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1. 一般的名称に係る文書

1.1　JAN

令和 3 年 2 月 15 日付薬生薬審発 0215 第 1 号により、以下のとおり通知された。

一般的名称（日本名）：チソツマブ　ベドチン（遺伝子組換え）

一般的名称（英　名）：Tisotumab Vedotin (Genetical Recombination)

1.2　INN

以下のとおり WHO Drug Information, Vol. 30, No. 1, 2016, p159-160, r-INN List 75 に掲載されている。

tisotumab vedotin

薬生薬審発 0215 第１号
令 和 ３ 年 ２ 月 15 日

各都道府県衛生主管部（局）長　殿

厚生労働省医薬・生活衛生局医薬品審査管理課長
（　　公　　印　　省　　略　　）

医薬品の一般的名称について

標記については、「医薬品の一般的名称の取扱いについて（平成 18 年３月 31 日薬食発第 0331001 号厚生労働省医薬食品局長通知）」等により取り扱っているところです。今般、我が国における医薬品の一般的名称（以下「JAN」という。）について、新たに別添１のとおり定めたので、御了知の上、貴管下関係業者に周知方よろしく御配慮願います。

また、「我が国における医薬品の一般的名称の変更について（その１）」（平成19年８月６日薬食審査発第0806001号厚生労働省医薬食品局審査管理課長通知）の別紙１及び参考中の記載内容について、別添２のとおり訂正するので併せて御留意願います。

（参照）
「日本医薬品一般的名称データベース」https://jpdb.nihs.go.jp/jan/Default.aspx
（別添の情報のうち、JAN 以外の最新の情報は、当該データベースの情報で対応することとしています。）

（別表２）INN に収載された品目の我が国における医薬品一般的名称

（平成 18 年 3 月 31 日薬食審査発第 0331001 号厚生労働省医薬食品局審査管理課長通知に示す別表２）

登録番号　302-3-B8

JAN（日本名）：チソツマブ　ベドチン（遺伝子組換え）

JAN（英　名）：Tisotumab Vedotin (Genetical Recombination)

アミノ酸配列及びジスルフィド結合

L 鎖

```
DIQMTQSPPS LSASAGDRVT ITCRASQGIS SRLAWYQQKP EKAPKSLIYA
ASSLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ YNSYPYTFGQ
GTKLEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG
LSSPVTKSFN RGEC
```

H 鎖

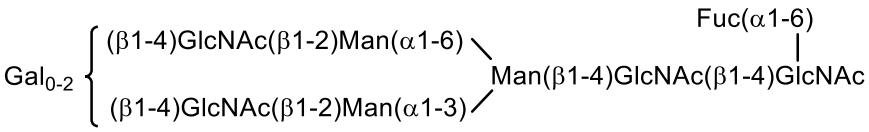
```
EVQLLESGGG LVQPGGSLRL SCAASGFTFS NYAMSWVRQA PGKGLEWVSS
ISGSGDYTYY TDSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARSP
WGYYLDSWGQ GTLVTVSSAS TKGPSVFPLA PSSKSTSGGT AALGCLVKDY
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTQTYI
CNVNHKPSNT KVDKRVEPKS CDKTHTCPPC PAPELLGGPS VFLFPPKPKD
TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYNST
YRVVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY
TLPPSREEMT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD
SDGSFFLYSK LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPGK
```

H 鎖 E1：部分的ピログルタミン酸；H 鎖 N298：糖鎖結合；H 鎖 K448：部分的プロセシング

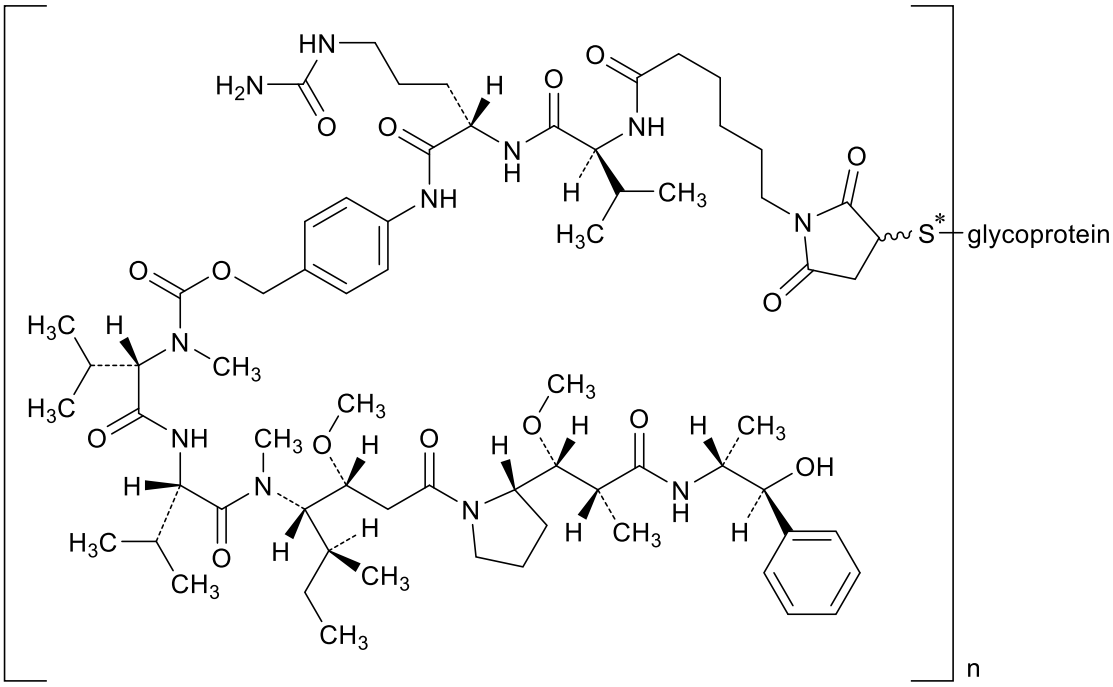
L 鎖 C214，H 鎖 C221，H 鎖 C227，H 鎖 C230：薬物結合可能部位

