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Norwegian Industrial Property Office

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(54) Title **PYRIDINES, PYRIMIDINES, AND PYRAZINES, AS BTK INHIBITORS AND USES THEREOF**

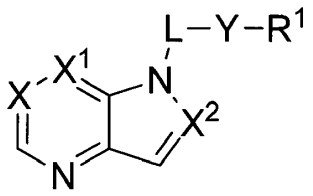
(56) References Cited:

WO-A2-2011/093672, EP-A1- 2 548 877, ZHENGYING PAN ET AL: "Discovery of Selective Irreversible Inhibitors for Brutons Tyrosine Kinase", CHEMMEDCHEM, WILEY - VCH VERLAG., WEINHEIM, DE, vol. 2, no. 1, 15 January 2007 (2007-01-15), pages 58-61, XP008118842, ISSN: 1860-7179, DOI: 10.1002/CMDC.200600221 [retrieved on 2006-12-12], WO-A1-2007/004749, ISHIKAWA, T. ET AL.: "Design and Synthesis of Novel Human Epidermal Growth Factor Receptor 2 (HER2)/Epidermal Growth Factor Receptor (EGFR) Dual Inhibitors Bearing a Pyrrolo[3,2-d]pyrimidine Scaffold", JOURNAL OF MEDICINAL CHEMISTRY, vol. 54, 2011, pages 8030-8050, XP002729528,, WO-A1-2006/010264, WO-A1-2012/158785, WO-A1-2012/158795, WO-A1-2013/010868, EP-A1- 1 752 457

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/

Patentkrav

1. Forbindelse med formel **I**,



I

eller et farmasøytisk akseptabelt salt derav, hvori:
X er N eller CR^2;
X^1 er N eller CR^2;
X^2 er N eller CR^2;
hver R^2 er uavhengig valgt blant -R, halogen, -halogenalkyl, -OR, -SR, -CN, $-NO_2$, $-SO_2R$, -SOR, -C(O)R, $-CO_2R$, $-C(O)N(R)_2$, -NRC(O)R, $-NRC(O)N(R)_2$, $-NRSO_2R$ eller $-N(R)_2$;
hver R er uavhengig hydrogen, C_{1-6}-alifatisk, C_{3-10}-aryl, en 3-8-leddet mettet eller delvis umettet karbosyklisk ring, en 3-7-leddet heterosyklisk ring som har 1-4 heteroatomer uavhengig valgt blant nitrogen, oksygen eller svovel eller en 5-6-leddet monosyklisk heteroarylring som har 1-4 heteroatomer uavhengig valgt blant nitrogen, oksygen eller svovel; hver av disse er eventuelt substituert; eller
to R-grupper på samme atom tas sammen med atomet som de er bundet til for å danne et C_{3-10}-aryl, en 3-8-leddet mettet eller delvis umettet karbosyklisk ring, en 3-7-leddet heterosyklisk ring som har 1-4 heteroatomer uavhengig valgt blant nitrogen, oksygen eller svovel eller en 5-6-leddet monosyklisk heteroarylring som har 1-4 heteroatomer uavhengig valgt blant nitrogen, oksygen eller svovel; hver av disse er eventuelt substituert;
L er en toverdig gruppe valgt blant C_{3-10}-aryl, en 3-8-leddet mettet eller delvis umettet karbosyklisk ring, en 3-7-leddet heterosyklisk ring som har 1-4 heteroatomer uavhengig valgt blant nitrogen, oksygen eller svovel og en 5-6-leddet monosyklisk heteroarylring som har 1-4 heteroatomer uavhengig valgt blant nitrogen, oksygen eller svovel; hver av disse er eventuelt substituert; eller L er en toverdig gruppe valgt blant C_{1-6}-alifatisk C_{3-10}-aryl, C_{1-6}-alifatisk 3-8 leddet mettet eller delvis umettet karbosyklisk ring, C_{1-6}-alifatisk 3-7-leddet heterosyklisk ring som har 1-4 heteroatomer uavhengig valgt blant nitrogen, oksygen eller svovel og en C_{1-6}-alifatisk 5-6-leddet monosyklisk heteroarylring som har 1-4 heteroatomer uavhengig valgt blant nitrogen, oksygen eller svovel; hver av disse er eventuelt substituert;

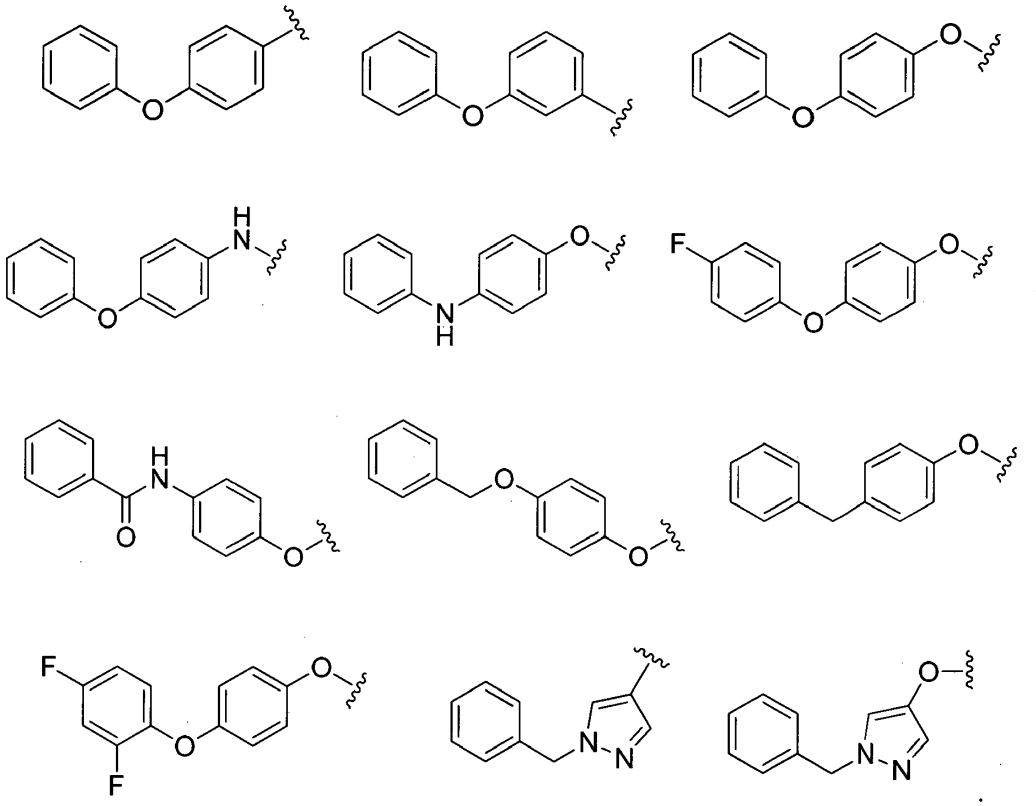
Y er O, S, SO_2, SO, C(O), CO_2, C(O)N(R), -NRC(O), -NRC(O)N(R), $-NRSO_2$, eller N(R); eller Y er fraværende;

