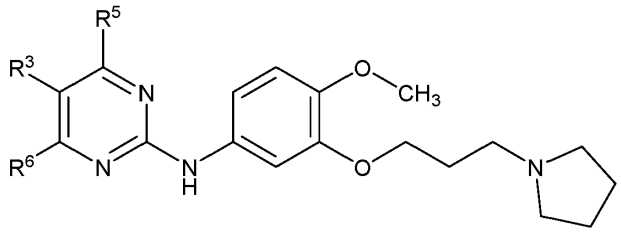




eller

4. Forbindelse for anvendelse ifølge et hvilket som helst av de foregående kravene, hvori n er 2 og forbindelsen videre omfatter en annen R^7 valgt fra halogen og metoksy.

5. Forbindelse for anvendelse ifølge krav 1, som er av formel (VI):

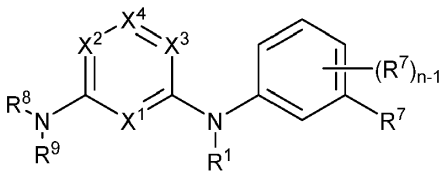


(VI),

hvori

R^5 velges fra gruppen som består av C_1-C_6alkyl og NR^8R^9; og R^6 er NR^8R^9.

6. Forbindelse for anvendelse ifølge et hvilket som helst av de foregående kravene, som er av formel (VIIIa):



(VIIIa),

hvori

X^1 er N;

X^2 er CR^3;

X^3 er N;

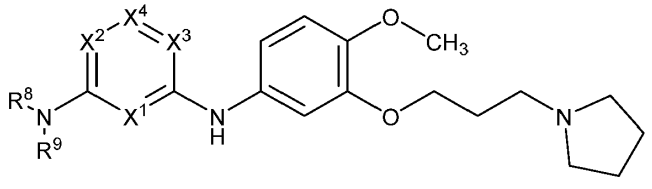
X^4 er CR^5;

R^3 er H; og

R^5 velges uavhengig fra gruppen som består av C_3-C_8sykloalkyl, og C_1-C_6alkyl eventuelt substituert med ett eller flere av halogen eller OR^a; eller

R^5 og R^3 sammen med atomene som de festes til danner fenyl eller et 5- eller 6-leddet heteroaryl.

7. Forbindelse for anvendelse ifølge et hvilket som helst av de foregående kravene, som er av formel (VIIIb):



(VIIIb),

hvori

X^1 er N;

X^2 er CR^3;

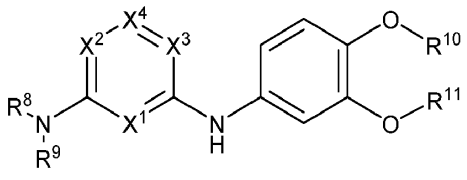
X^3 er N;

X^4 er CR^5;

R^5 velges fra gruppen som består av C_3-C_8sykloalkyl og C_1-C_6alkyl; eller

R^5 og R^3 sammen med atomene som de festes til danner fenyl eller et 5- eller 6-leddet heteroaryl.

8. Forbindelse for anvendelse ifølge et hvilket som helst av de foregående kravene, som er av formel (VIIIc):



(VIIIc),

hvori

X^1 er N;

X^2 er CR^3;

X^3 er N;

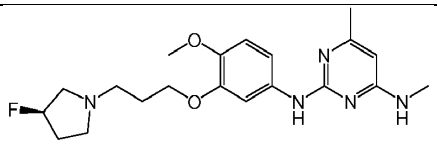
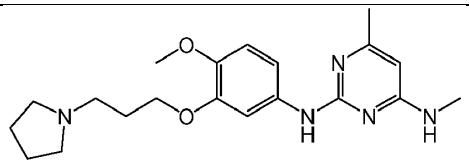
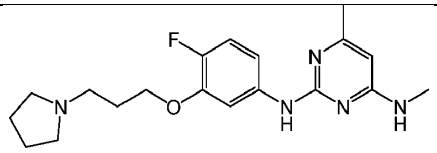
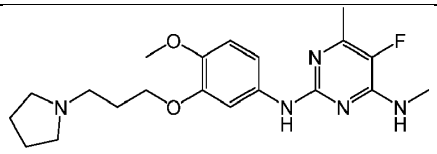
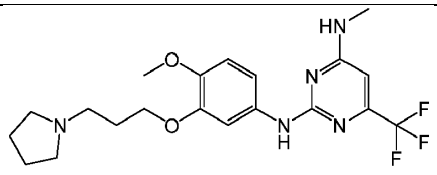
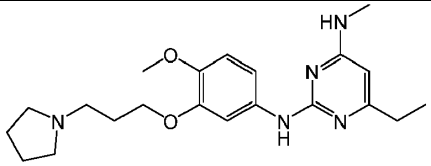
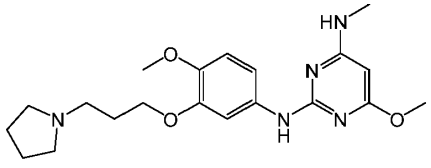
X^4 er CR^5;

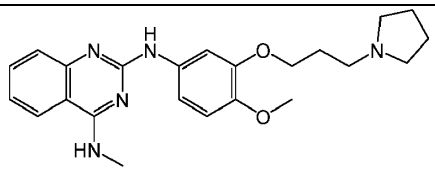
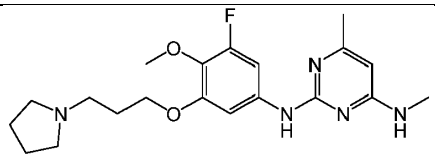
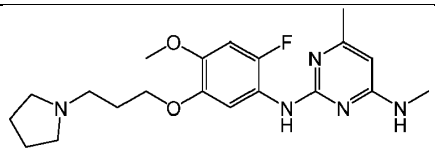
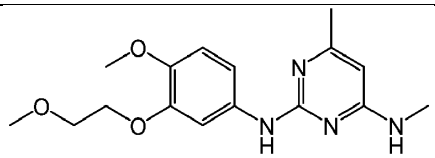
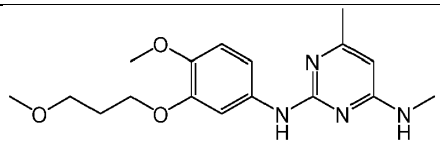
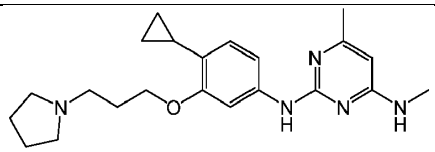
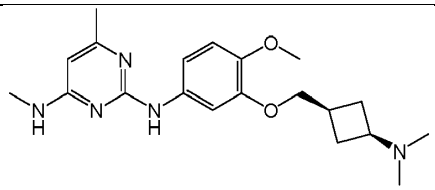
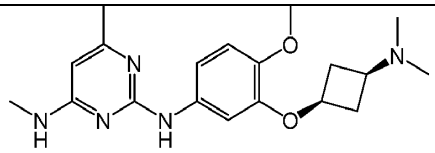
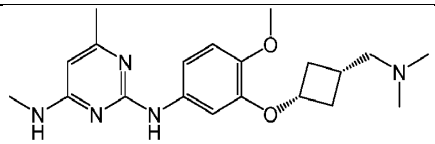
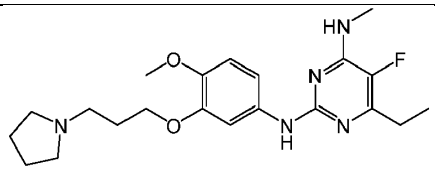
R^5 velges fra gruppen som består av C_3-C_8sykloalkyl og C_1-C_6alkyl; eller

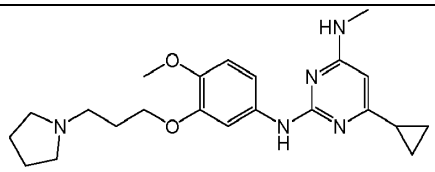
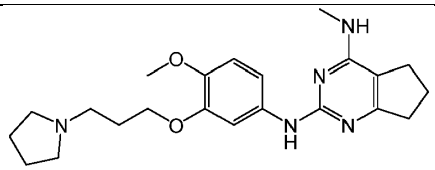
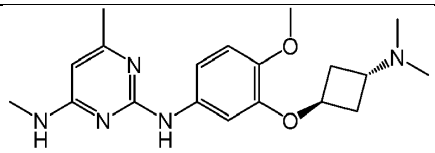
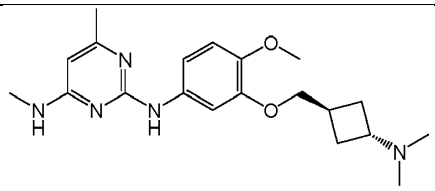
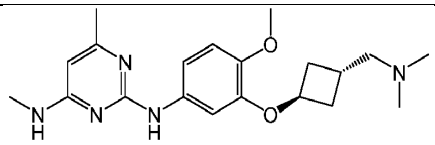
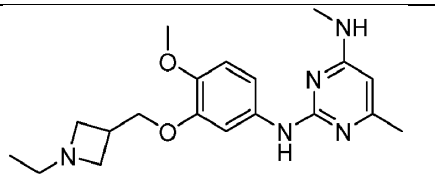
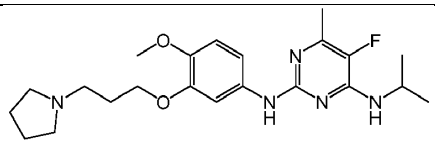
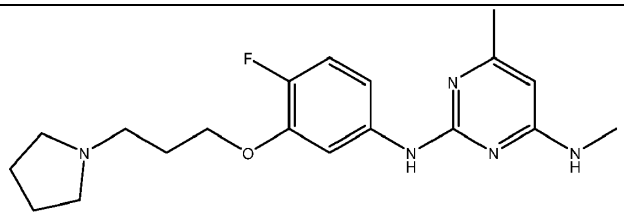
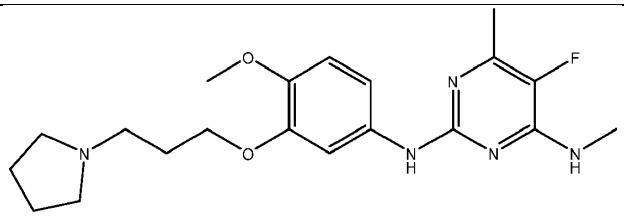
R^5 og R^3 sammen med atomene som de festes til danner fenyl eller et 5- eller 6-leddet heteroaryl.