L 鎖 C214－H 鎖 C221，H 鎖 C227－H 鎖 C227，H 鎖 C230－H 鎖 C230：ジスルフィド結合

主な糖鎖の推定構造



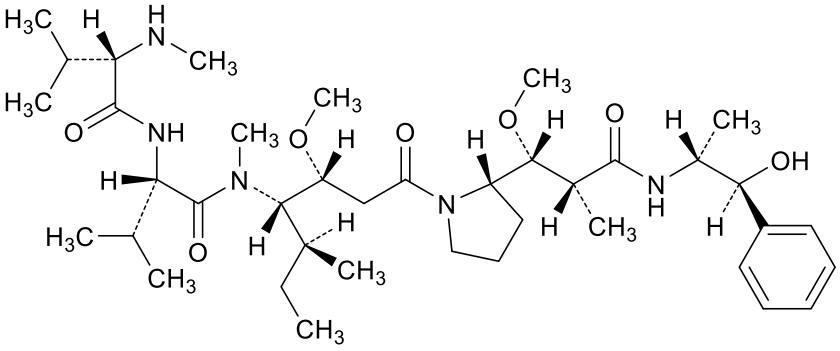
ベドチン部位の構造式



n は平均 4 である

*抗体部分の Cys 残基の硫黄原子

モノメチルアウリスタチン E の構造式



$C_{6418}H_{9906}N_{1710}O_{2022}S_{44}$（タンパク質部分，4 本鎖）

H 鎖　$C_{2183}H_{3367}N_{579}O_{674}S_{16}$

L 鎖　$C_{1026}H_{1590}N_{276}O_{337}S_{6}$

チソツマブ　ベドチンは，抗体薬物複合体（分子量：約153,000）であり，遺伝子組換えモノクローナル抗体の平均4個のCys残基に，モノメチルアウリスタチンEとリンカーからなるベドチン（(3*RS*)-1-(6-{[(2*S*)-1-{[(2*S*)-5-(カルバモイルアミノ)-1-{4-[({[(2*S*)-1-{[(2*S*)-1-{[(3*R*,4*S*,5*S*)-1-{(2*S*)-2-[(1*R*,2*R*)-3-{[(1*S*,2*R*)-1-ヒドロキシ-1-フェニルプロパン-2-イル]アミノ}-1-メトキシ-2-メチル-3-オキソプロピル]ピロリジン-1-イル}-3-メトキシ-5-メチル-1-オキソヘプタン-4-イル](メチル)アミノ}-3-メチル-1-オキソブタン-2-イル]アミノ}-3-メチル-1-オキソブタン-2-イル](メチル)カルバモイル}オキシ)メチル]アニリノ}-1-オキソペンタン-2-イル]アミノ}-3-メチル-1-オキソブタン-2-イル]アミノ}-6-オキソヘキシル)-2,5-ジオキソピロリジン-3-イル基（$C_{68}H_{106}N_{11}O_{15}$；分子量：1,317.63））が結合している．抗体部分は，ヒト組織因子に対する遺伝子組換えヒトIgG1モノクローナル抗体であり，チャイニーズハムスター卵巣細胞により産生される．タンパク質部分は，448個のアミノ酸残基からなるH鎖（γ1鎖）2本及び214個のアミノ酸残基からなるL鎖（κ鎖）2本で構成される糖タンパク質（分子量：約147,500）である．

Tisotumab Vedotin is an antibody-drug-conjugate (molecular weight: ca. 153,000) consisting of Vedotin ((3*RS*)-1-(6-{[(2*S*)-1-{[(2*S*)-5-(carbamoylamino)-1-{4-[({[(2*S*)-1-{[(2*S*)-1-{[(3*R*,4*S*,5*S*)-1-{(2*S*)-2-[(1*R*,2*R*)-3-{[(1*S*,2*R*)-1-hydroxy-1-phenylpropan-2-yl]amino}-1-methoxy-2-methyl-3-oxopropyl]pyrrolidin-1-yl}-3-methoxy-5-methyl-1-oxoheptan-4-yl](methyl)amino}-3-methyl-1-oxobutan-2-yl]amino}-3-methyl-1-oxobutan-2-yl](methyl)carbamoyl}oxy)methyl]anilino}-1-oxopentan-2-yl]amino}-3-methyl-1-oxobutan-2-yl]amino}-6-oxohexyl)-2,5-dioxopyrrolidin-3-yl group ($C_{68}H_{106}N_{11}O_{15}$; molecular weight: 1,317.63)), which is composed of monomethyl auristatin E and linker, attached to an average of 4 Cys residues of the recombinant monoclonal antibody. The monoclonal antibody moiety is a recombinant human IgG1 monoclonal antibody against human tissue factor and produced in a Chinese hamster ovary cells. The protein moiety is a glycoprotein (molecular weight: ca. 147,500) composed of 2 H-chains (γ1-chains) consisting of 448 amino acid residues each and 2 L-chains (κ-chains) consisting of 214 amino acid residues each.

International Nonproprietary Names for Pharmaceutical Substances (INN)

RECOMMENDED International Nonproprietary Names: List 75

Notice is hereby given that, in accordance with paragraph 7 of the Procedure for the Selection of Recommended International Nonproprietary Names for Pharmaceutical Substances [*Off. Rec. Wld Health Org.*, 1955, **60**, 3 (Resolution EB15.R7); 1969, **173**, 10 (Resolution EB43.R9); Resolution EB115.R4 (EB115/2005/REC/1)], the following names are selected as Recommended International Nonproprietary Names. The inclusion of a name in the lists of Recommended International Nonproprietary Names does not imply any recommendation of the use of the substance in medicine or pharmacy.
Lists of Proposed (1–113) and Recommended (1–74) International Nonproprietary Names can be found in *Cumulative List No. 16, 2015* (available in CD-ROM only).

Dénominations communes internationales des Substances pharmaceutiques (DCI)

Dénominations communes internationales RECOMMANDÉES: Liste 75

Il est notifié que, conformément aux dispositions du paragraphe 7 de la Procédure à suivre en vue du choix de Dénominations communes internationales recommandées pour les Substances pharmaceutiques [*Actes off. Org. mond. Santé*, 1955, **60**, 3 (résolution EB15.R7); 1969, **173**, 10 (résolution EB43.R9); résolution EB115.R4 (EB115/2005/REC/1)] les dénominations ci-dessous sont choisies par l'Organisation mondiale de la Santé en tant que dénominations communes internationales recommandées. L'inclusion d'une dénomination dans les listes de DCI recommandées n'implique aucune recommandation en vue de l'utilisation de la substance correspondante en médecine ou en pharmacie.
On trouvera d'autres listes de Dénominations communes internationales proposées (1–113) et recommandées (1–74) dans la *Liste récapitulative No. 16, 2015* (disponible sur CD-ROM seulement).

Denominaciones Comunes Internacionales para las Sustancias Farmacéuticas (DCI)

Denominaciones Comunes Internacionales RECOMENDADAS: Lista 75

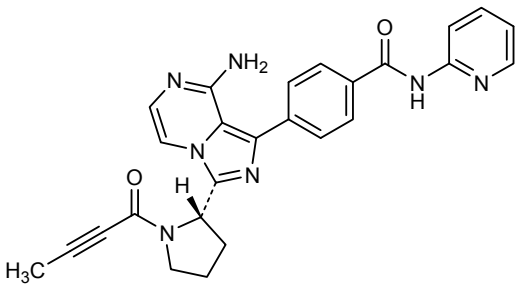
De conformidad con lo que dispone el párrafo 7 del Procedimiento de Selección de Denominaciones Comunes Internacionales Recomendadas para las Sustancias Farmacéuticas [*Act. Of. Mund. Salud*, 1955, **60**, 3 (Resolución EB15.R7); 1969, **173**, 10 (Resolución EB43.R9); Résolution EB115.R4 (EB115/2005/REC/1) EB115.R4 (EB115/2005/REC/1)], se comunica por el presente anuncio que las denominaciones que a continuación se expresan han sido seleccionadas como Denominaciones Comunes Internacionales Recomendadas. La inclusión de una denominación en las listas de las Denominaciones Comunes Recomendadas no supone recomendación alguna en favor del empleo de la sustancia respectiva en medicina o en farmacia.
Las listas de Denominaciones Comunes Internacionales Propuestas (1–113) y Recomendadas (1–74) se encuentran reunidas en *Cumulative List No. 16, 2015* (disponible sólo en CD-ROM).

Latin, English, French, Spanish: *Recommended INN*	*Chemical name or description; Molecular formula; Graphic formula*
DCI Recommandée	*Nom chimique ou description; Formule brute; Formule développée*
DCI Recomendada	*Nombre químico o descripción; Fórmula molecular; Fórmula desarrollada*

acalabrutinibum

acalabrutinib	4-{8-amino-3-[(2*S*)-1-(but-2-ynoyl)pyrrolidin-2-yl]imidazo[1,5-*a*]pyrazin-1-yl}-*N*-(pyridin-2-yl)benzamide
acalabrutinib	4-{8-amino-3-[(2*S*)-1-(but-2-ynoyl)pyrrolidin-2-yl]imidazo[1,5-*a*]pyrazin-1-yl}-*N*-(pyridin-2-yl)benzamide
acalabrutinib	4-{8-amino-3-[(2*S*)-1-(but-2-inoil)pirrolidin-2-il]imidazo[1,5-*a*]pirazin-1-il}-*N*-(piridin-2-il)benzamida