R^1 er C_{2-6}-alkenyl eller C_{2-6} alkynyl, som eventuelt er substituert; eller R^1 er CN.

2. Forbindelsen ifølge krav 1, hvori hver R^2 er uavhengig fenyl eller pyrazolyl.

3. Forbindelsen ifølge krav 1, hvori hver R^2 er uavhengig -OR eller $-N(R)_2$.

4. Forbindelsen ifølge krav 1, hvori hver R^2 er uavhengig hydrogen,



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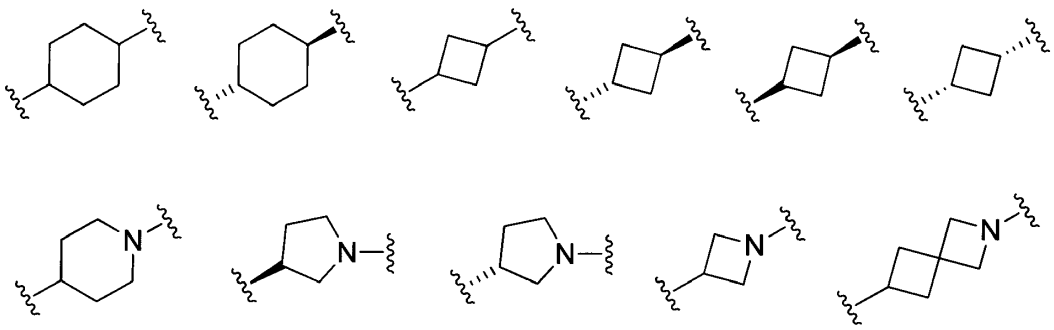

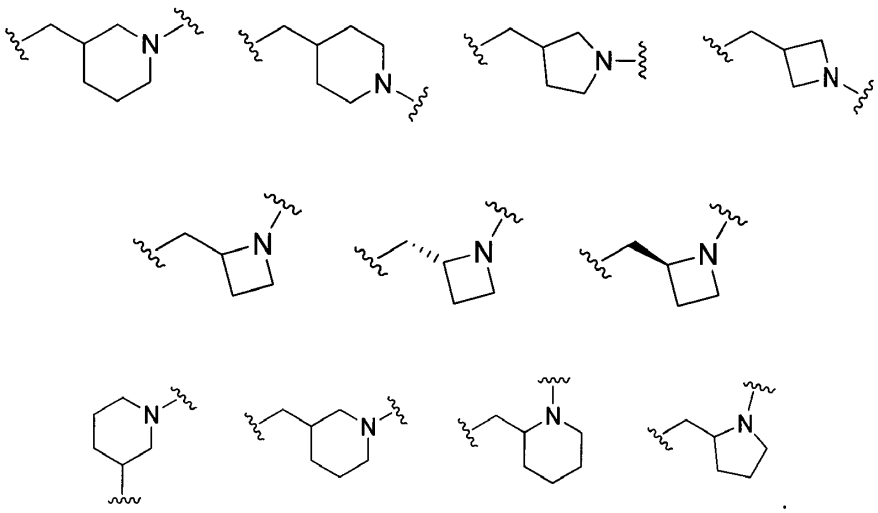

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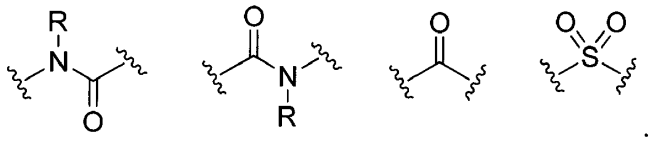
6. Forbindelsen ifølge krav 1, hvori Y er NR,



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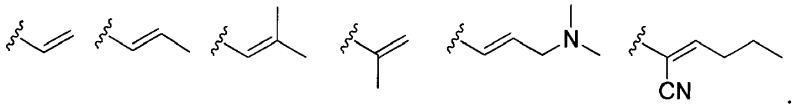
7. Forbindelsen ifølge krav 1, hvori Y er fraværende.

8. Forbindelsen ifølge krav 1, hvori R^1 er -CN, $-CH_2CN$,



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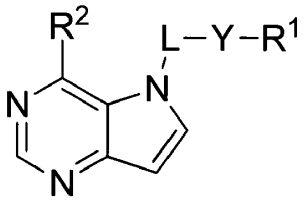
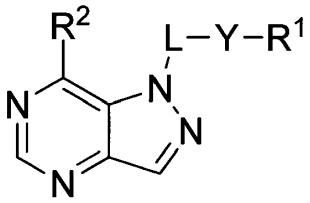


I-a1;

eller et farmasøytisk akseptabelt salt derav.

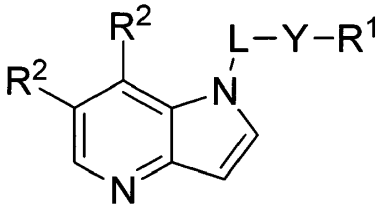
10. Forbindelsen ifølge krav 1, med formel **I-a2**,



I-a2;

eller et farmasøytisk akseptabelt salt derav.

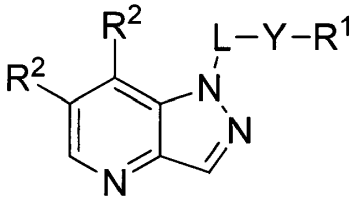
11. Forbindelsen ifølge krav 1, med formel **I-b1**,



I-b1;

eller et farmasøytisk akseptabelt salt derav.