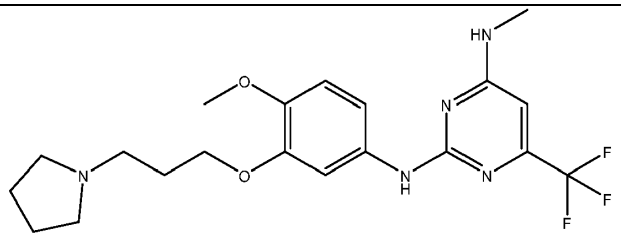
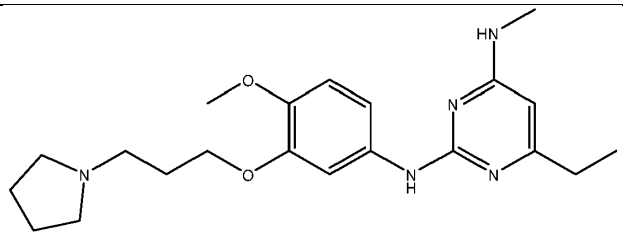
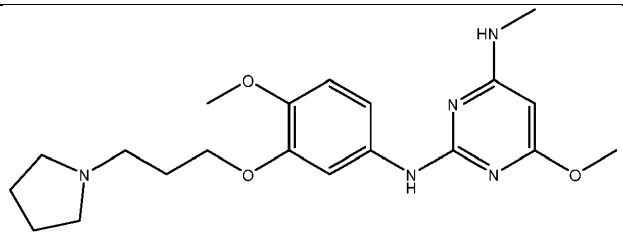
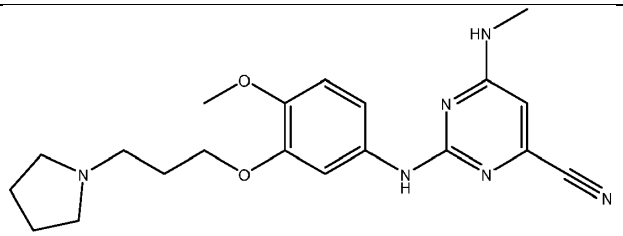
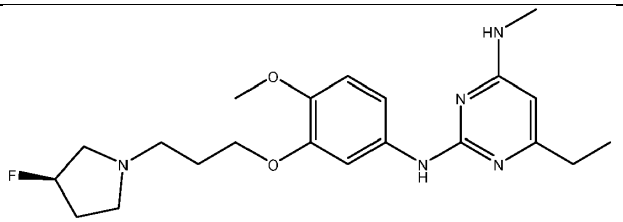
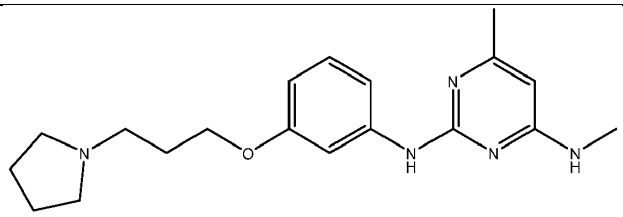
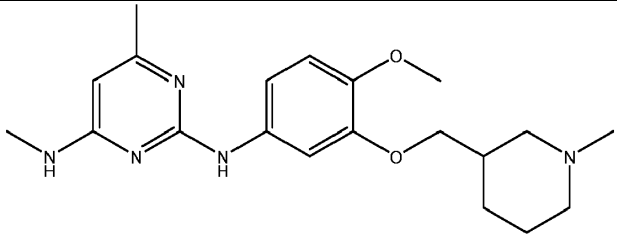
9. Forbindelse for anvendelse ifølge et hvilket som helst av de foregående kravene, hvori R^5 er C_{1-6}alkyl eller R^5 og R^3 sammen med atomene som de festes til danner fenyl eller en 5- til 6-leddet heteroarylring.

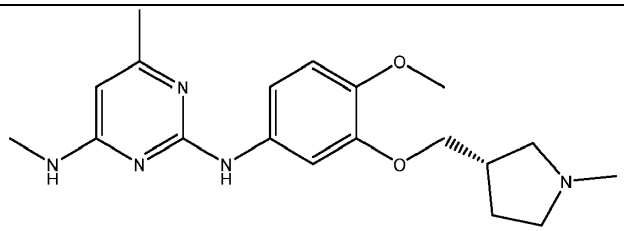
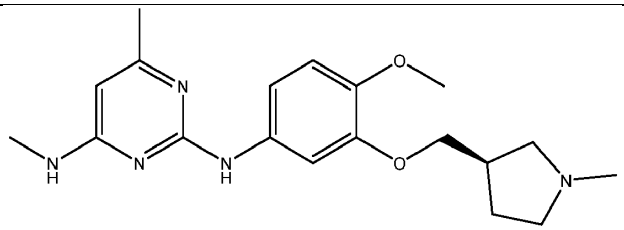
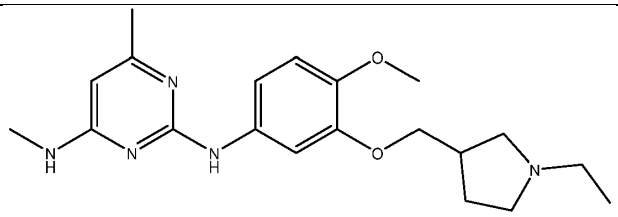
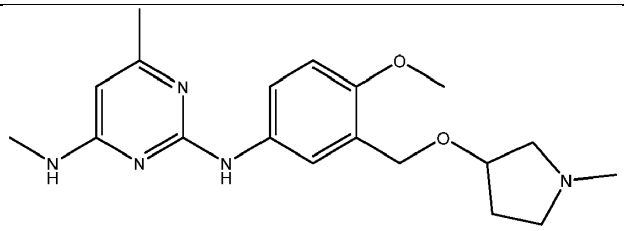
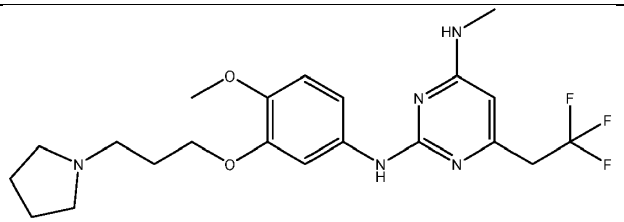
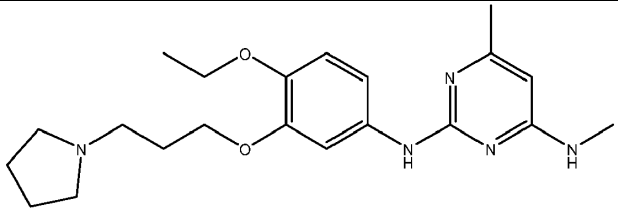
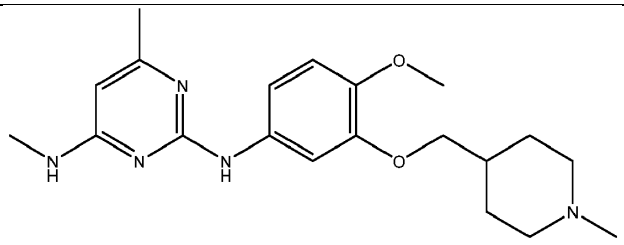
10. Forbindelse for anvendelse ifølge et hvilket som helst av de foregående kravene, hvori forbindelsen velges fra de følgende forbindelsene og farmasøytisk akseptable salter derav:

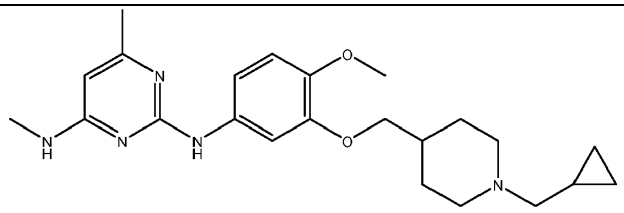
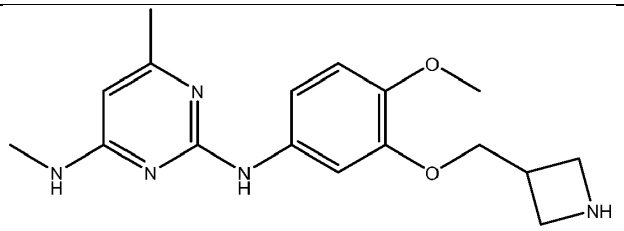
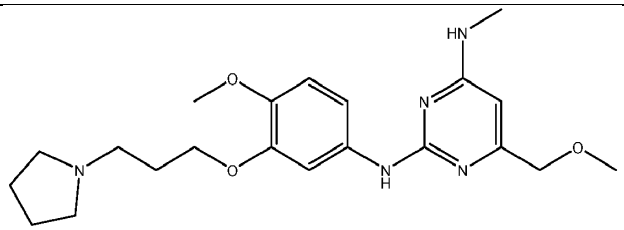
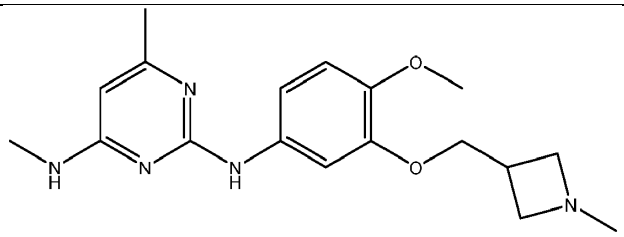
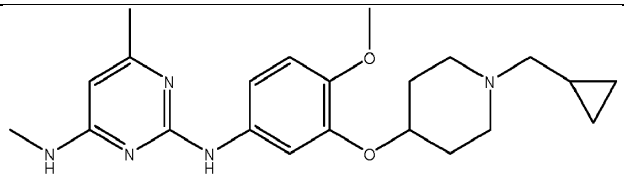
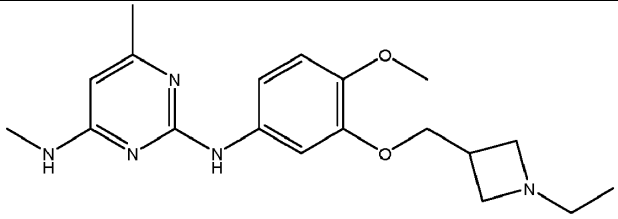
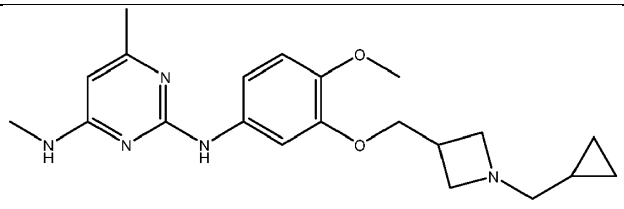
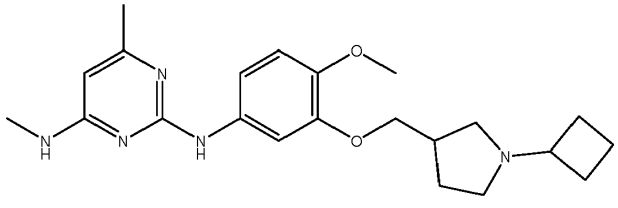
Forbindelse nr.	**Struktur**
186	
205	
232	
236	
238	
240	
261	