$C_{26}H_{23}N_7O_2$



afasevikumabum #

afasevikumab	immunoglobulin G1-kappa, anti-[*Homo sapiens* IL17A (interleukin 17A, IL-17A) and *Homo sapiens* IL17F (interleukin 17F, IL-17F)], *Homo sapiens* monoclonal antibody; gamma1 heavy chain (1-453) [*Homo sapiens* VH (IGHV3-9*01 (96.00%) -(IGHD)-IGHJ2*01) [8.8.16] (1-123) -IGHG1*03, G1m3 (CH1 (124-221), hinge (222-236), CH2 (237-346), CH3 (347-451), CHS (452-453)) (124-453)], (226-215')-disulfide with kappa light chain (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-11*01 (98.90%) -IGKJ4*01) [6.3.10] (1'-108') -IGKC*01, Km3 (109'-215')]; dimer (232-232'':235-235'')-bisdisulfide
afasévikumab	immunoglobuline G1-kappa, anti-[*Homo sapiens* IL17A (interleukine 17A, IL-17A) et *Homo sapiens* IL17F (interleukine 17F, IL-17F)], *Homo sapiens* anticorps monoclonal;

chaîne lourde gamma1 (1-453) [*Homo sapiens* VH (IGHV3-9*01 (96.00%) -(IGHD)-IGHJ2*01) [8.8.16] (1-123) -IGHG1*03, G1m3 (CH1 (124-221), charnière (222-236), CH2 (237-346), CH3 (347-451), CHS (452-453)) (124-453)], (226-215')-disulfure avec la chaîne légère kappa (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-11*01 (98.90%) -IGKJ4*01) [6.3.10] (1'-108') -IGKC*01, Km3 (109'-215')]; dimère (232-232":235-235")-bisdisulfure

afasevikumab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* IL17A (interleukina 17A, IL-17A) y *Homo sapiens* IL17F (interleukina 17F, IL-17F)], anticuerpo monoclonal de *Homo sapiens*;
cadena pesada gamma1 (1-453) [*Homo sapiens* VH (IGHV3-9*01 (96.00%) -(IGHD)-IGHJ2*01) [8.8.16] (1-123) -IGHG1*03, G1m3 (CH1 (124-221), bisagra (222-236), CH2 (237-346), CH3 (347-451), CHS (452-453)) (124-453)], (226-215')-disulfuro con la cadena ligera kappa (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-11*01 (98.90%) -IGKJ4*01) [6.3.10] (1'-108') -IGKC*01, Km3 (109'-215')]; dímero (232-232":235-235")-bisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGRSLRL SCAASGFTFD DYAMHWVRQA PGKGLEWVSG  50
INWSSGGIGY ADSVKGRFTI SRDNAKNSLY LQMNSLRAED TALYYCARDI 100
GGFGEFYWNF GLWGRGTLVT VSSASTKGPS VFPLAPSSKS TSGGTAALGC 150
LVKDYFPEPV TVSWNSGALT SGVHTFPAVL QSSGLYSLSS VVTVPSSSLG 200
TQTYICNVNH KPSNTKVDKR VEPKSCDKTH TCPPCPAPEL LGGPSVFLFP 250
PKPKDTLMIS RTPEVTCVVV DVSHEDPEVK FNWYVDGVEV HNAKTKPREE 300
QYNSTYRVVS VLTVLHQDWL NGKEYKCKVS NKALPAPIEK TISKAKGQPR 350
EPQVYTLPPS REEMTKNQVS LTCLVKGFYP SDIAVEWESN GQPENNYKTT 400
PPVLDSDGSF FLYSKLTVDK SRWQQGNVFS CSVMHEALHN HYTQKSLSLS 450
PGK                                                     453
```

Light chain / Chaîne légère / Cadena ligera

```
EIVLTQSPAT LSLSPGERAT LSCRASQSVR SYLAWYQQKP GQAPRLLIYD  50
ASNRATGIPA RFSGSGSGTD FTLTISSLEP EDFAVYYCQQ RSNWPPATFG 100
GGTKVEIKRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK 150
VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ 200
GLSSPVTKSF NRGEC                                        215
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-96	150-206	267-327	373-431
	22"-96"	150"-206"	267"-327"	373"-431"
Intra-L (C23-C104)	23'-88'	135'-195'		
	23'"-88'"	135'"-195'"		
Inter-H-L (h 5-CL 126)	226-215'	226"-215'"		
Inter-H-H (h 11, h 14)	232-232"	235-235"		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilaciónH VH N57: 52, 52" (2% of the glycans)
H CH2 N84.4:
303, 303" (98% of the glycans)
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

aglatimagenum besadenovecum #
aglatimagene besadenovec

adenovirus (serotype 5) non replicant with a deletion in the E1/E2 region containing the herpes virus thymidine kinase gene (*Herpes simplex virus* HSV-tk) under the control of a *Rous sarcoma virus* (RSV) long terminal repeat promoter

aglatimagène bésadénovec

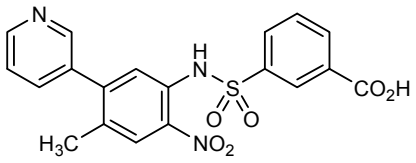
adénovirus (sérotype 5) non répliquant, délété de la région E1/E2, contenant le gène de la thymidine kinase du virus de l'herpès (*virus Herpes simplex* HSV-tk) sous le contrôle de la séquence LTR (terminale longue répétée) du virus du sarcome de Rous (RSV)

aglatimagén besadenovec	adenovirus (serotipo 5), no replicante, con una deleción en la región E1/E2, que contiene el gen de la timidina kinasa del virus del herpes (*Herpes simplex virus* HSV-tk) bajo el control de la secuencia LTR (secuencia larga terminal repetida) del virus del sarcoma de Rous (RSV)

alofanibum

alofanib	3-{[4-methyl-2-nitro-5-(pyridin-3-yl)phenyl]sulfamoyl}benzoic acid
alofanib	acide 3-{[4-méthyl-2-nitro-5-(pyridin-3-yl)phenyl]sulfamoyl}benzoïque
alofanib	ácido 3-{[4-metil-2-nitro-5-(piridin-3-il)fenil]sulfamoil}benzoico

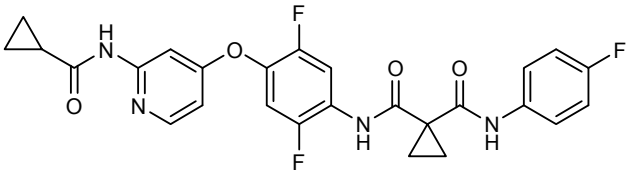
$C_{19}H_{15}N_3O_6S$



altiratinibum

altiratinib	*N*-{4-[(2-cyclopropanecarboxamidopyridin-4-yl)oxy]-2,5-difluorophenyl}-*N*'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
altiratinib	*N*-{4-[(2-cyclopropanecarboxamidopyridin-4-yl)oxy]-2,5-difluorophényl}-*N*'-(4-fluorophényl)cyclopropane-1,1-dicarboxamide
altiratinib	*N*-{4-[(2-ciclopropanocarboxamidopiridin-4-il)oxi]-2,5-difluorofenil}-*N*'-(4-fluorofenil)ciclopropano-1,1-dicarboxamida

$C_{26}H_{21}F_3N_4O_4$



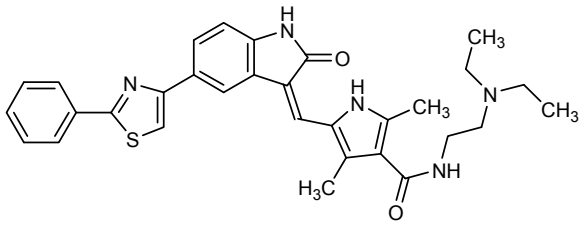
amcasertibum

amcasertib	*N*-[2-(diethylamino)ethyl]-2,4-dimethyl-5-{[2-oxo-5-(2-phenyl-1,3-thiazol-4-yl)-1,2-dihydro-3*H*-indol-3-ylidene]methyl}-1*H*-pyrrole-3-carboxamide
amcasertib	*N*-[2-(diéthylamino)éthyl]-2,4-diméthyl-5-{[2-oxo-5-(2-phényl-1,3-thiazol-4-yl)-1,2-dihydro-3*H*-indol-3-ylidène]méthyl}-1*H*-pyrrole-3-carboxamide

amcasertib

N-[2-(dietilamino)etil]-2,4-dimetil-5-{[5-(2-fenil-1,3-tiazol-4-il)- 2-oxo-1,2-dihidro-3*H*-indol-3-ilideno]metil}-1*H*-pirrol-3-carboxamida