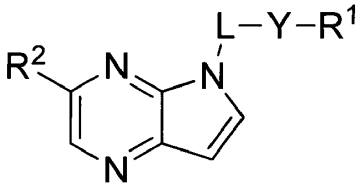
12. Forbindelsen ifølge krav 1, med formel **I-b2**,



I-b2;

eller et farmasøytisk akseptabelt salt derav.

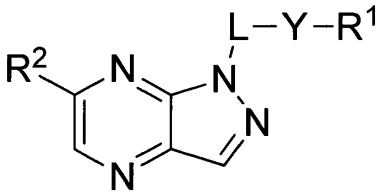
13. Forbindelsen ifølge krav 1, med formel **I-c1**:



I-c1;

eller et farmasøytisk akseptabelt salt derav.

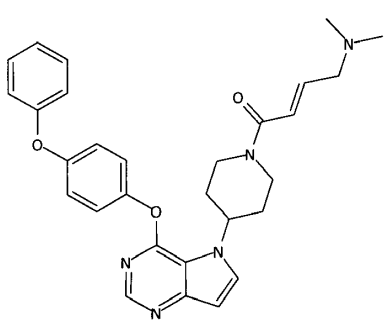
14. Forbindelsen ifølge krav 1, med formel **I-c2**:



I-c2;

eller et farmasøytisk akseptabelt salt derav.

15. Forbindelsen ifølge krav 1, valgt blant



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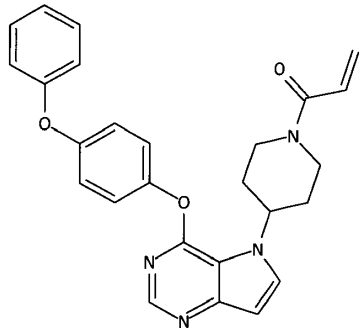

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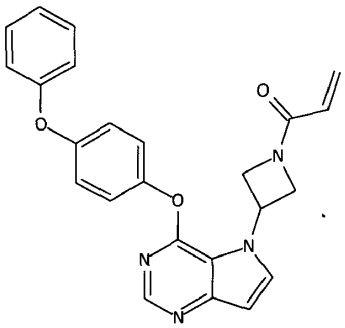

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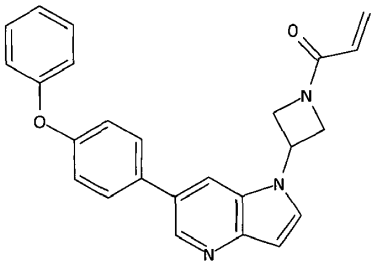

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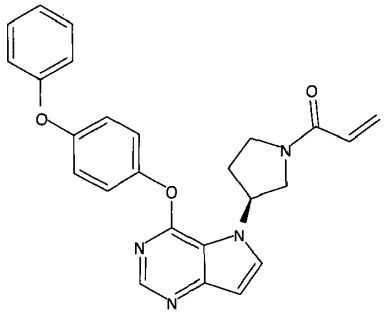

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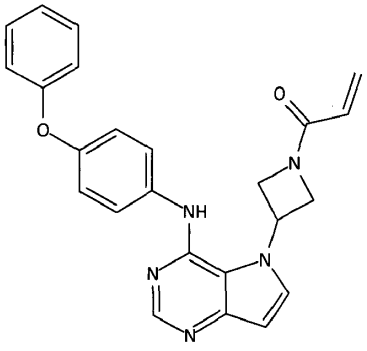

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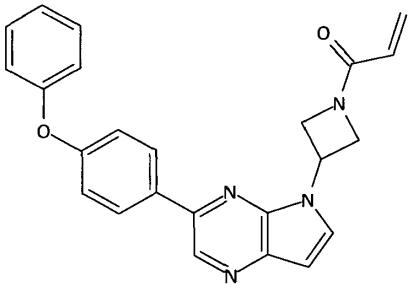

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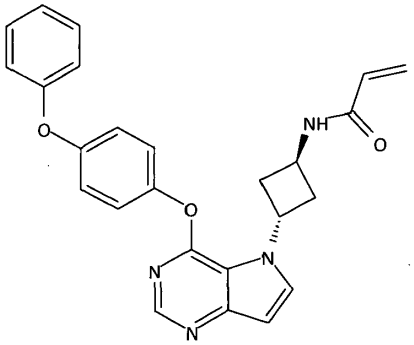

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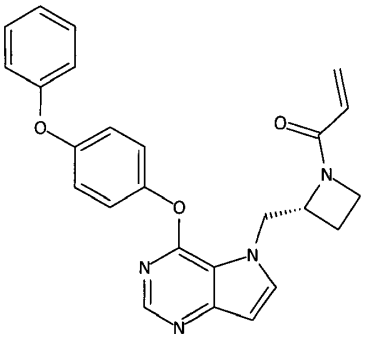

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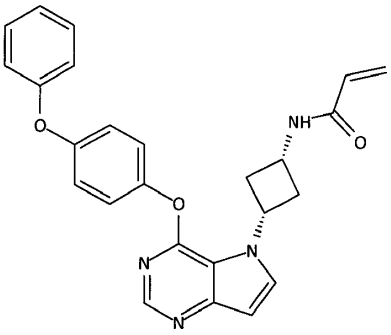

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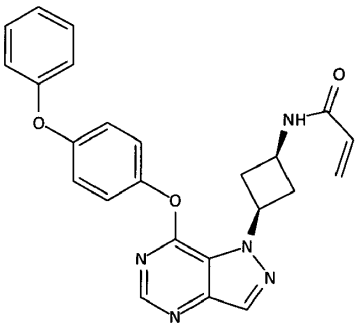

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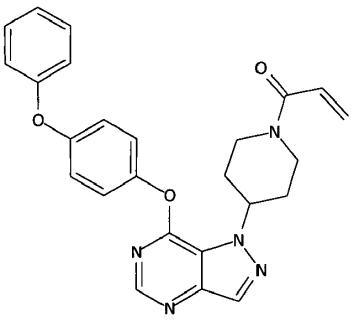