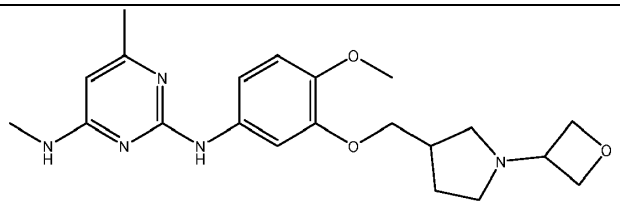
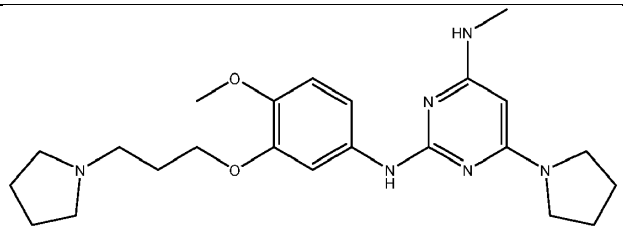
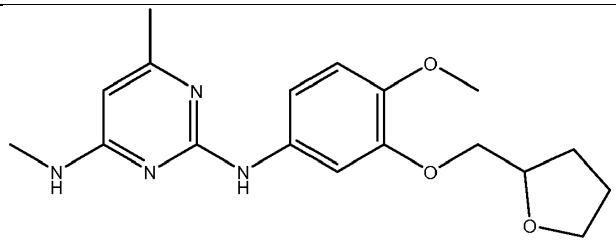
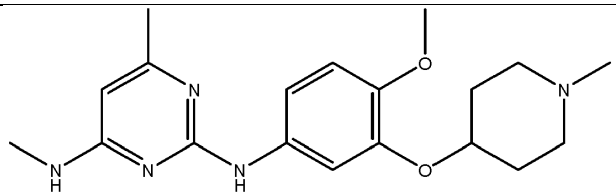
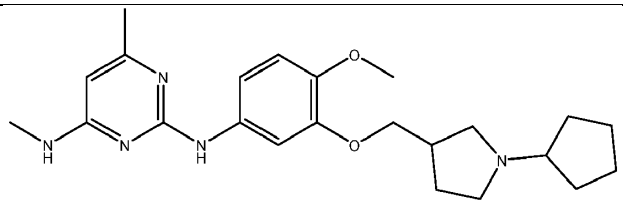
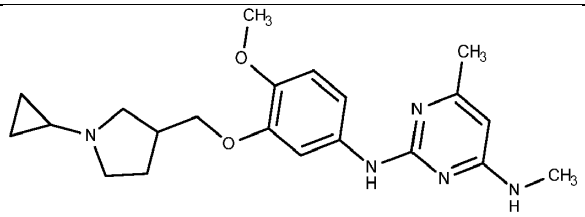
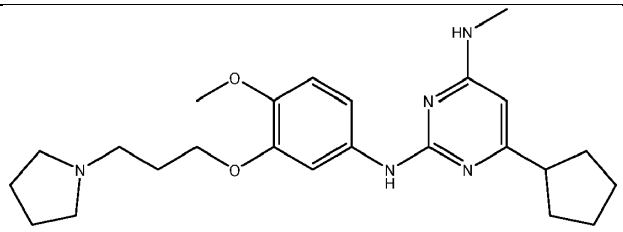
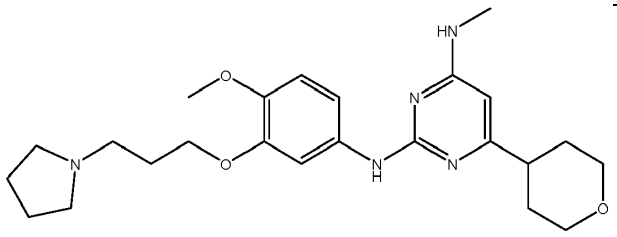
263	
301	
302	
311	
312	
313	
316	
317	
318	
319	

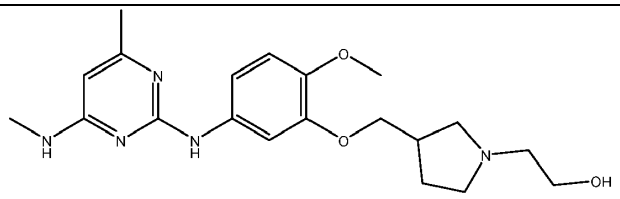
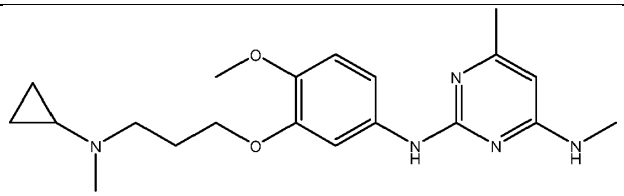
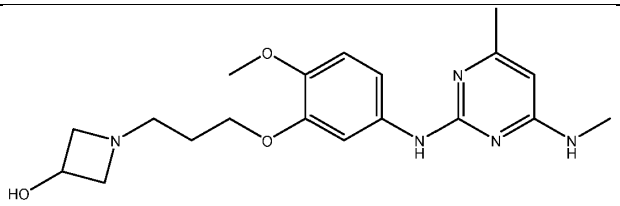
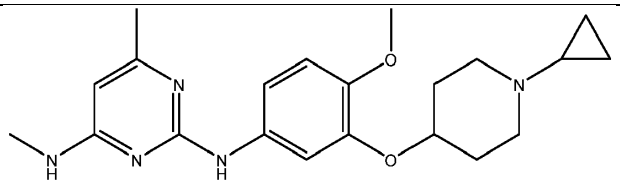
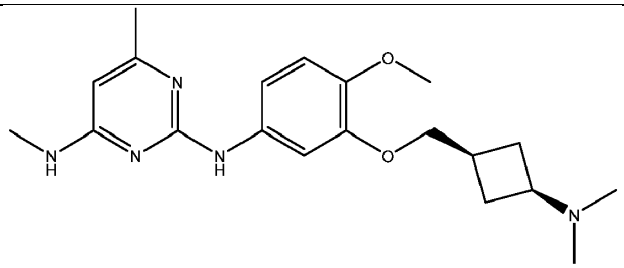
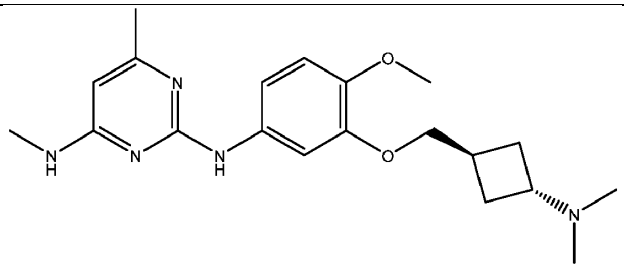
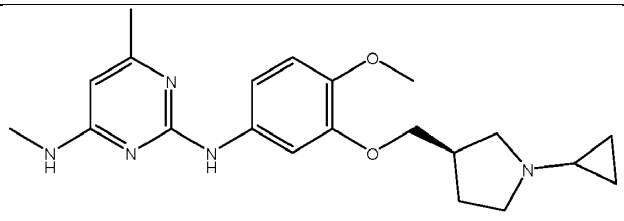
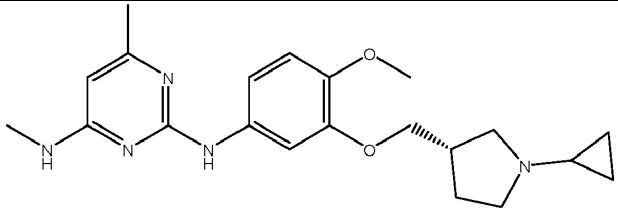
320	
328	
329	
330	
331	
334	
337	
356	
360	

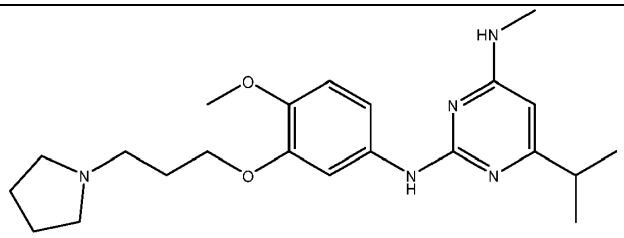
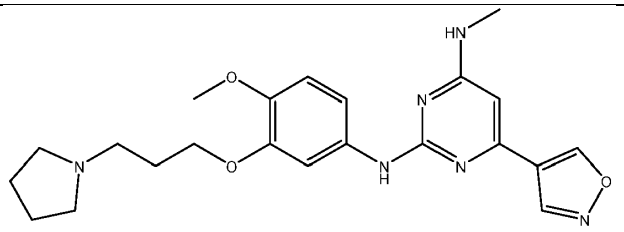
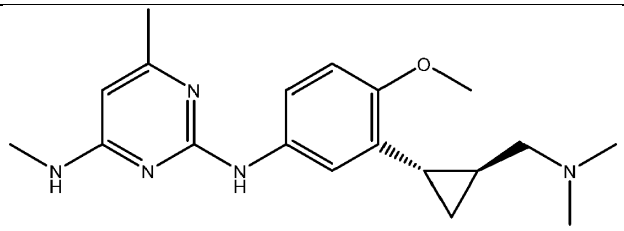
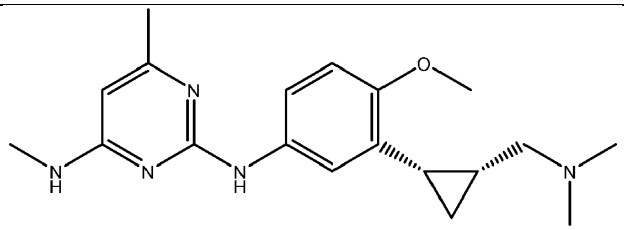
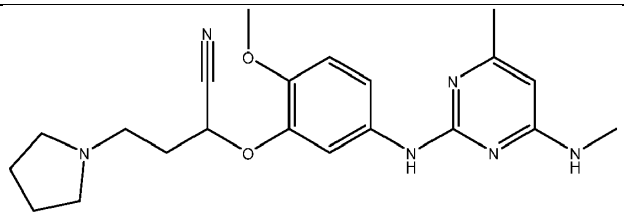
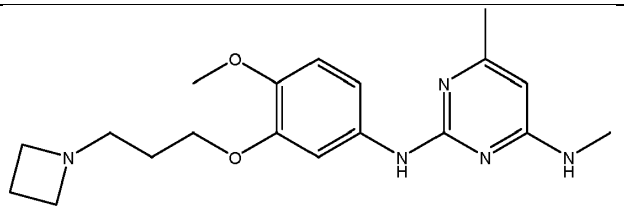
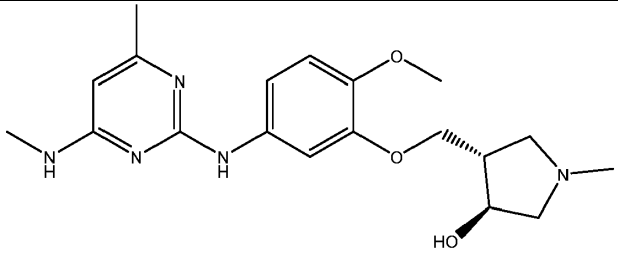
362	
364	
380	
384	
385	
391	
413	

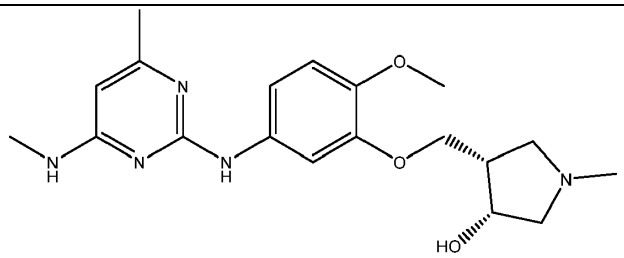
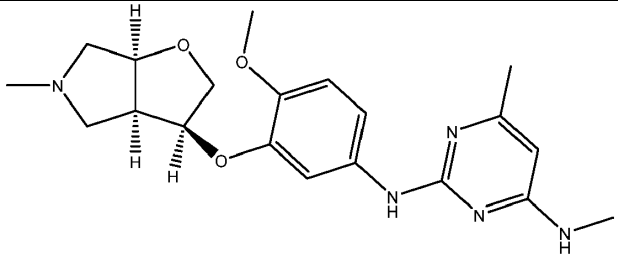
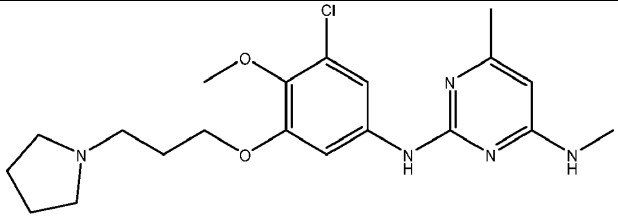
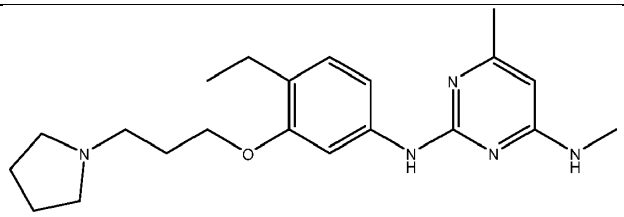
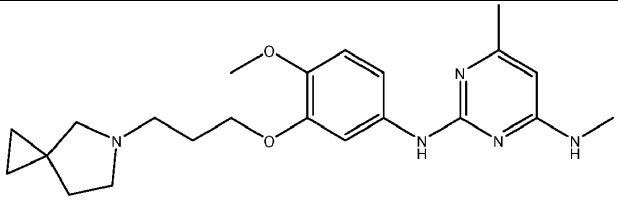
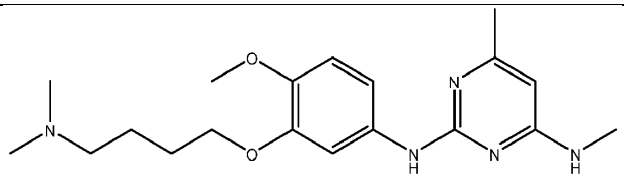
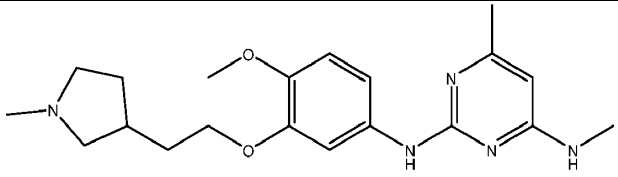
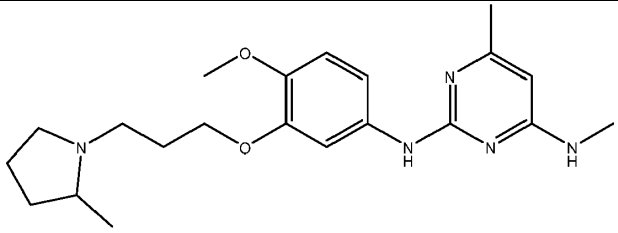
417	
418	
419	
421	
428	
432	
435	