$C_{31}H_{33}N_5O_2S$



apalutamidum

apalutamide

4-{7-[6-cyano-5-(trifluoromethyl)pyridin-3-yl]-8-oxo-6-thioxo-5,7-diazaspiro[3.4]octan-5-yl}-2-fluoro-*N*-methylbenzamide

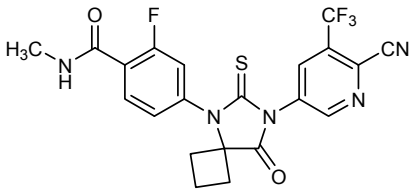
apalutamide

4-{7-[6-cyano-5-(trifluorométhyl)pyridin-3-yl]-8-oxo-6-thioxo-5,7-diazaspiro[3.4]octan-5-yl}-2-fluoro-*N*-méthylbenzamide

apalutamida

4-{7-[6-ciano-5-(trifluorometil)piridin-3-il]-8-oxo-6-tioxo-5,7-diazaspiro[3.4]octan-5-il}-2-fluoro-*N*-metilbenzamida

$C_{21}H_{15}F_4N_5O_2S$



ascrinvacumabum #

ascrinvacumab

immunoglobulin G2-kappa, anti-[*Homo sapiens* ACVRL1 (activin A receptor type II-like 1, activin receptor-like kinase 1, ALK1, ALK-1, serine/threonine-protein kinase receptor R3, SKR3, transforming growth factor-beta superfamily receptor type I, TGF-B superfamily receptor type I, TSR-I, HHT2, ORW2)], *Homo sapiens* monoclonal antibody; gamma2 heavy chain (1-444) [*Homo sapiens* VH (IGHV4-31*02 (98.00%) -(IGHD) -IGHJ4*01) [10.7.10] (1-118) -IGHG2*01, G2m.. (CH1 (119-216), hinge (217-228), CH2 (229-337), CH3 (338-442), CHS (443-444)) (119-444)], (132-215')-disulfide with kappa light chain (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-20*01 (99.00%) -IGKJ5*01) [7.3.9] (1'-108') -IGKC*01, Km3 (109'-215')]; dimer (220-220":221-221":224-224":227-227")-tetrakisdisulfide

ascrinvacumab

immunoglobuline G2-kappa, anti-[*Homo sapiens* ACVRL1 (réceptor de type II-like 1 de l'activine A, kinase 1 réceptor-like de l'activine, ALK1, ALK-1, récepteur R3 sérine/thréonine-protéine kinase, SKR3, récepteur de type I de la superfamille du facteur de croissance transformant bêta, récepteur de type I de la superfamille TGF-B, TSR-I, HHT2, ORW2)], *Homo sapiens* anticorps monoclonal; chaîne lourde gamma2 (1-444) [*Homo sapiens* VH (IGHV4-31*02 (98.00%) -(IGHD) -IGHJ4*01) [10.7.10] (1-118) -IGHG2*01, G2m.. (CH1 (119-216), charnière (217-228), CH2 (229-337), CH3 (338-442), CHS (443-444)) (119-444)], (132-215')-disulfure avec la chaîne légère kappa (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-20*01 (99.00%) -IGKJ5*01) [7.3.9] (1'-108') -IGKC*01, Km3 (109'-215')]; dimère (220-220'':221-221'':224-224'':227-227'')-tétrakisdisulfure

ascrinvacumab

inmunoglobulina G2-kappa, anti-[*Homo sapiens* ACVRL1 (receptor de tipo II-like 1 de la activina A, kinasa 1 receptor-like de la activina, ALK1, ALK-1, receptor R3 serina/treonina-proteína kinasa, SKR3, receptor de tipo I de la superfamilia del factor de crecimiento transformador beta, receptor de type I de la superfamilia TGF-B, TSR-I, HHT2, ORW2)], *Homo sapiens* anticuerpo monoclonal; cadena pesada gamma2 (1-444) [*Homo sapiens* VH (IGHV4-31*02 (98.00%) -(IGHD) -IGHJ4*01) [10.7.10] (1-118) -IGHG2*01, G2m.. (CH1 (119-216), bisagra (217-228), CH2 (229-337), CH3 (338-442), CHS (443-444)) (119-444)], (132-215')-disulfuro con la cadena ligera kappa (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-20*01 (99.00%) -IGKJ5*01) [7.3.9] (1'-108') -IGKC*01, Km3 (109'-215')]; dimero (220-220'':221-221'':224-224'':227-227'')-tetrakisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLQESGPG LVKPSQTLSL TCTVSGGSIS SGEYYWNWIR QHPGKGLEWI  50
GYIYYSGSTY YNPSLKSRVT ISVDTSKNQF SLKLSSVTAA DTAVYYCARE 100
SVAGFDYWGQ GTLVTVSSAS TKGPSVFPLA PCSRSTSEST AALGCLVKDY 150
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSNFGTQTYT 200
CNVDHKPSNT KVDKTVERKC CVECPPCPAP PVAGPSVFLF PPKPKDTLMI 250
SRTPEVTCVV VDVSHEDPEV QFNWYVDGVE VHNAKTKPRE EQFNSTFRVV 300
SVLTVVHQDW LNGKEYKCKV SNKGLPAPIE KTISKTKGQP REPQVYTLPP 350
SREEMTKNQV SLTCLVKGFY PSDIAVEWES NGQPENNYKT TPPMLDSDGS 400
FFLYSKLTVD KSRWQQGNVF SCSVMHEALH NHYTQKSLSL SPGK       444
```

Light chain / Chaîne légère / Cadena ligera

```
EIVLTQSPGT LSLSPGERAT LSCRASQSVS SSYLAWYQQK PGQAPRLLIY  50
GTSSRATGIP DRFSGSGSGT DFTLTISRLE PEDFAVYYCQ QYGSSPITFG 100
QGTRLEIKRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK 150
VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ 200
GLSSPVTKSF NRGEC                                       215
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104) 22-97 145-201 258-318 364-422
22''-97'' 145''-201'' 258''-318'' 364''-422''
Intra-L (C23-C104) 23'-89' 135'-195'
23'''-89''' 135'''-195'''
Inter-H-L (CH1 10-CL 126) 132-215' 132''-215'''
Inter-H-H (h 4, h 5, h 8, h 11) 220-220'' 221-221'' 224-224'' 227-227''

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
294, 294''
Fucosylated complex bi-antennary NS0-type glycans / glycanes de type NS0 bi-antennaires complexes fucosylés / glicanos de tipo NS0 biantenarios complejos fucosilados