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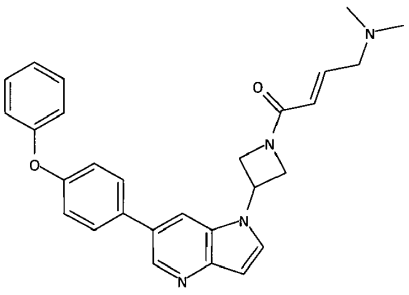

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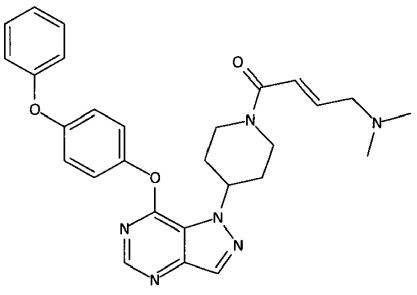

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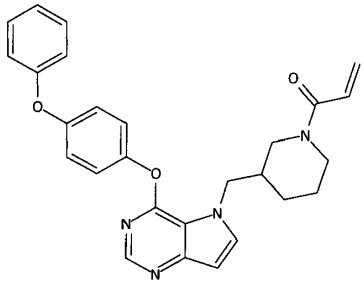

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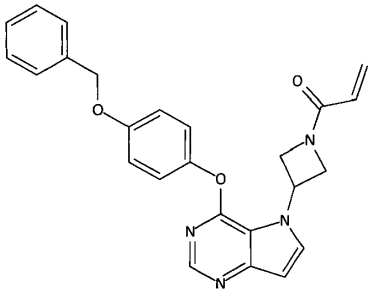

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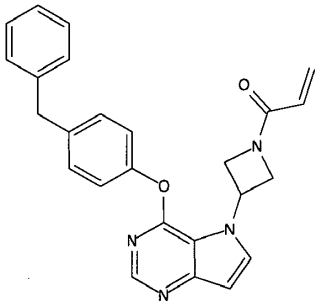

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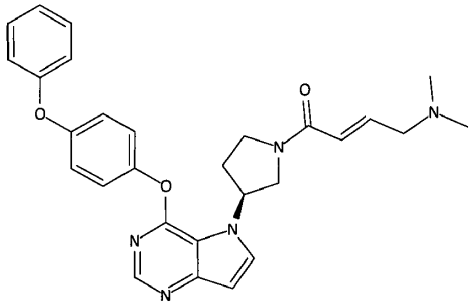

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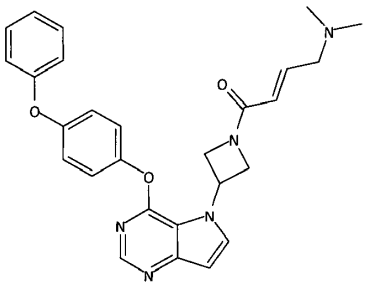

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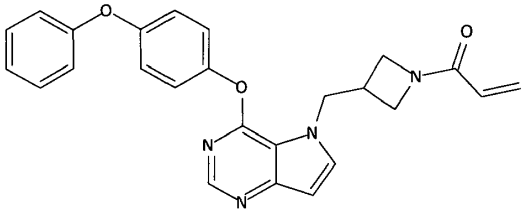

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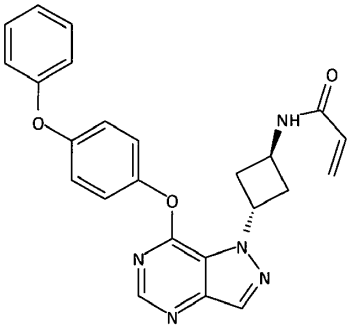

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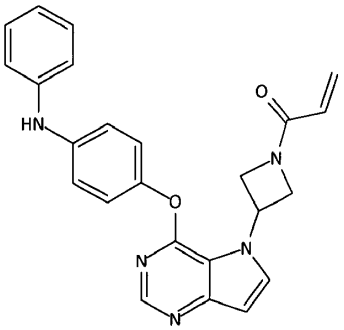

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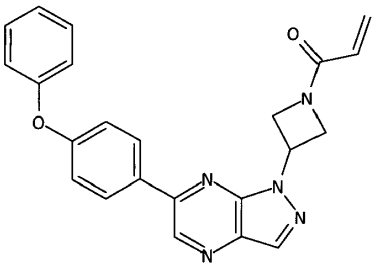

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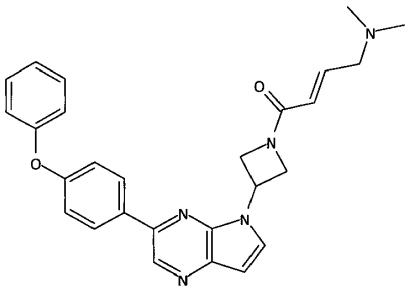

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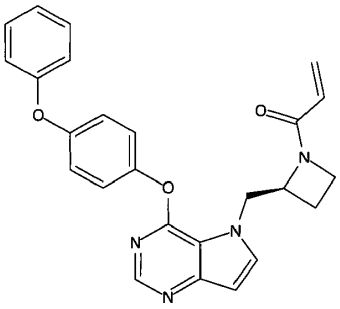

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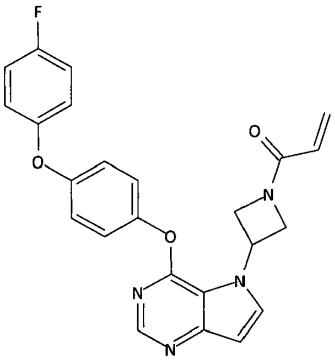

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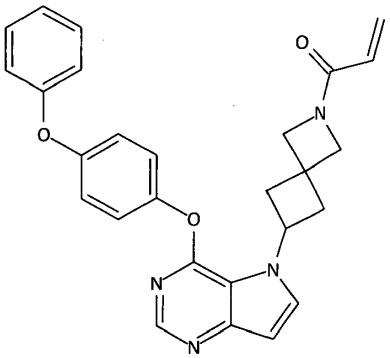

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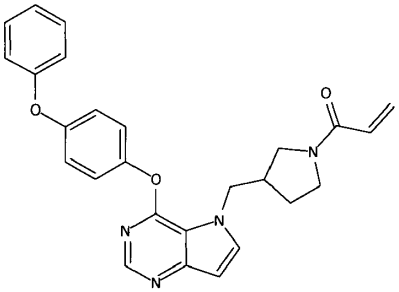