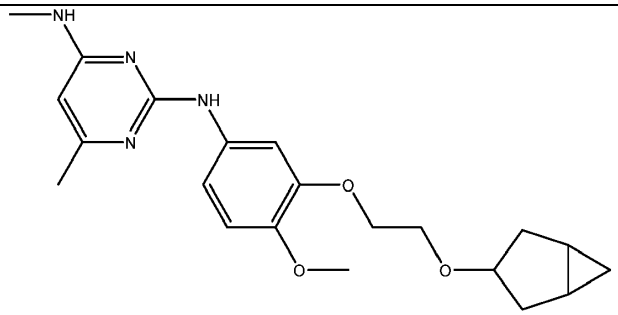
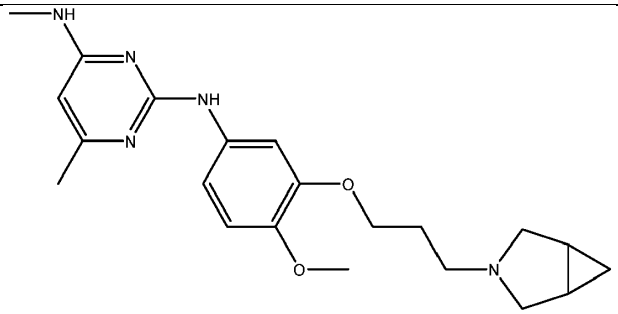
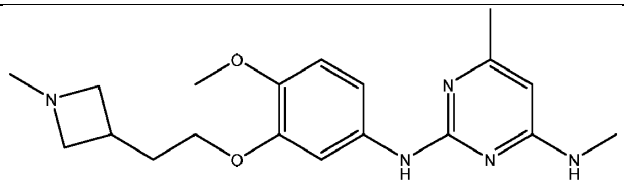
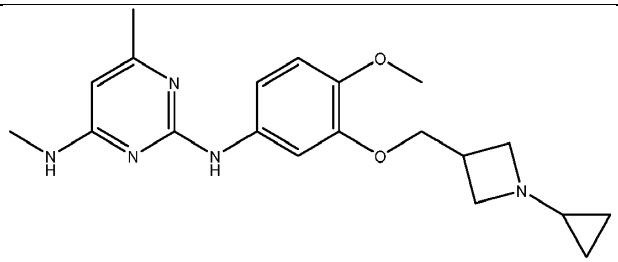
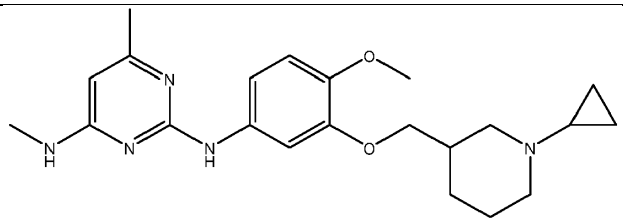
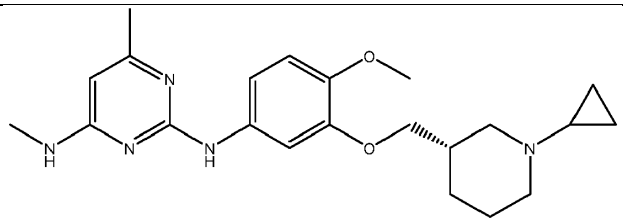
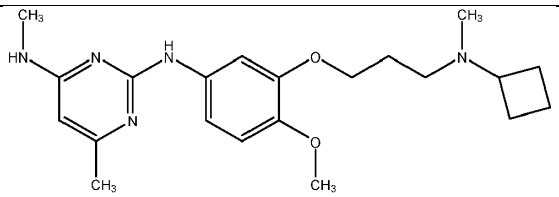
436	
437	
441	
442	
443	
444	
445	
446	

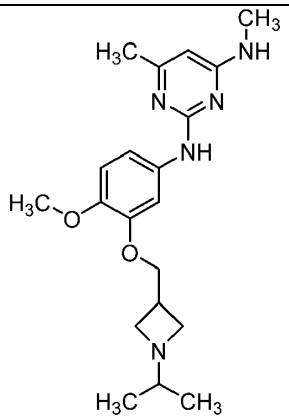
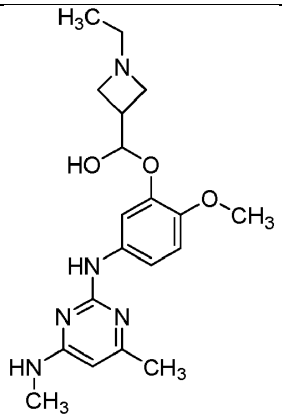
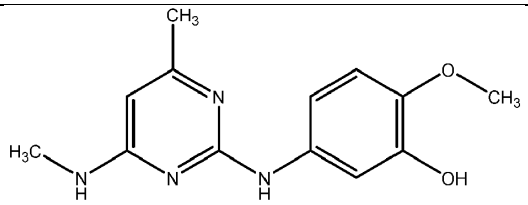
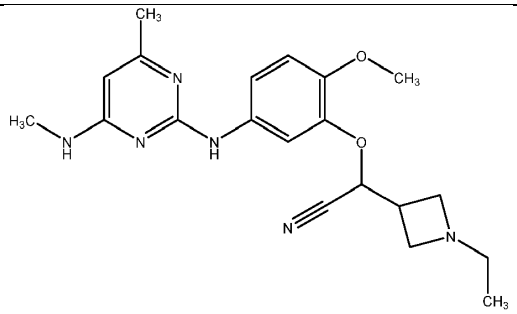
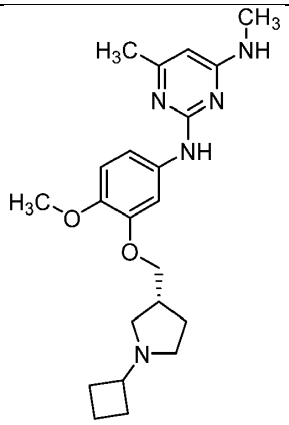
449	
450	
452	
455	
456	
457	
458	
459	

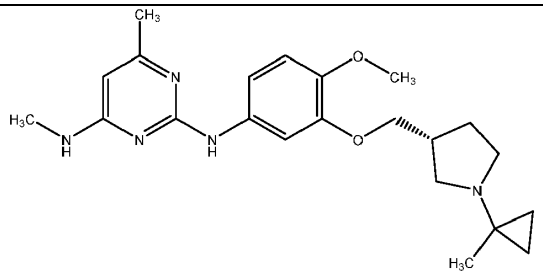
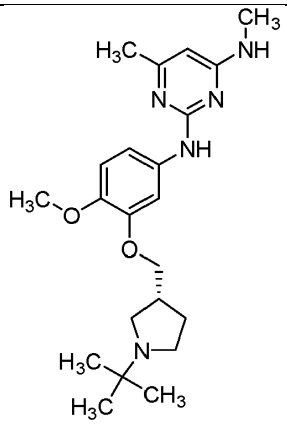
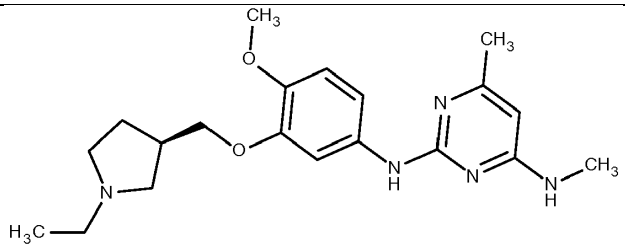
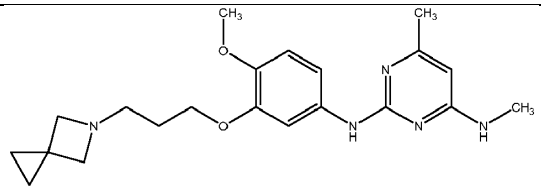
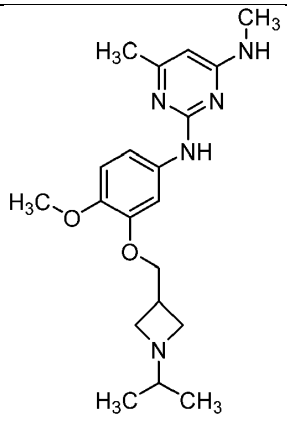
461	
463	
465	
466	
468	
470	
481	
482	

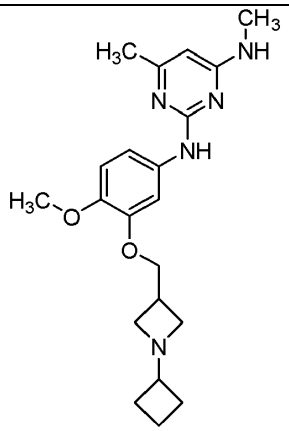
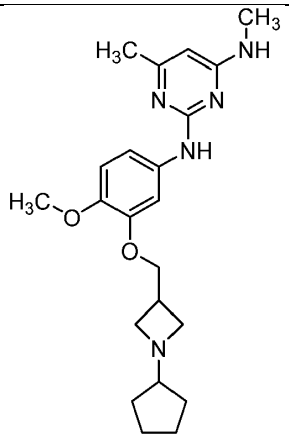
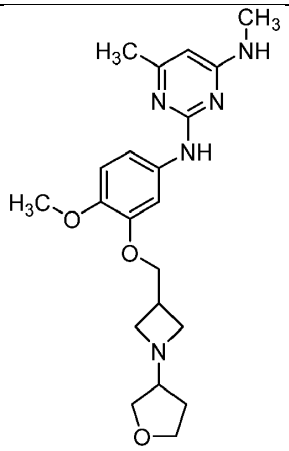
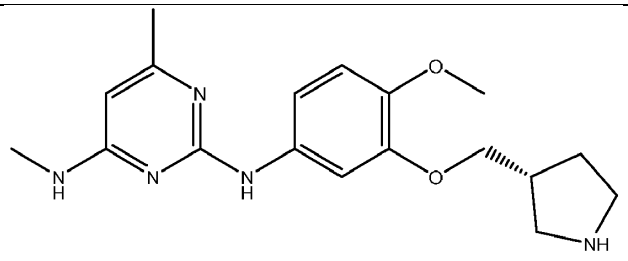
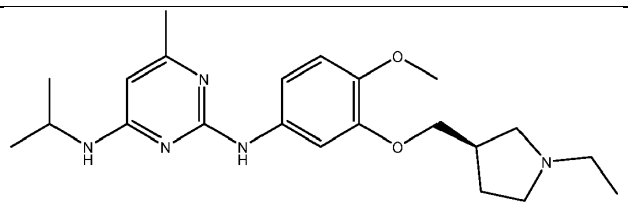
483	
484	
487	
488	
489	
490	
491	