Other post-translational modifications / Autres modifications post-traductionnelles / Otras modificaciones post-traduccionales
C-terminal trimming of the *C*-terminal lysine (K)
H CHS K2:
444, 444''

avacincaptadum pegolum	
avacincaptad pegol	5'-*O*-({[6-(1-{(2*RS*)-2,3-bis[ω-methoxypoly(oxyethane-1,2-diyl)]propoxy}formamido)hexyl]oxy}hydroxyphosphoryl)-2'-deoxy-2'-fluoro-cytidylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-guanylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-guanylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-adenylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→3')-thymidine
avacincaptad pégol	5'-*O*-({[6-(1-{(2*RS*)-2,3-bis[ω-méthoxypoly(oxyéthane-1,2-diyl)]propoxy}formamido)hexyl]oxy}hydroxyphosphoryl)-2'-déoxy-2'-fluoro-cytidylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-déoxy-2'-fluorocytidylyl-(3'→5')-2'-déoxy-2'-fluorocytidylyl-(3'→5')-guanylyl-(3'→5')-2'-déoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-déoxy-2'-fluorouridylyl-(3'→5')-2'-déoxy-2'-fluorocytidylyl-(3'→5')-2'-déoxy-2'-fluorouridylyl-(3'→5')-2'-déoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-déoxy-2'-fluorocytidylyl-(3'→5')-guanylyl-(3'→5')-2'-déoxy-2'-fluorocytidylyl-(3'→5')-2'-déoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-déoxy-2'-fluorouridylyl-(3'→5')-2'-déoxy-2'-fluorocytidylyl-(3'→5')-2'-déoxy-2'-fluorocytidylyl-(3'→5')-2'-déoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-déoxy-2'-fluorouridylyl-(3'→5')-2'-déoxy-2'-fluorouridylyl-(3'→5')-2'-déoxy-2'-fluorouridylyl-(3'→5')-adénylyl-(3'→5')-2'-déoxy-2'-fluorocytidylyl-(3'→5')-2'-déoxy-2'-fluorocytidylyl-(3'→5')-2'-déoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-déoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→3')-thymidine

avacincaptad pegol

5'-*O*-({[6-(1-{(2*RS*)-2,3-bis[ω-metoxipoli(oxietano-1,2-diil)]propoxi}formamido)hexil]oxi}hidroxifosforil)-2'-desoxi-2'-fluoro-citidilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-guanilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-guanilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-adenilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-*O*-metilguanilil-(3'→3')-timidina

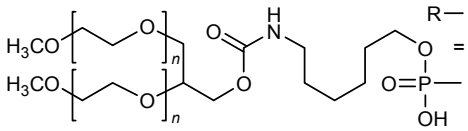
$C_{395}H_{492}F_{21}N_{142}O_{262}P_{39}\ (C_2H_4O)_{2n}$

(3'-5') R-dflC-mG-dflC-dflC-G-dflC-mG-mG-dflU-dflC-dflU-dflC-mA-mG-mG-dflC-G-dflC-dflU-mG-mA-mG-dflU-dflC-dflU-mG-mA-mG-dflU-dflU-dflU-A-dflC-dflC-dflU-mG-dflC-mG3'-3'dT

Legend

dfl = 2'-deoxy-2'-fluoro

m = 2'-*O*-methyl



avelumabum #

avelumab

immunoglobulin G1-lambda1, anti-[*Homo sapiens* CD274 (programmed death ligand 1, PDL1, PD-L1, B7 homolog 1, B7H1)], *Homo sapiens* monoclonal antibody; gamma1 heavy chain (1-450) [*Homo sapiens* VH (IGHV3-23*01 (90.80%) -(IGHD)-IGHJ4*01) [8.8.13] (1-120) -IGHG1*01, Gm17,1 (CH1 (121-218), hinge (219-233), CH2 (234-343), CH3 (344-448), CHS (449-450) (121-450)], (223-215')-disulfide with lambda1 light chain (1'-216') [*Homo sapiens* V-LAMBDA (IGLV2-14*01 (99.00%) -IGLJ1*01) [9.3.10] (1'-110') -IGLC1*02 (111'-216')]; dimer (229-229'':232-232'')-bisdisulfide

avélumab

immunoglobuline G1-lambda1, anti-[*Homo sapiens* CD274 (ligand 1 de mort programmée, PDL1, PD-L1, homologue 1 de B7, B7H1)], *Homo sapiens* anticorps monoclonal; chaîne lourde gamma1 (1-450) [*Homo sapiens* VH (IGHV3-23*01 (90.80%) -(IGHD)-IGHJ4*01) [8.8.13] (1-120) -IGHG1*01, Gm17,1 (CH1 (121-218), charnière (219-233), CH2 (234-343), CH3 (344-448), CHS (449-450) (121-450)], (223-215')-disulfure avec la chaîne légère lambda1 (1'-216') [*Homo sapiens* V-LAMBDA (IGLV2-14*01 (99.00%) -IGLJ1*01) [9.3.10] (1'-110') -IGLC1*02 (111'-216')]; dimère (229-229'':232-232'')-bisdisulfure

avelumab

inmunoglobulina G1-lambda1, anti-[*Homo sapiens* CD274 (ligando 1 de muerte programada, PDL1, PD-L1, homólogo 1 de B7, B7H1)], anticuerpo monoclonal de *Homo sapiens*;
cadena pesada gamma1 (1-450) [*Homo sapiens* VH (IGHV3-23*01 (90.80%) -(IGHD)-IGHJ4*01) [8.8.13] (1-120) -IGHG1*01, Gm17,1 (CH1 (121-218), bisagra (219-233), CH2 (234-343), CH3 (344-448), CHS (449-450) (121-450)], (223-215')-disulfuro con la cadena ligera lambda1 (1'-216') [*Homo sapiens*
V-LAMBDA (IGLV2-14*01 (99.00%) -IGLJ1*01) [9.3.10] (1'-110') -IGLC1*02 (111'-216')]; dímero (229-229":232-232")-bisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYIMMWVRQA PGKGLEWVSS  50
IYPSGGITFY ADTVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARIK 100
LGTVTTVDYW GQGTLVTVSS ASTKGPSVFP LAPSSKSTSG GTAALGCLVK 150
DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT 200
YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG PSVFLFPPKP 250
KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ 350
VYTLPPSRDE LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPGK 450
```

Light chain / Chaîne légère / Cadena ligera

```
QSALTQPASV SGSPGQSITI SCTGTSSDVG GYNYVSWYQQ HPGKAPKLMI  50
YDVSNRPSGV SNRFSGSKSG NTASLTISGL QAEDEADYYC SSYTSSSTRV 100
FGTGTKVTVL GQPKANPTVT LFPPSSEELQ ANKATLVCLI SDFYPGAVTV 150
AWKADGSPVK AGVETTKPSK QSNNKYAASS YLSLTPEQWK SHRSYSCQVT 200
HEGSTVEKTV APTECS                                      216
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-96	147-203	264-324	370-428
	22"-96"	147"-203"	264"-324"	370"-428"
Intra-L (C23-C104)	22'-90'	138'-197'		
	22'"-90'"	138'"-197'"		
Inter-H-L (h 5-CL 126)	223-215'	223"-215'"		
Inter-H-H (h 11, h 14)	229-229"	232-232"		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
300, 300"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

Other post-translational modifications / Autres modifications post-traductionnelles / Otras modificaciones post-traduccionales
H CHS K2 C-terminal lysine clipping:
450, 450'

belizatinibum

belizatinib

4-fluoro-*N*-(6-{[4-(2-hydroxypropan-2-yl)piperidin-1-yl]methyl}-1-{*cis*-4-[(propan-2-yl)carbamoyl]cyclohexyl}-1*H*-benzimidazol-2-yl)benzamide

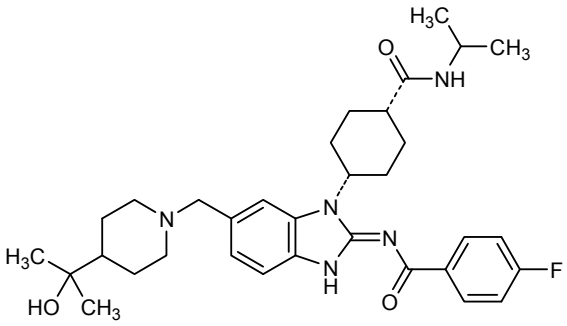
bélizatinib

4-fluoro-*N*-(6-{[4-(2-hydroxypropan-2-yl)pipéridin-1-yl]méthyl}-1-{*cis*-4-[(propan-2-yl)carbamoyl]cyclohexyl}-1*H*-benzimidazol-2-yl)benzamide

belizatinib

4-fluoro-*N*-(6-{[4-(2-hidroxipropan-2-il)piperidin-1-il]metil}-1-{*cis*-4-[(propan-2-il)carbamoil]ciclohexil}-1*H*-benzoimidazol-2-il)benzamida