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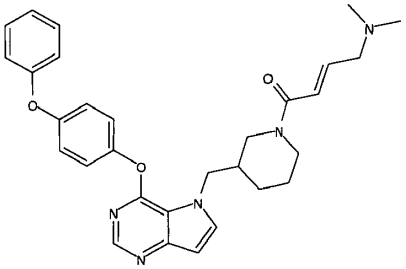

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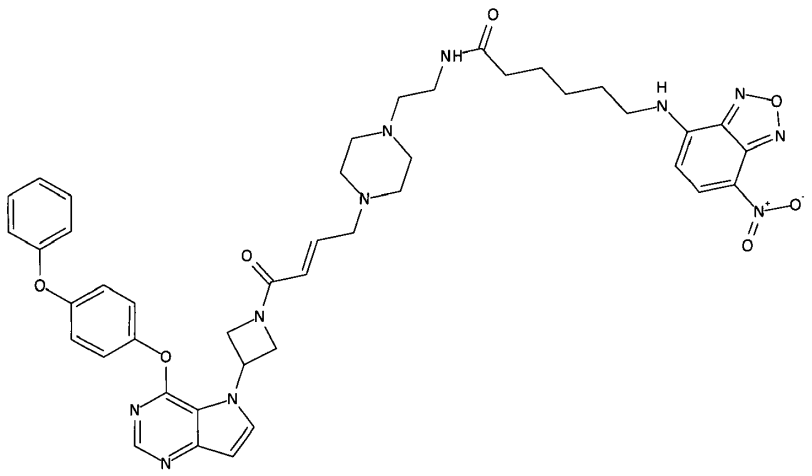

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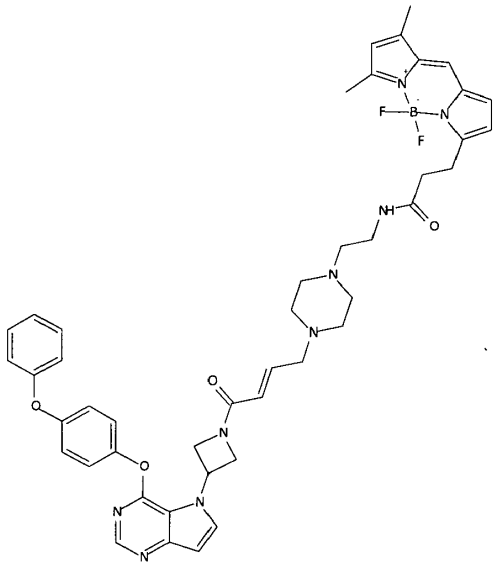

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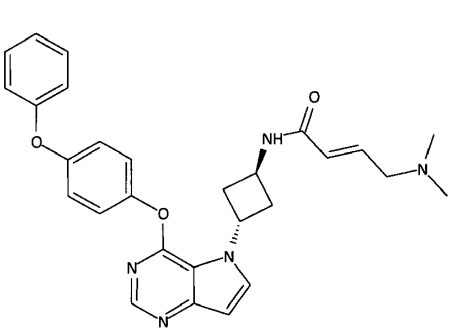

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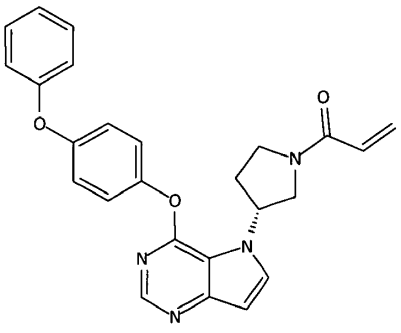

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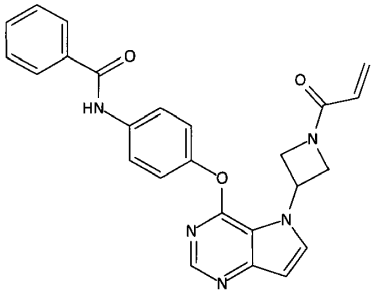

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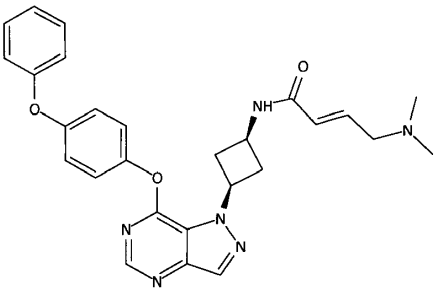

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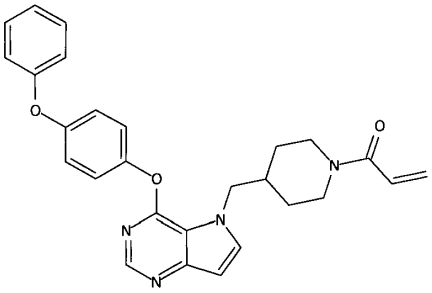

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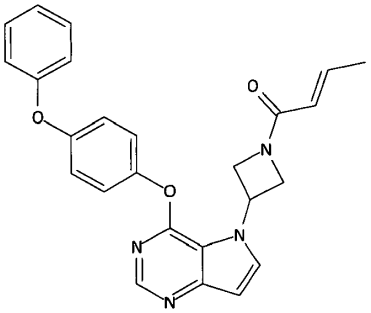

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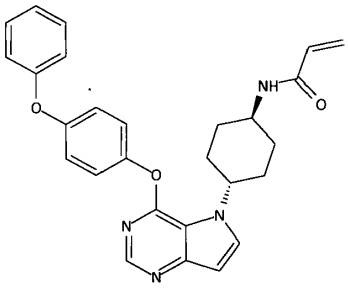

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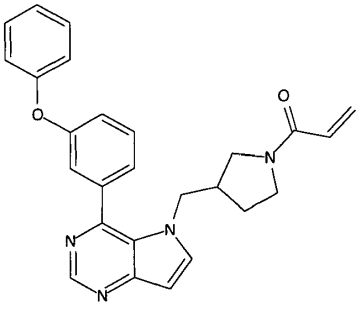