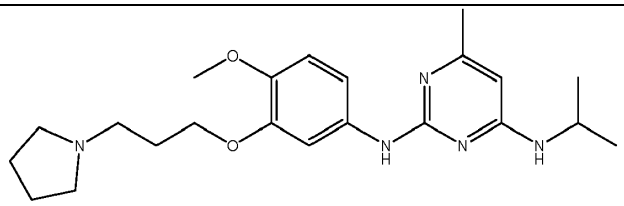
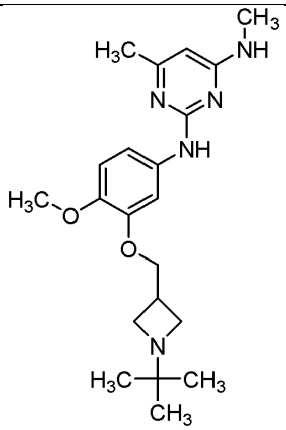
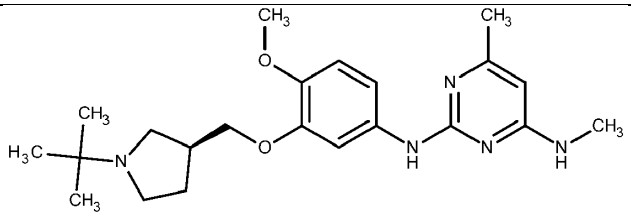
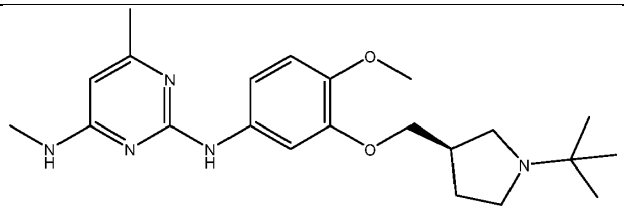
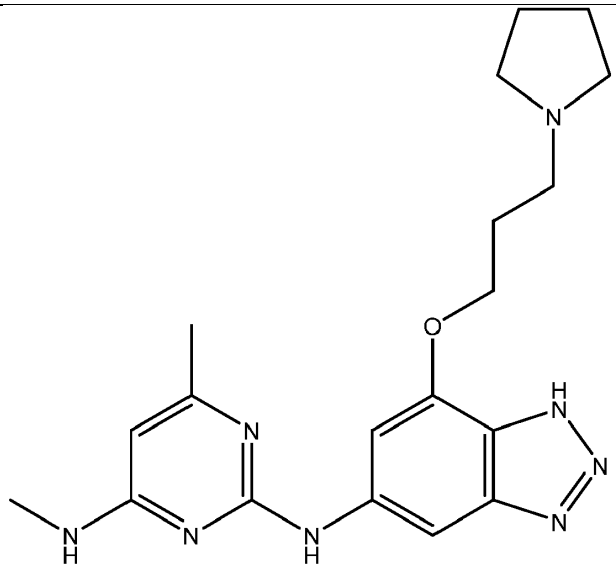
492	
493	
496	
497	
498	
502	
503	
504	

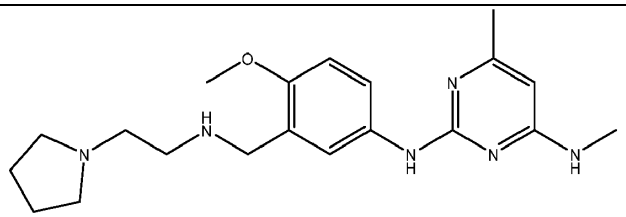
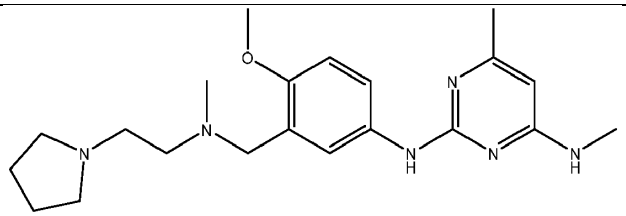
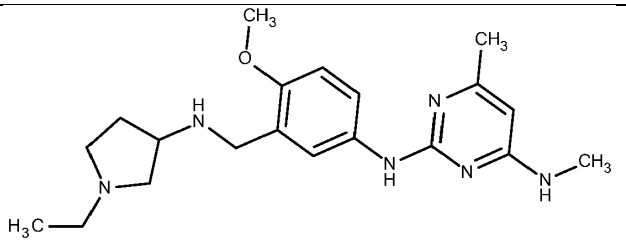
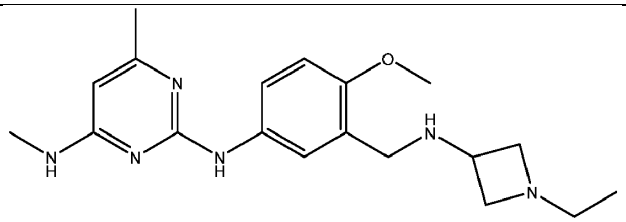
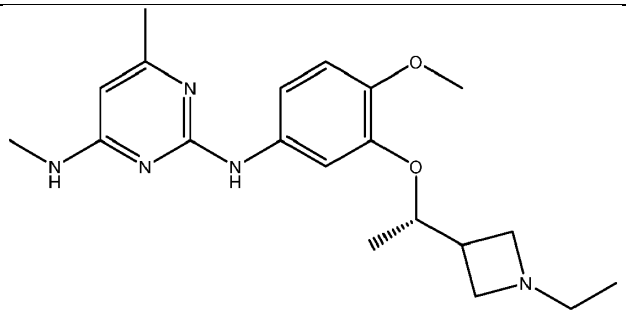
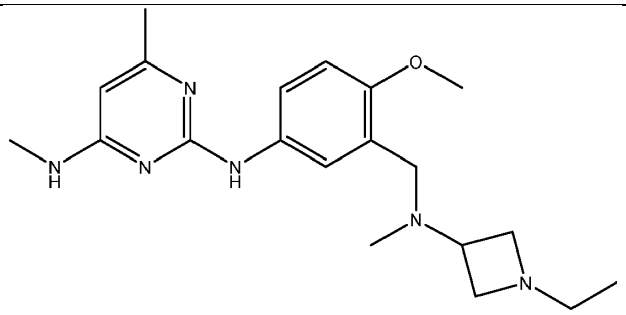
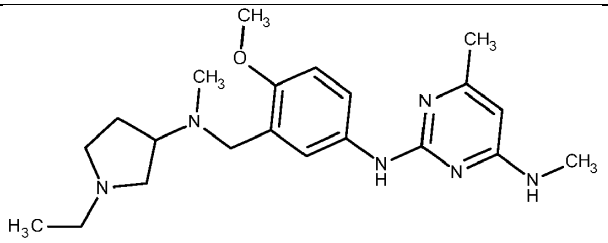
505	
506	
508	
510	
517a	
517b	
551	

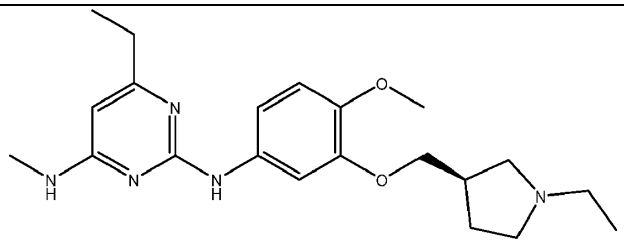
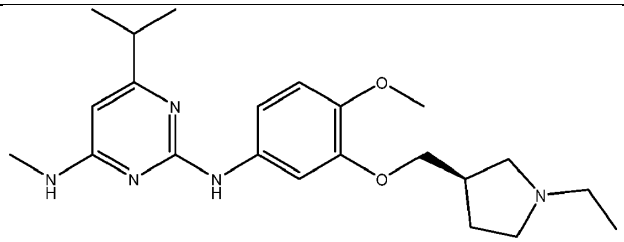
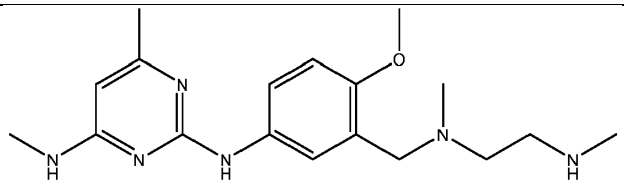
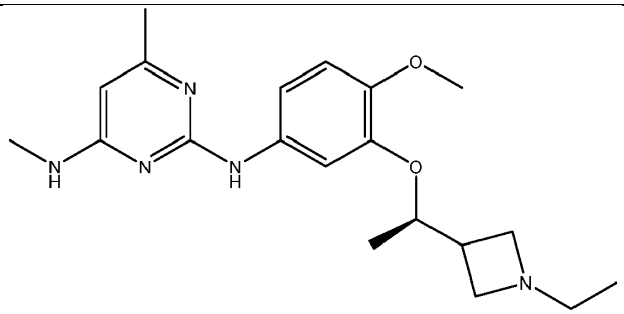
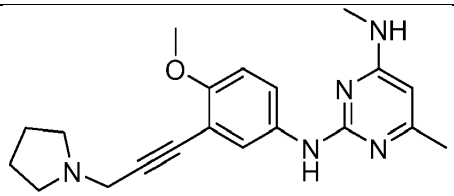
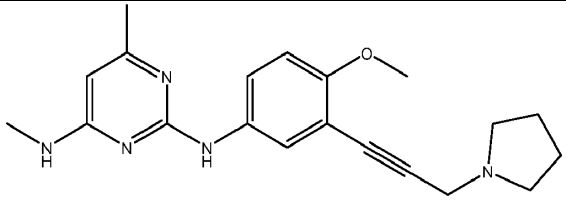
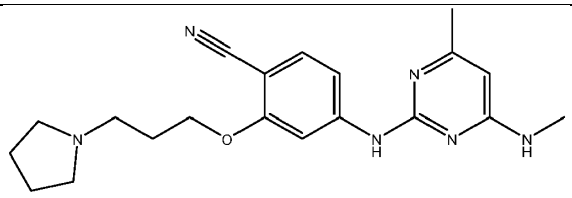
559	
560	
561	
562	
563	