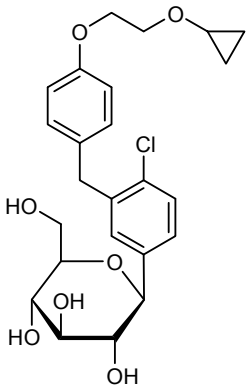
$C_{33}H_{44}FN_5O_3$



bexagliflozinum

bexagliflozin	(1*S*)-1,5-anhydro-1-*C*-[4-chloro-3-({4-[2-(cyclopropyloxy)ethoxy]phenyl}methyl)phenyl]-D-glucitol
bexagliflozine	(1*S*)-1,5-anhydro-1-*C*-[4-chloro-3-({4-[2-(cyclopropyloxy)éthoxy]phényl}méthyl)phényl]-D-glucitol
bexagliflozina	(1*S*)-1,5-anhidro-1-*C*-[3-({4-[2-(ciclopropiloxi)etoxi]fenil}metil)-4-clorofenil]-D-glucitol

$C_{24}H_{29}ClO_7$



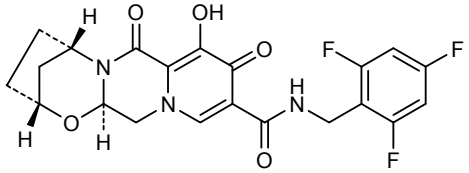
bictegravirum

bictegravir	(2*R*,5*S*,13a*R*)-8-hydroxy-7,9-dioxo-*N*-[(2,4,6-trifluorophenyl)methyl]-2,3,4,5,7,9,13,13a-octahydro-2,5-methanopyrido[1',2':4,5]pyrazino[2,1-*b*][1,3]oxazepine-10-carboxamide
bictégravir	(2*R*,5*S*,13a*R*)-8-hydroxy-7,9-dioxo-*N*-[(2,4,6-trifluorophényl)méthyl]-2,3,4,5,7,9,13,13a-octahydro-2,5-méthanopyrido[1',2':4,5]pyrazino[2,1-*b*][1,3]oxazépine-10-carboxamide

bictegravir

(2*R*,5*S*,13a*R*)-8-hidroxi-7,9-dioxo-*N*-[(2,4,6-trifluorofenil)metil]-2,3,4,5,7,9,13,13a-octahidro-2,5-metanopirido[1',2':4,5]pirazino[2,1-*b*][1,3]oxazepina-10-carboxamida

$C_{21}H_{18}F_3N_3O_5$



bleselumabum #

bleselumab

immunoglobulin G4-kappa, anti-[*Homo sapiens* CD40 (tumor necrosis factor receptor superfamily member 5, TNFRSF5)], human monoclonal antibody;
gamma4 heavy chain (1-448) [*Homo sapiens* VH (IGHV4-39*01 (92.90%) -(IGHD)-IGHJ5*01) [10.7.13] (1-121) -IGHG4*01 (CH1 (122-219), hinge S10>P (229) (220-231), CH2 (232-341), CH3 (342-446), CHS (447-448)) (122-448)], (135-213')-disulfide with kappa light chain (1'-213') [*Homo sapiens* (V-KAPPA (IGKV1-13*02 (98.90%) -IGKJ1*01) [6.3.8] (1'-106') -IGKC*01, Km3 (107'-213')]; dimer (227-227":230-230")-bisdisulfide

blésélumab

immunoglobuline G4-kappa, anti-[*Homo sapiens* CD40 (membre 5 de la superfamille des récepteurs du TNF, TNFRSF5)], anticorps monoclonal humain;
chaîne lourde gamma4 (1-448) [*Homo sapiens* VH (IGHV4-39*01 (92.90%) -(IGHD)-IGHJ5*01) [10.7.13] (1-121) -IGHG4*01 (CH1 (122-219), charnière S10>P (229) (220-231), CH2 (232-341), CH3 (342-446), CHS (447-448)) (122-448)], (135-213')-disulfure avec la chaîne légère kappa (1'-213') [*Homo sapiens* (V-KAPPA (IGKV1-13*02 (98.90%) -IGKJ1*01) [6.3.8] (1'-106') -IGKC*01, Km3 (107'-213')]; dimère (227-227":230-230")-bisdisulfure

bleselumab

inmunoglobulina G4-kappa, anti-[*Homo sapiens* CD40 (miembro 5 de la superfamilia de receptores del TNF, TNFRSF5)], anticuerpo monoclonal humano;
cadena pesada gamma4 (1-448) [*Homo sapiens* VH (IGHV4-39*01 (92.90%) -(IGHD)-IGHJ5*01) [10.7.13] (1-121) -IGHG4*01 (CH1 (122-219), bisagra S10>P (229) (220-231), CH2 (232-341), CH3 (342-446), CHS (447-448)) (122-448)], (135-213')-disulfuro con la cadena ligera kappa (1'-213') [*Homo sapiens* (V-KAPPA (IGKV1-13*02 (98.90%) -IGKJ1*01) [6.3.8] (1'-106') -IGKC*01, Km3 (107'-213')]; dímero (227-227":230-230")-bisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
QLQLQESGPG LLKPSETLSL TCTVSGGSIS SPGYYGGWIR QPPGKGLEWI  50
GSIYKSGSTY HNPSLKSRVT ISVDTSKNQF SLKLSSVTAA DTAVYYCTRP 100
VVRYFGWFDP WGQGTLVTVS SASTKGPSVF PLAPCSRSTS ESTAALGCLV 150
KDYFPEPVTV SWNSGALTSG VHTFPAVLQS SGLYSLSSVV TVPSSSLGTK 200
TYTCNVDHKP SNTKVDKRVE SKYGPPCPPC PAPEFEGGPS VFLFPPKPKD 250
TLMISRTPEV TCVVVDVSQE DPEVQFNWYV DGVEVHNAKT KPREEQFNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKGLP SSIEKTISKA KGQPREPQVY 350
TLPPSQEEMT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD 400
SDGSFFLYSR LTVDKSRWQE GNVFSCSVMH EALHNHYTQK SLSLSLGK   448
```

Light chain / Chaîne légère / Cadena ligera

```
AIQLTQSPSS LSASVGDRVT ITCRASQGIS SALAWYQQKP GKAPKLLIYD  50
ASNLESGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ FNSYPTFGQG 100
TKVEIKRTVA APSVFIFPPS DEQLKSGTAS VVCLLNNFYP REAKVQWKVD 150
NALQSGNSQE SVTEQDSKDS TYSLSSTLTL SKADYEKHKV YACEVTHQGL 200
SSPVTKSFNR GEC                                         213
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-97	148-204	262-322	368-426
	22''-97''	148''-204''	262''-322''	368''-426''
Intra-L (C23-C104)	23'-88'	133'-193'		
	23'''-88'''	133'''-193'''		
Inter-H-L (CH1 10-CL 126)	135-213'	135''-213'''		
Inter-H-H (h 8, h 11)	227-227''	230-230''		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación

H CH2 N84.4:
298, 298''

Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

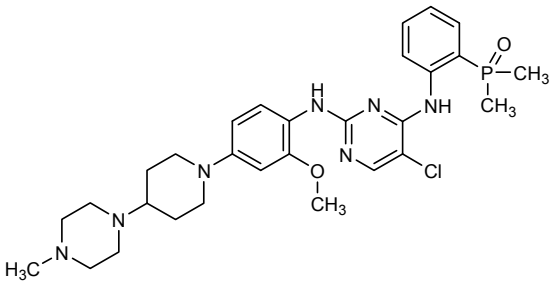
brigatinibum

brigatinib — 2-[(5-chloro-2-{2-methoxy-4-[4-(4-methylpiperazin-1-yl)piperidin-1-yl]anilino}pyrimidin-4-yl)amino]phenyl}dimethyl-λ^5-phosphanone

brigatinib — 2-[(5-chloro-2-{2-méthoxy-4-[4-(4-méthylpipérazin-1-yl)pipéridin-1-yl]anilino}pyrimidin-4-yl)amino]phényl}diméthyl-λ^5-phosphanone

brigatinib — 2-[(5-cloro-2-{2-metoxi-4-[4-(4-metilpiperazin-1-il)piperidin-1-il]anilino}pirimidin-4-il)amino]fenil}dimetil-λ^5-fosfanona

$C_{29}H_{39}ClN_7O_2P$



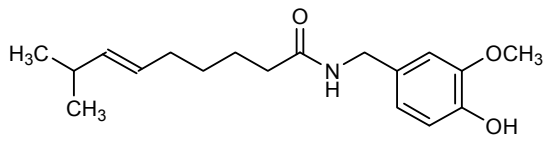
capsaicinum

capsaicin — (6*E*)-*N*-[(4-hydroxy-3-methoxyphenyl)methyl]-8-methylnon-6-enamide

capsaïcine — (6*E*)-*N*-[(4-hydroxy-3-méthoxyphényl)méthyl]-8-méthylnon-6-énamide

capsaicina — (6*E*)-*N*-[(4-hidroxi-3-metoxifenil)metil]-8-metilnon-6-enamida

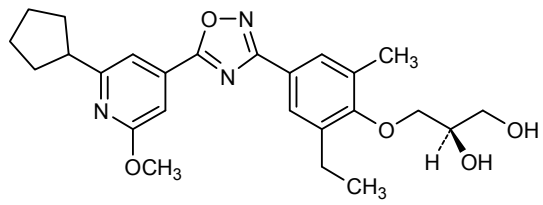
$C_{18}H_{27}NO_3$



cenerimodum

cenerimod	(2*S*)-3-{4-[5-(2-cyclopentyl-6-methoxypyridin-4-yl)-1,2,4-oxadiazol-3-yl]-2-ethyl-6-methylphenoxy}propane-1,2-diol
cénérimod	(2*S*)-3-{4-[5-(2-cyclopentyl-6-méthoxypyridin-4-yl)-1,2,4-oxadiazol-3-yl]-2-éthyl-6-méthylphénoxy}propane-1,2-diol
cenerimod	(2*S*)-3-{4-[5-(2-ciclopentil-6-metoxipiridin-4-il)-1,2,4-oxadiazol-3-il]-2-etil-6-metilfenoxi}propano-1,2-diol

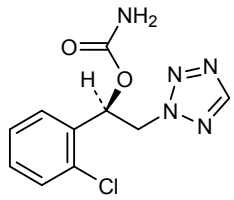
$C_{25}H_{31}N_3O_5$



cenobamatum

cenobamate	(1*R*)-1-(2-chlorophenyl)-2-(2*H*-tetrazol-2-yl)ethyl carbamate
cénobamate	carbamate de (1*R*)-1-(2-chlorophényl)-2-(2*H*-tétrazol-2-yl)éthyle
cenobamato	carbamato de (1*R*)-1-(2-clorofenil)-2-(2*H*-tetrazol-2-il)etilo

$C_{10}H_{10}ClN_5O_2$



cergutuzumabum amunaleukinum #

cergutuzumab amunaleukin	immunoglobulin G1-kappa fused to IL2 (interleukin 2), anti-[*Homo sapiens* CEACAM5 (carcinoembryonic antigen-related cell adhesion molecule 5, CEA, CD66e)], humanized monoclonal antibody fused to IL2; gamma1 heavy chain (1-451) [humanized VH (*Homo sapiens* IGHV1-18*01 (82.70%) -(IGHD)-IGHJ6*01) [8.8.14] (1-121) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (122-219), hinge (220-234), CH2 L1.3>A (238), L1.2>A (239), P114>G (333) (235-344), CH3 Y5>C (353), T22>S (370), L24>A (372), Y86>V (411) (345-449), CHS (450-451)) (122-451)], (224-215')-disulfide with kappa light chain (1'-215') [humanized V-KAPPA (*Homo sapiens* IGKV1-16*01 (82.10%) -IGKJ2*01) [6.3.10] (1'-108') -*Homo sapiens* IGKC*01, Km3 (109'-215')]; gamma1 heavy chain fused to IL2 (1''-598'') [humanized VH (*Homo sapiens* IGHV1-18*01 (82.70%) -(IGHD)-IGHJ6*01) [8.8.14] (1''-121'') -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (122''-219''), hinge (220''-234''), CH2 L1.3>A (238''), L1.2>A (239''), P114>G (333'') (235''-344''), CH3 S10>C (358''), T22>W (370''), (345''-449''), CHS K2>del (450'')) (122''-450'') -15-mer (tris(tetraglycyl-seryl)) linker (451''-465'') -*Homo sapiens* IL2 (Pr21-153) T23>A (468''), F62>A (507''), Y65>A (510''), L92>G (547''), C145>A (590'') (466''-598'')], (224''-215''')-disulfide with kappa light chain (1'''-215''') [humanized V-KAPPA (*Homo sapiens* IGKV1-16*01 (82.10%) -IGKJ2*01) [6.3.10] (1'''-108''') -*Homo sapiens* IGKC*01, Km3 (109'''-215''')]; dimer (230-230'':233-233'')-bisdisulfide
cergutuzumab amunaleukine	immunoglobuline G1-kappa fusionnée à l'IL2 (interleukine 2), anti-[*Homo sapiens* CEACAM5 (molécule d'adhésion cellulaire 5 apparentée à l'antigène carcinoembryonaire, CEA, CD66e)], anticorps monoclonal humanisé fusionné à l'IL2; chaîne lourde gamma1 (1-451) [VH humanisé (*Homo sapiens* IGHV1-18*01 (82.70%) -(IGHD)-IGHJ6*01) [8.8.14] (1-121) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (122-219), charnière (220-234), CH2 L1.3>A (238), L1.2>A (239), P114>G (333) (235-344), CH3 Y5>C (353), T22>S (370), L24>A (372), Y86>V (411) (345-449), CHS (450-451)) (122-451)], (224-215')-disulfure avec la chaîne légère kappa (1'-215') [V-KAPPA humanisé (*Homo sapiens* IGKV1-16*01 (82.10%) -IGKJ2*01) [6.3.10] (1'-108') -*Homo sapiens* IGKC*01, Km3 (109'-215')]; chaîne lourde gamma1 fusionnée à l'IL2 (1''-598'') [VH humanisé (*Homo sapiens* IGHV1-18*01 (82.70%) -(IGHD)-IGHJ6*01) [8.8.14] (1''-121'') -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (122''-219''), charnière (220''-234''), CH2 L1.3>A (238''), L1.2>A (239''), P114>G (333'') (235''-344''), CH3 S10>C (358''), T22>W (370''), (345''-449''), CHS K2>del (450'')) (122''-450'') -15-mer (tris(tétraglycyl-séryl)) linker (451''-465'') -*Homo sapiens* IL2 (Pr21-153) T23>A (468''), F62>A (507''), Y65>A (510''), L92>G (547''), C145>A (590'') (466''-598'')], (224''-215''')- disulfure avec la chaîne légère kappa (1'''-215''') [V-KAPPA humanisé (*Homo sapiens* IGKV1-16*01 (82.10%) -IGKJ2*01) [6.3.10] (1'''-108''') -*Homo sapiens* IGKC*01, Km3 (109'''-215''')]; dimère (230-230'':233-233'')-bisdisulfure