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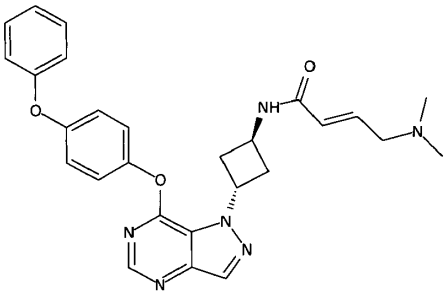

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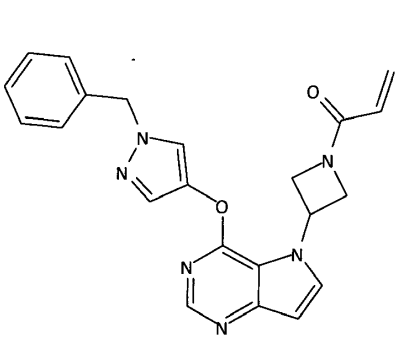

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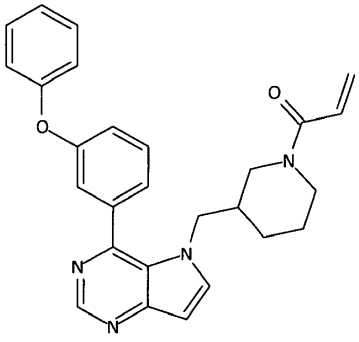

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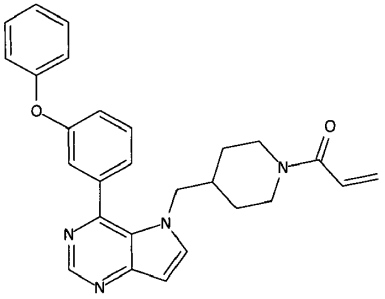

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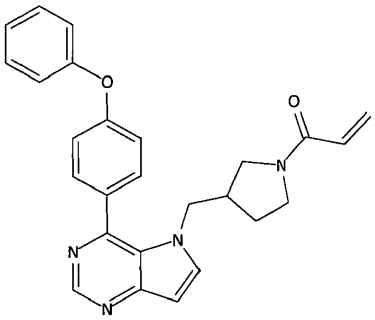

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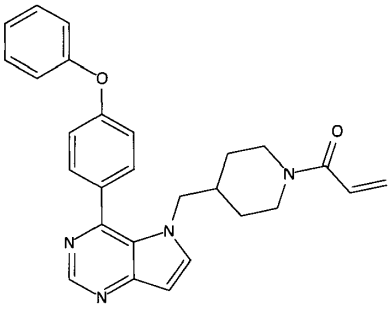

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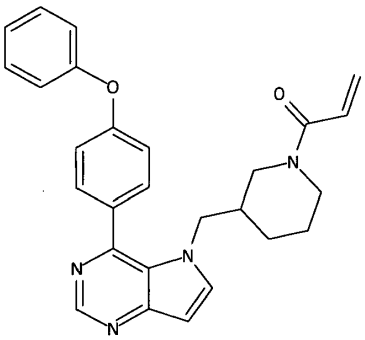

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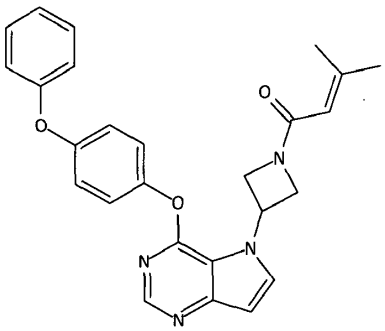

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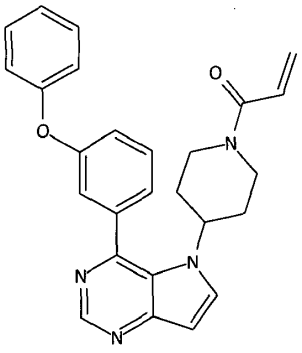

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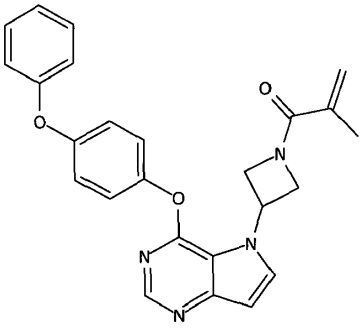

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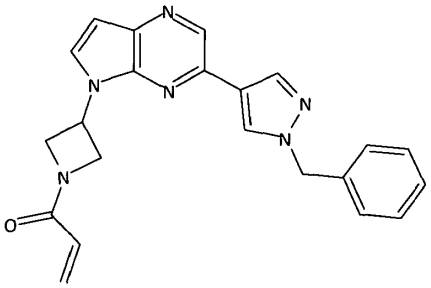

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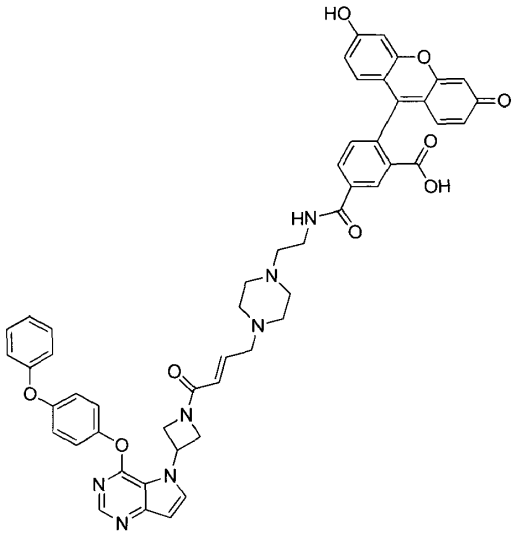