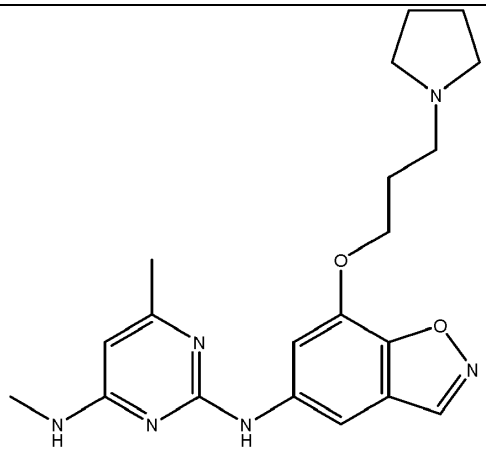
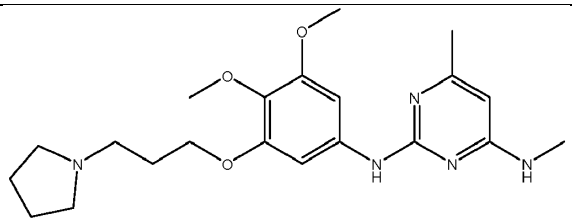
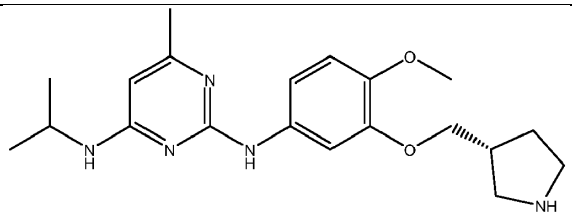
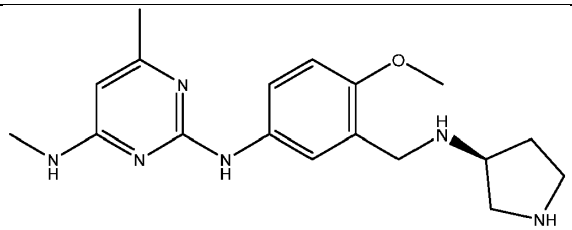
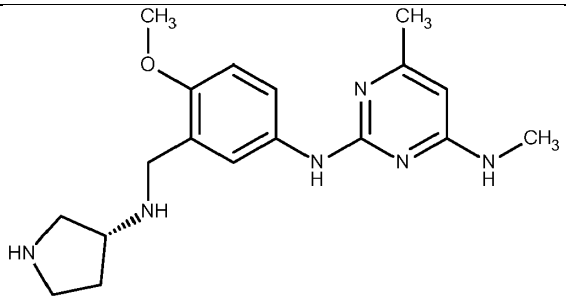
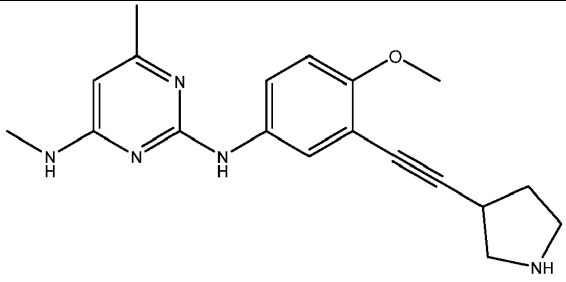
568	
570	
571	
574	
575	

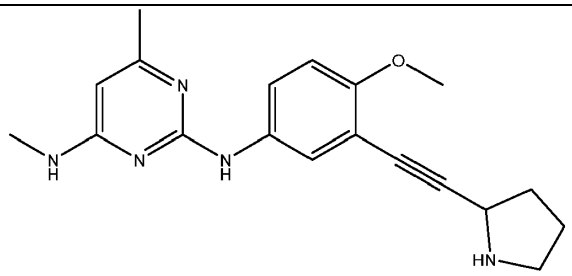
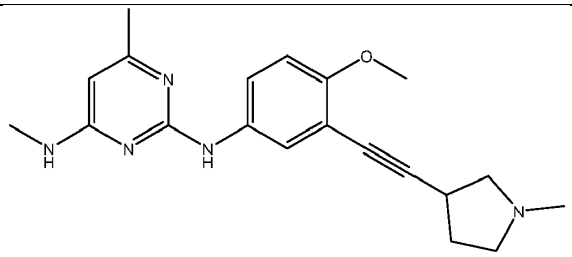
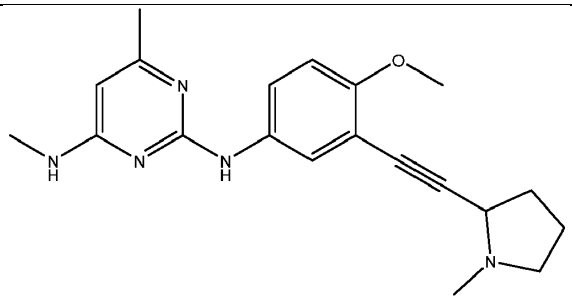
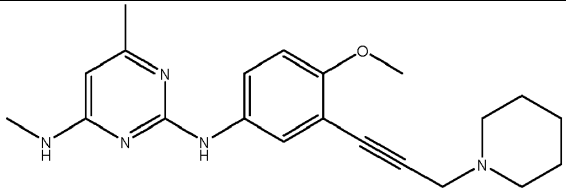
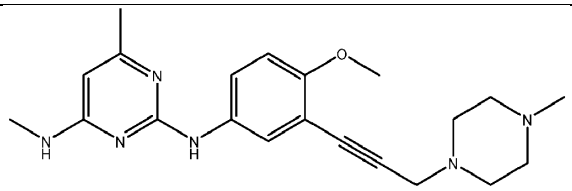
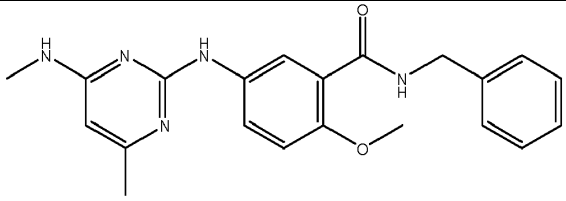
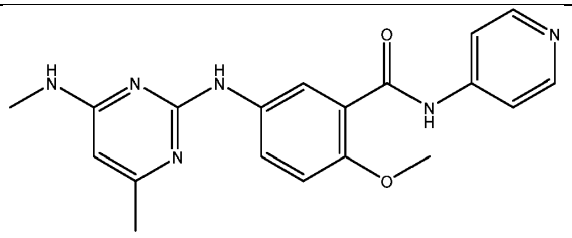
576	
577	
580	
600	
602	

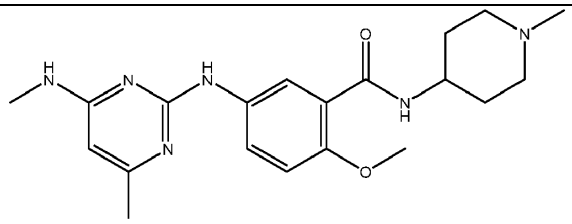
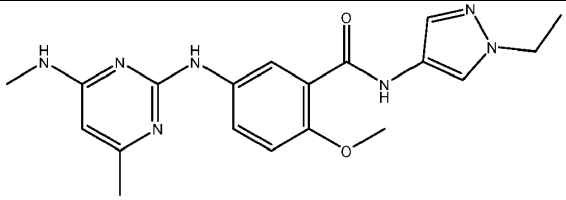
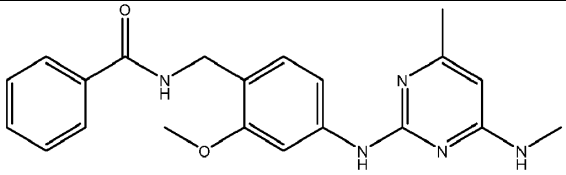
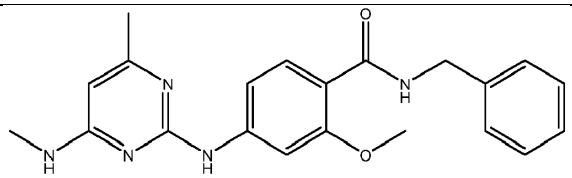
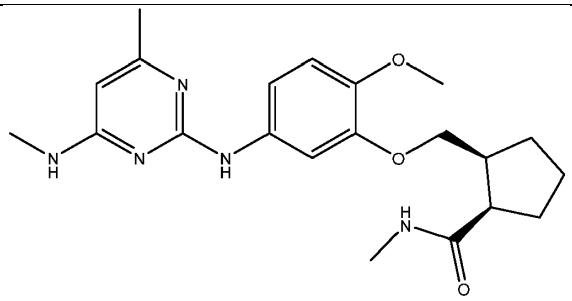
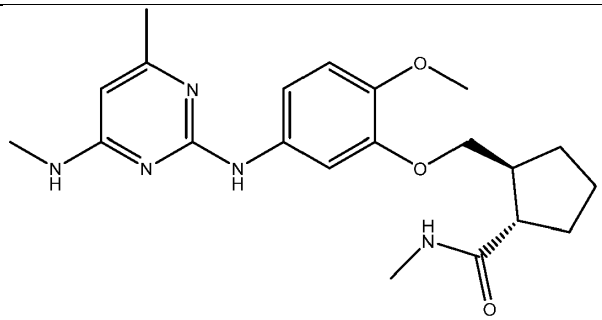
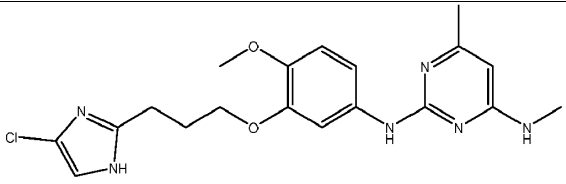
603	
606	
610	
614	
624	

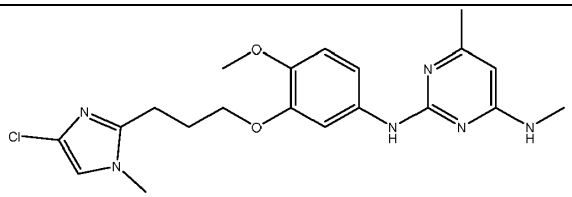
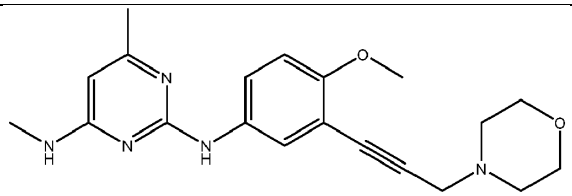
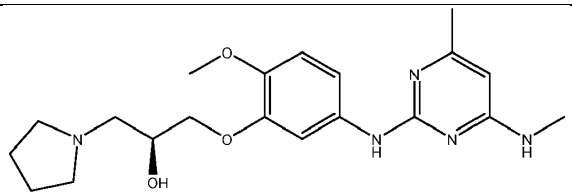
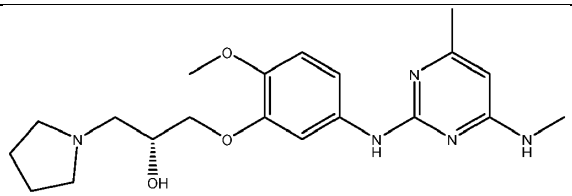
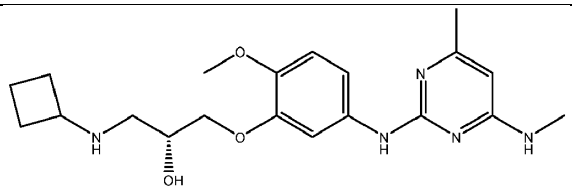
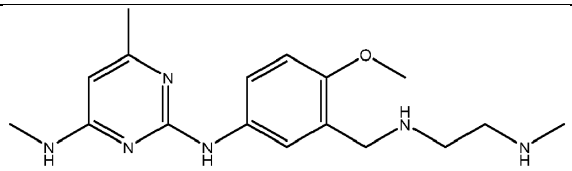
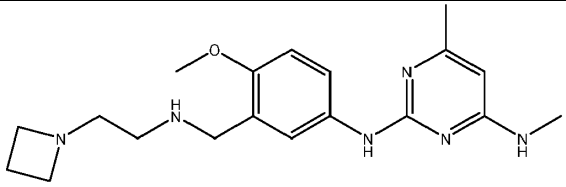
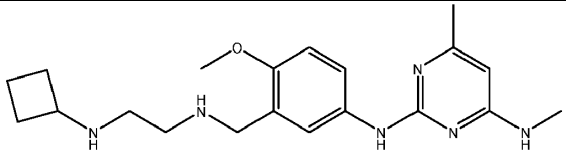
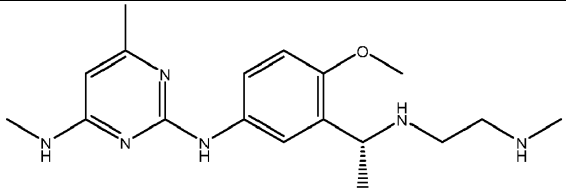
644	
645	
646	
647	
649	
650	
651	

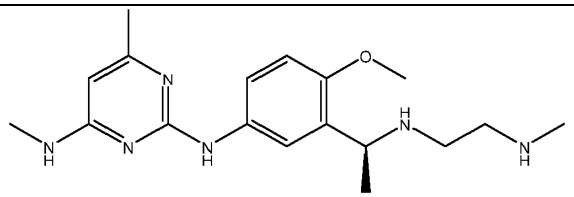
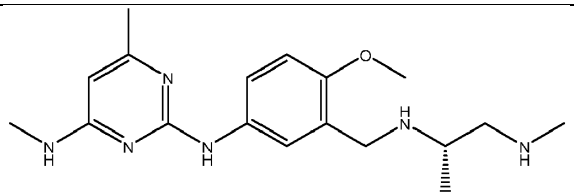
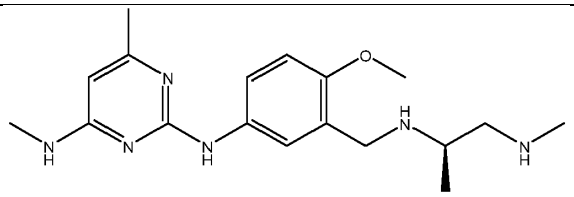
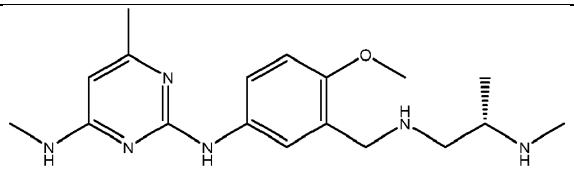
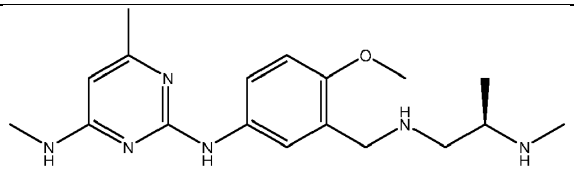
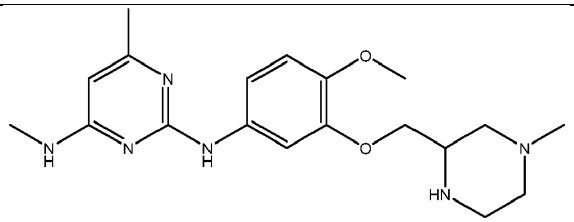
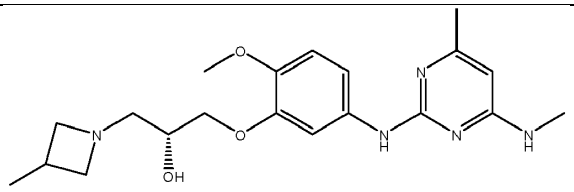
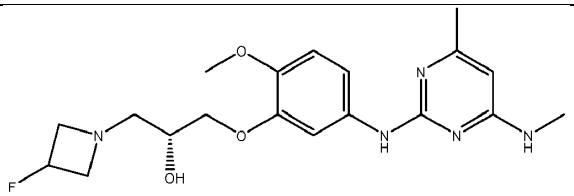
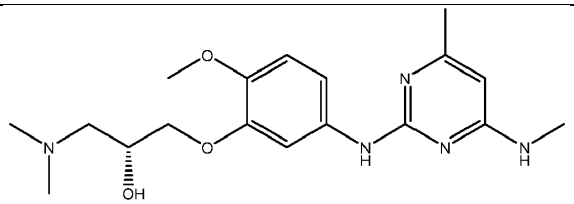
671	
672	
680	
687	
765	
786	
791	

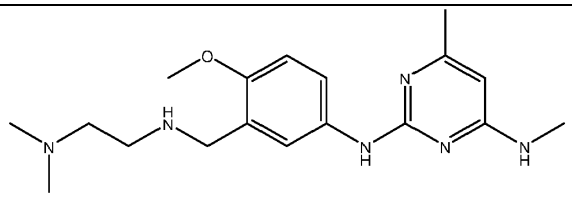
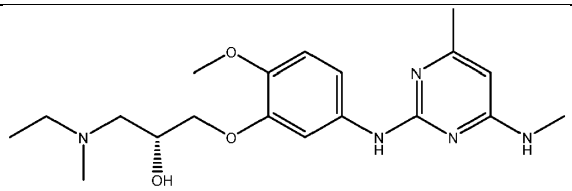
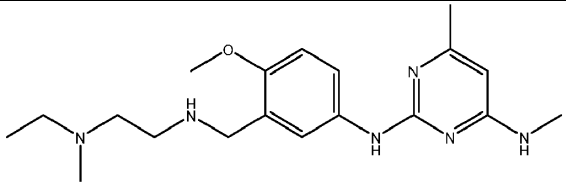
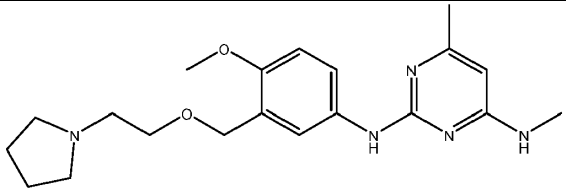
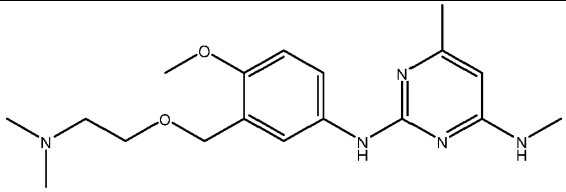
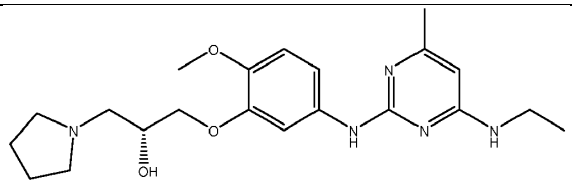
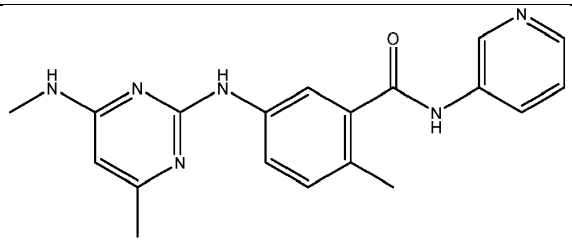
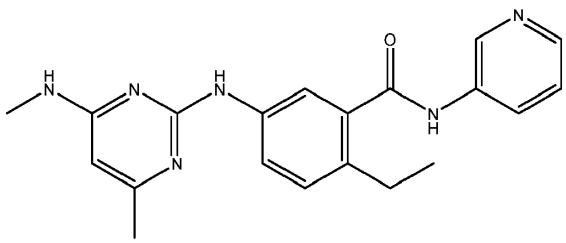
793	
799	
800	
813	
814	
845	

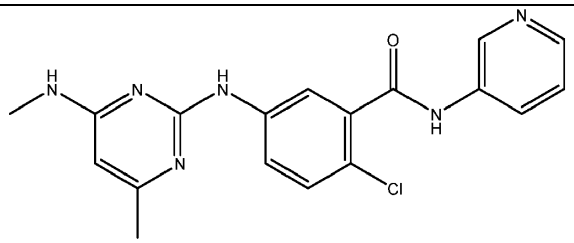
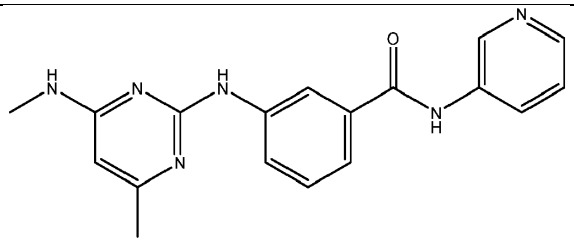
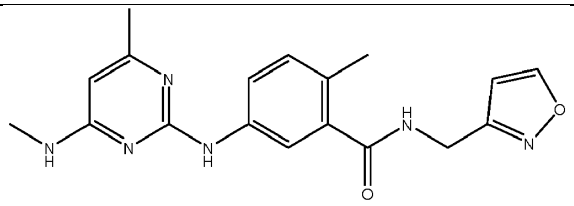
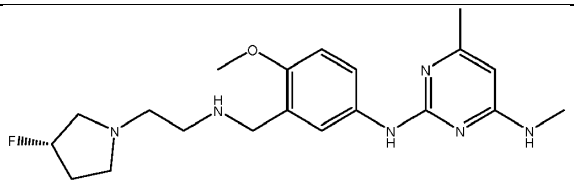
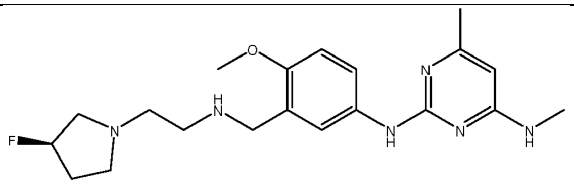
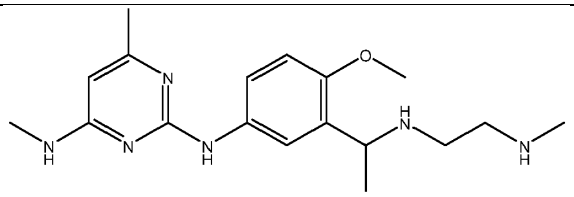
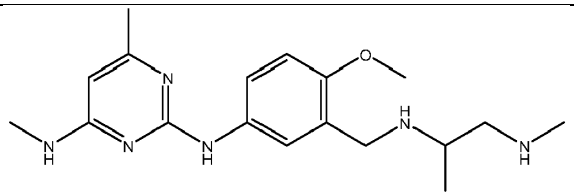
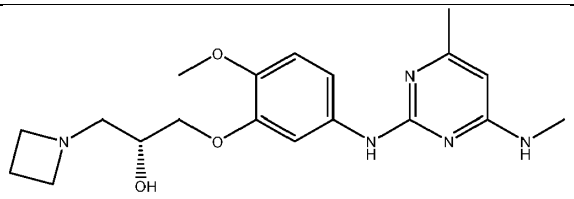
846	
847	
848	
855	
860	
871	
872	