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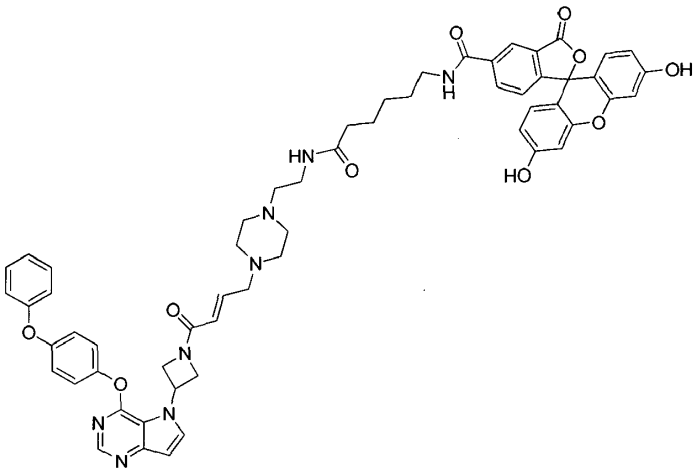

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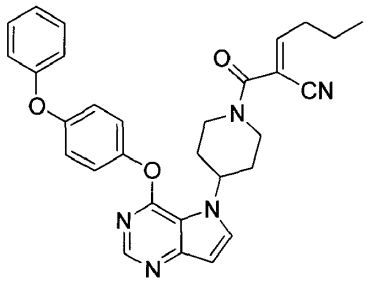

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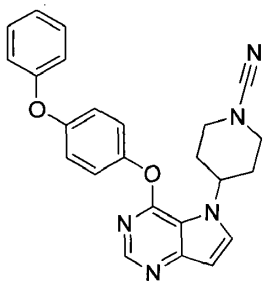

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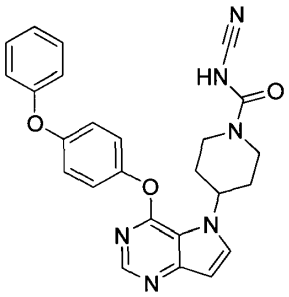

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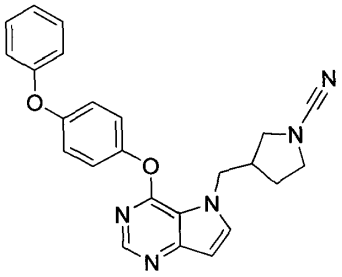

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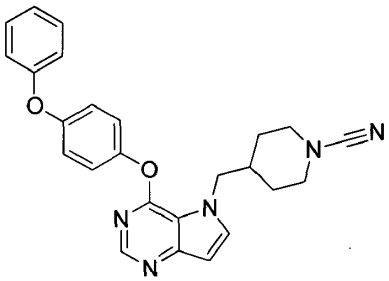

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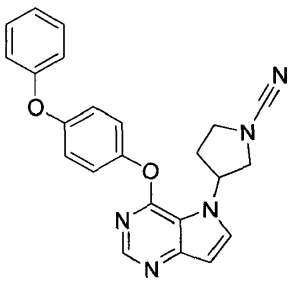

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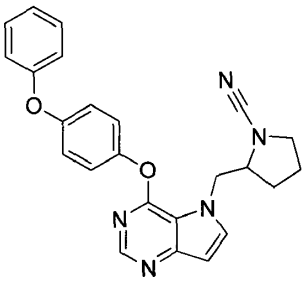

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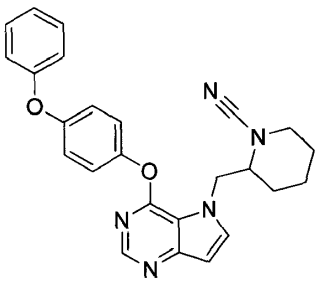

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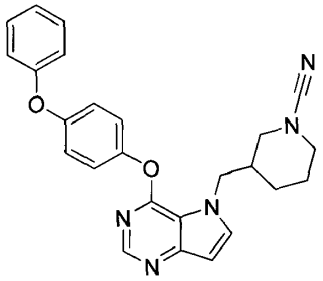

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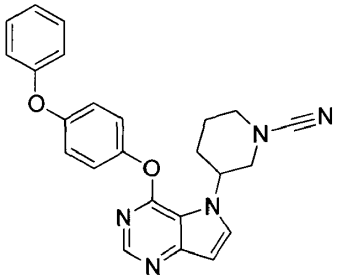

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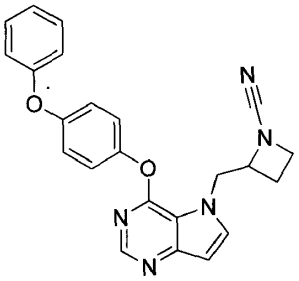

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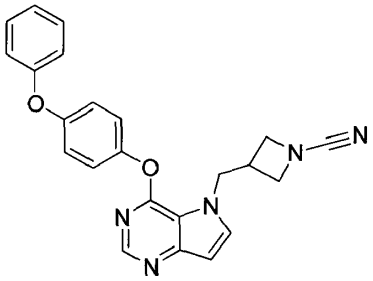

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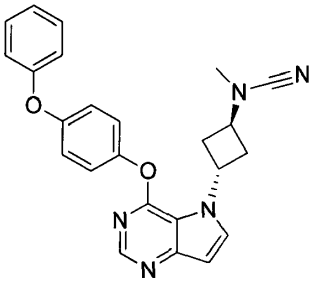

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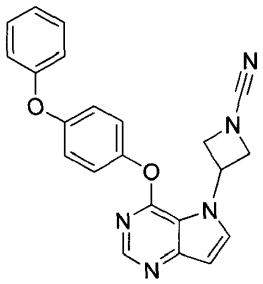

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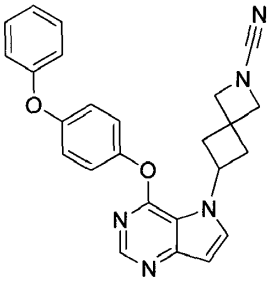

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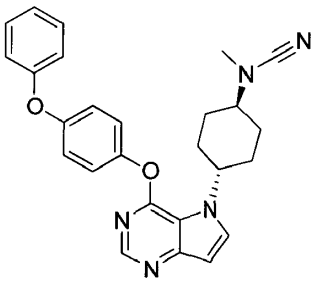

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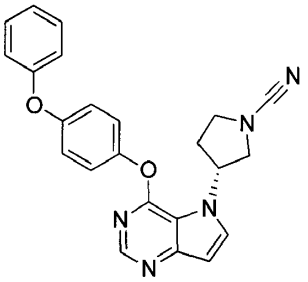