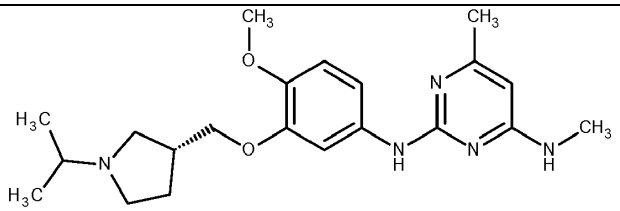
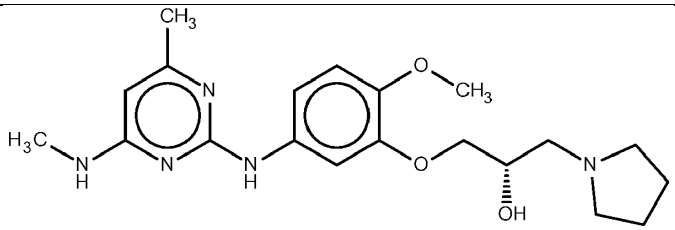
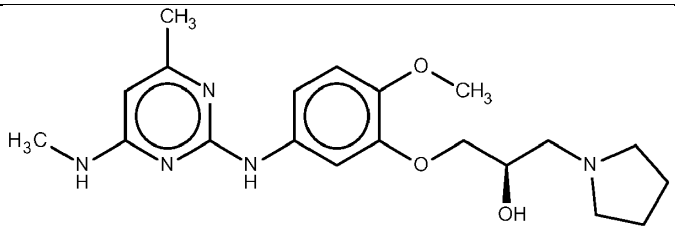
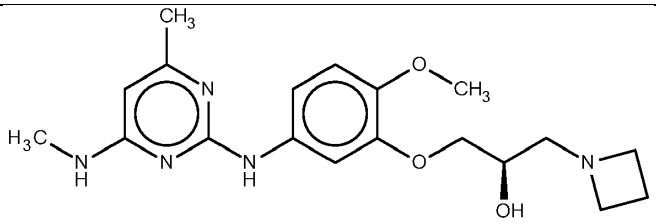
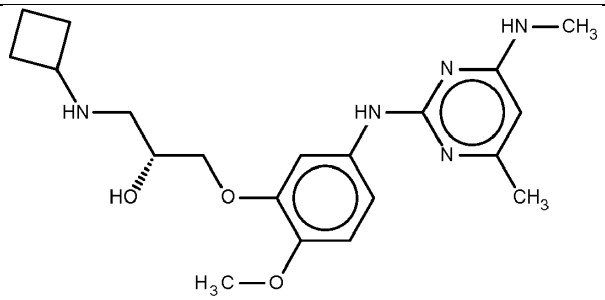
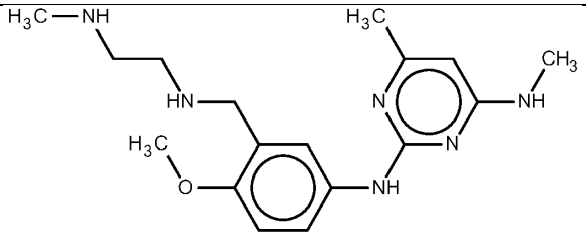
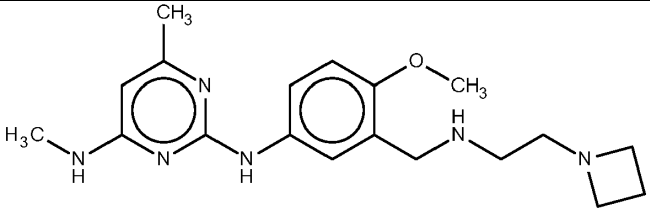
873	
874	
876	
877	
878	
879	
890	

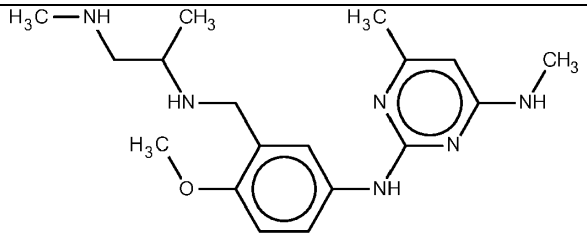
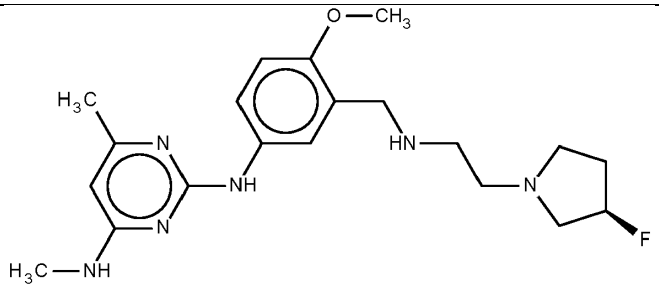
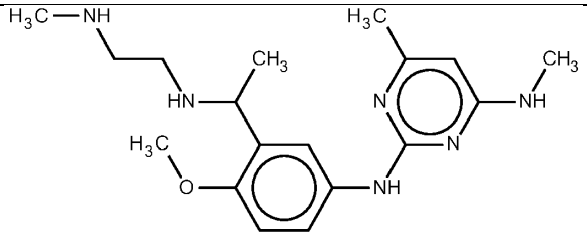
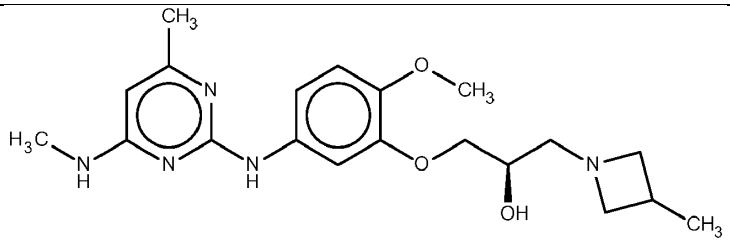
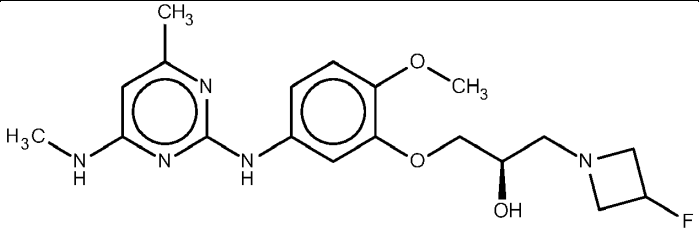
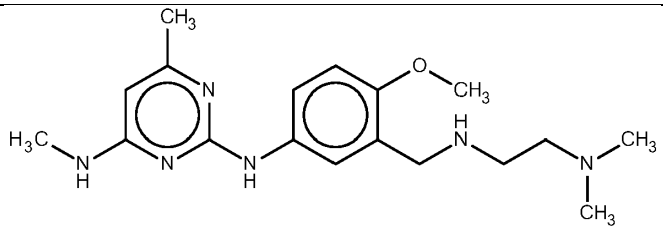
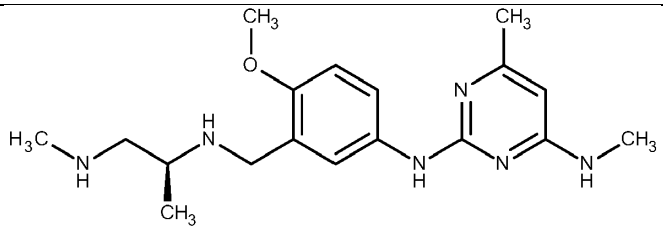
891	
904	
905	
906	
962	
964	
965	
966	
967	

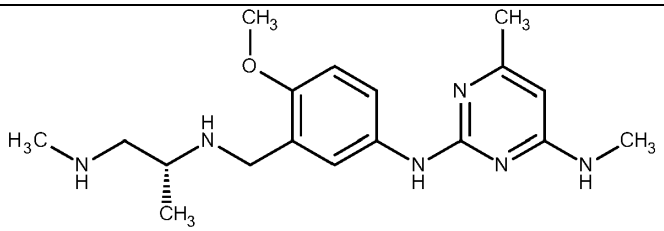
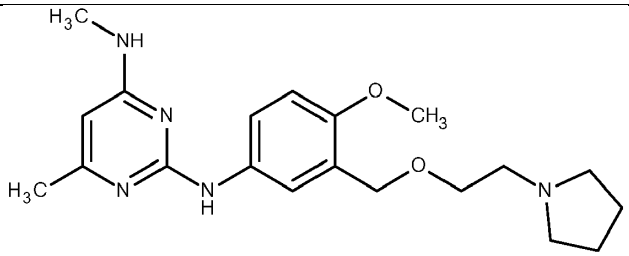
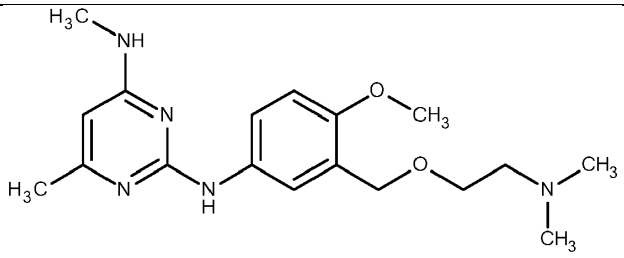
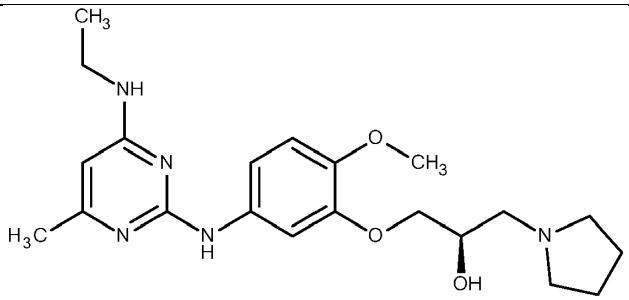
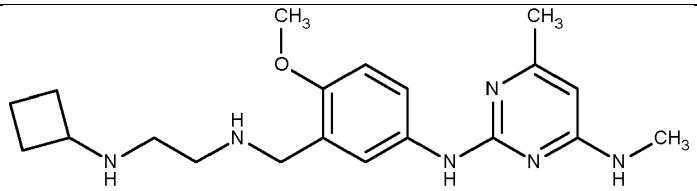
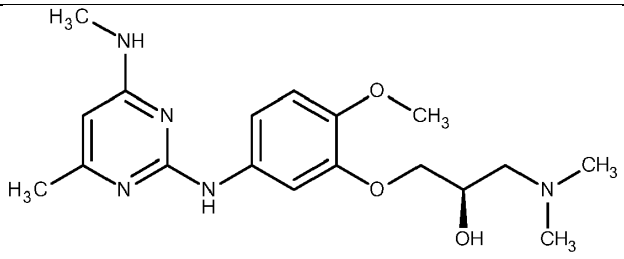
968	
969	
970	
971	
972	
977	
985	
986	
989	

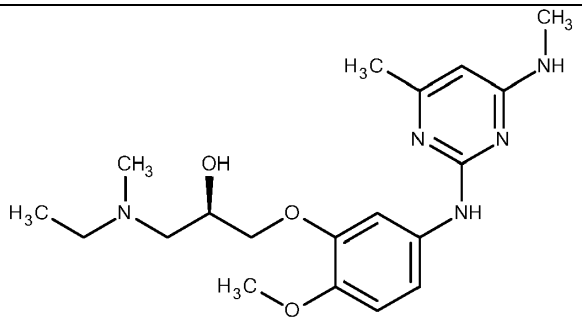
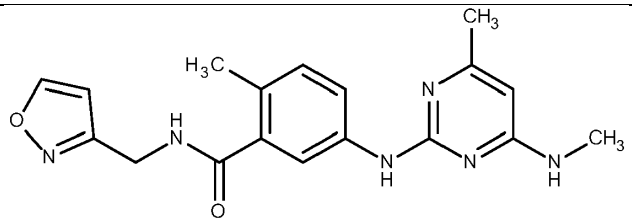
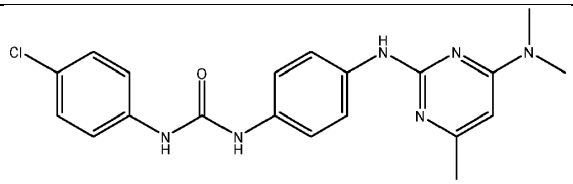
990	
991	
992	
993	
994	
997	
998	
999	

1000	
1001	
1004	
1029	
1030	
1036	
1037	
1038	

1040	
1044	
1045	
1078	
1079	
1080	
1081	

1090	
1094	
1095	
1099	
1100	
1101	
1102	

1103	
1104	
1105	
1106	
1109	
1112	

1113	
1114	
1117	

11. Forbindelse for anvendelse som definert i et hvilket som helst av kravene 1–10, hvori blodsykdommen er sigdcelleanemi eller β-talassemi.

12. Forbindelse for anvendelse som definert i et hvilket som helst av kravene 1–10, hvori blodsykdommen er en hematologisk kreft.

13. Forbindelse for anvendelse som definert i krav 12, hvori den hematologiske kreften er akutt myelogen leukemi (AML) eller kronisk lymfatisk leukemi (KLL).

14. Forbindelse for anvendelse som definert i et hvilket som helst av de foregående kravene, hvori forbindelsen er en selektiv inhibitor av EHMT2.