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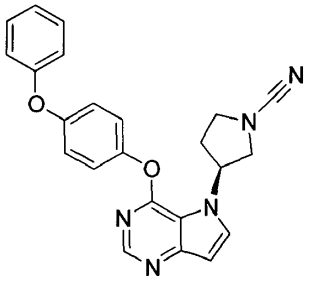

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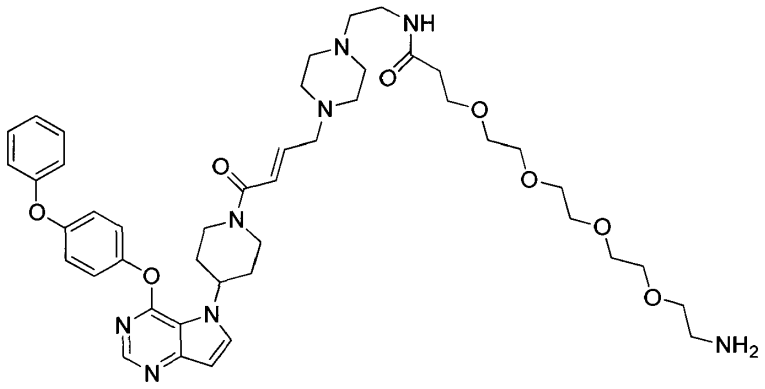

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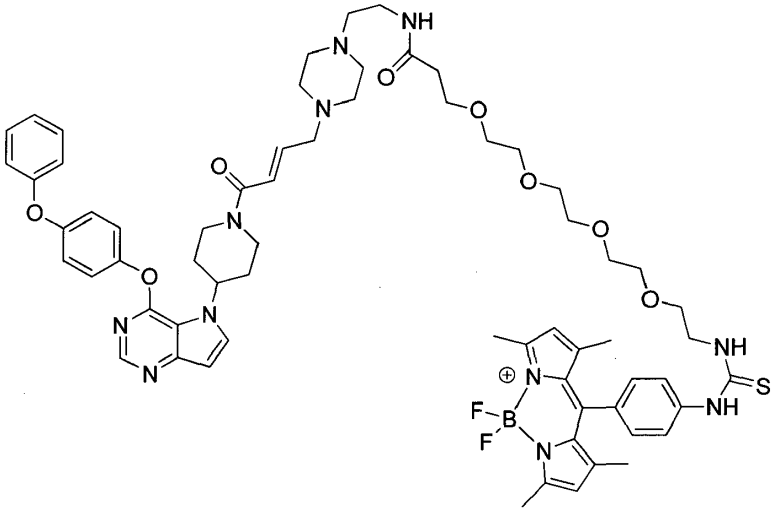

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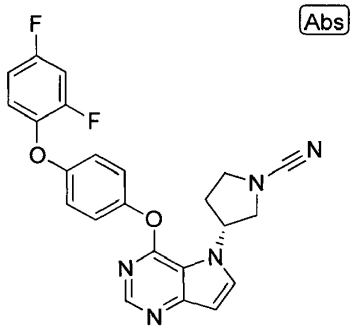

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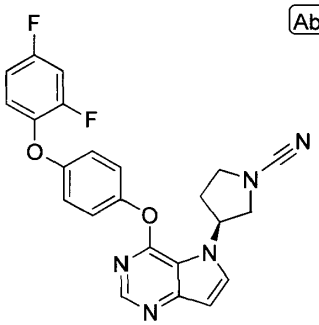

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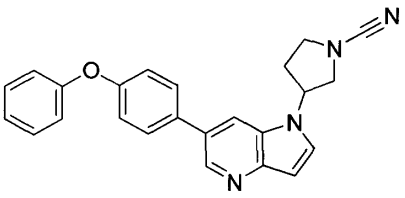


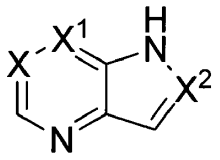
77.

16. Farmasøytisk sammensetning som omfatter en forbindelse ifølge krav 1 og en farmasøytisk akseptabel adjuvans, bærer eller vehikkel.

17. Forbindelse ifølge ett av kravene 1 til 15 og/eller et fysiologisk akseptabelt salt derav for anvendelse i behandlingen av en BTK-mediert forstyrrelse, hvori den BTK-medierte forstyrrelsen er inflammatorisk tarmsykdom, leddgikt, systemisk lupus erytematose (SLE eller lupus), lupus nefritt, vaskulitt, idiopatisk trombocytopenisk purpura (ITP), revmatoid artritt, psoriasisartritt, osteoartritt, Stills sykdom, juvenil artritt, diabetes, myasthenia gravis, Hashimotos tyreoiditt, Ords tyreoiditt, Graves sykdom, autoimmun tyreoiditt, Sjøgrens syndrom, multippel sklerose, systemisk sklerose, Lymes nevroborreliose, Guillain-Barre syndrom, akutt spredt encefalomyelitt, Addisons sykdom, opsoklonus-myoklonus syndrom, ankyloserende spondylose, antifosfolipid antistoffsyndrom, aplastisk anemi, autoimmun hepatitt, autoimmun gastritt, pernistisk anemi, cøliaki, Goodpastures syndrom, idiopatisk trombocytopenisk purpura, optisk nevritt, sklerodermi, primær biliær cirrhose, Reiters syndrom, Takayasus arteritt, temporal arteritt, varm autoimmun hemolytisk anemi, Wegeners granulomatose, psoriasis, alopecia universalis, Behcets sykdom, kronisk tretthet, dysautonomi, membranøs glomerulonefropati, endometriose, interstitial cystitt, pemphigus vulgaris, bulløst pemfigoid, nevromyotoni, skleroderma eller vulvodyni.

18. Fremgangsmåte for fremstilling av en forbindelse med formel I ifølge krav 1, som omfatter trinnene:

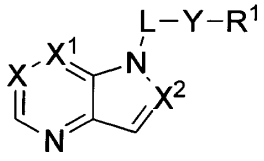
å omsette en forbindelse med formel (II-a)



II-a

hvori X, X^1 og X^2 er som definert i krav 1;

med en forbindelse for å gi en forbindelse med formel **I**:



I

hvori X, X^1, X^2, R^1, L og Y er som definert i krav 1.