cergutuzumab amunaleukina

inmunoglobulina G1-kappa fusionada con IL2 (interleukina 2), anti-[*Homo sapiens* CEACAM5 (molécula de adhesión celular 5 relacionada con el antígeno carcinoembrionario, CEA, CD66e)], anticuerpo monoclonal humanizado fusionado IL2;
cadena pesada gamma1 (1-451) [VH humanizado (*Homo sapiens* IGHV1-18*01 (82.70%) -(IGHD)-IGHJ6*01) [8.8.14] (1-121) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (122-219), bisagra (220-234), CH2 L1.3>A (238), L1.2>A (239), P114>G (333) (235-344), CH3 Y5>C (353), T22>S (370), L24>A (372), Y86>V (411) (345-449), CHS (450-451)) (122-451)], (224-215')-disulfuro con la cadena ligera kappa (1'-215') [V-KAPPA humanizado (*Homo sapiens* IGKV1-16*01 (82.10%) -IGKJ2*01) [6.3.10] (1'-108') -*Homo sapiens* IGKC*01, Km3 (109'-215')]; cadena pesada fusionada con 'IL2 (1"-598") [VH humanizado (*Homo sapiens* IGHV1-18*01 (82.70%) -(IGHD)-IGHJ6*01) [8.8.14] (1"-121") -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (122"-219"), bisagra (220"-234"), CH2 L1.3>A (238"), L1.2>A (239"), P114>G (333") (235"-344"), CH3 S10>C (358"), T22>W (370"), (345"-449"), CHS K2>del (450")) (122"-450") -15-mer (tris(tetraglicil-seril)) espaciador (451"-465") -*Homo sapiens* IL2 (Pr21-153) T23>A (468"), F62>A (507"), Y65>A (510"), L92>G (547"), C145>A (590") (466"-598")], (224"-215'")- disulfuro con la cadena ligera kappa (1'"-215'") [V-KAPPA humanizado (*Homo sapiens* IGKV1-16*01 (82.10%) -IGKJ2*01) [6.3.10] (1'"-108'") -*Homo sapiens* IGKC*01, Km3 (109'"-215'")]; dímero (230-230":233-233")-bisdisulfuro

Heavy chain H/ Chaîne lourde H/ Cadena pesada H

```
QVQLVQSGAE VKKPGASVKV SCKASGYTFT EFGMNWVRQA PGQGLEWMGW  50
INTKTGEATY VEEFKGRVTF TTDTSTSTAY MELRSLRSDD TAVYYCARWD 100
FAYYVEAMDY WGQGTTVTVS SASTKGPSVF PLAPSSKSTS GGTAALGCLV 150
KDYFPEPVTV SWNSGALTSG VHTFPAVLQS SGLYSLSSVV TVPSSSLGTQ 200
TYICNVNHKP SNTKVDKKVE PKSCDKTHTC PPCPAPEAAG GPSVFLFPPK 250
PKDTLMISRT PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY 300
NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK ALGAPIEKTI SKAKGQPREP 350
QVCTLPPSRD ELTKNQVSLS CAVKGFYPSD IAVEWESNGQ PENNYKTTPP 400
VLDSDGSFFL VSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG 450
K                                                       451
```

Heavy chain H" (fused to IL2) / Chaîne lourde H" (fusionnée to IL2) / Cadena pesada H" (fusionada con IL2)

```
QVQLVQSGAE VKKPGASVKV SCKASGYTFT EFGMNWVRQA PGQGLEWMGW  50
INTKTGEATY VEEFKGRVTF TTDTSTSTAY MELRSLRSDD TAVYYCARWD 100
FAYYVEAMDY WGQGTTVTVS SASTKGPSVF PLAPSSKSTS GGTAALGCLV 150
KDYFPEPVTV SWNSGALTSG VHTFPAVLQS SGLYSLSSVV TVPSSSLGTQ 200
TYICNVNHKP SNTKVDKKVE PKSCDKTHTC PPCPAPEAAG GPSVFLFPPK 250
PKDTLMISRT PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY 300
NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK ALGAPIEKTI SKAKGQPREP 350
QVYTLPPCRD ELTKNQVSLW CLVKGFYPSD IAVEWESNGQ PENNYKTTPP 400
VLDSDGSFFL YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG 450
GGGGSGGGGS GGGGSAPASS STKKTQLQLE HLLLDLQMIL NGINNYKNPK 500
LTRMLTAKFA MPKKATELKH LQCLEEELKP LEEVLNGAQS KNFHLRPRDL 550
ISNINVIVLE LKGSETTFMC EYADETATIV EFLNRWITFA QSIISTLT   598
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS LSASVGDRVT ITCKASAAVG TYVAWYQQKP GKAPKLLIYS  50
ASYRKRGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCHQ YYTYPLFTFG 100
QGTKLEIKRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK 150
VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ 200
GLSSPVTKSF NRGEC                                       215
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104) 22-96 148-204 265-325 371-429
Intra-H (C23-C104) 22"-96" 148"-204" 265"-325" 371"-429"
-IL2 (Pr C78-C125) 523"-570"
Intra-L (C23-C104) 23'-88' 135'-195'
23'"-88'" 135'"-195'"
Inter-H-L (h 5-CL 126) 224-215' 224"-215'"
Inter-H-H (h 11, h 14) 230-230" 233-233"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación

H CH2 N84.4:
301, 301"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

Other post-translational modifications / Autres modifications post-traductionnelles / Otras modificaciones post-traduccionales

H CHS K2 C-terminal lysine clipping:
451

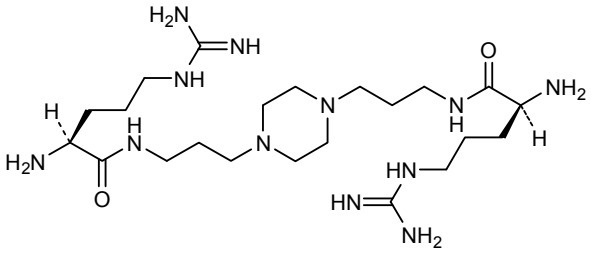
ciraparantagum

ciraparantag — $N^1,N^{1'}$-[piperazine-1,4-diylbis(propane-1,3-diyl)]bis-L-argininamide

ciraparantag — $N^1,N^{1'}$-[pipérazine-1,4-diylbis(propane-1,3-diyl)]bis-L-argininamide

ciraparantag — $N^1,N^{1'}$-[piperazina-1,4-diilbis(propano-1,3-diil)]bis-L-argininamida

$C_{22}H_{48}N_{12}O_2$



cobitolimodum

cobitolimod — *all-P-ambo*-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-deoxy-*P*-thioadenylyl-(3'→5')-2'-deoxyadenylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-2'-deoxyadenylyl-(3'→5')-2'-deoxyguanylyl-(3'→5')-thymidylyl-(3'→5')-thymidylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-2'-deoxyguanylyl-(3'→5')-thymidylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-2'-deoxyadenylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-deoxycytidine

cobitolimod — *tout-P-ambo*-2'-déoxy-*P*-thioguanylyl-(3'→5')-2'-déoxy-*P*-thioguanylyl-(3'→5')-2'-déoxy-*P*-thioadénylyl-(3'→5')-2'-déoxyadénylyl-(3'→5')-2'-déoxycytidylyl-(3'→5')-2'-déoxyadénylyl-(3'→5')-2'-déoxyguanylyl-(3'→5')-thymidylyl-(3'→5')-thymidylyl-(3'→5')-2'-déoxycytidylyl-(3'→5')-2'-déoxyguanylyl-(3'→5')-thymidylyl-(3'→5')-2'-déoxycytidylyl-(3'→5')-2'-déoxycytidylyl-(3'→5')-2'-déoxyadénylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-déoxy-*P*-thioguanylyl-(3'→5')-2'-déoxy-*P*-thioguanylyl-(3'→5')-2'-déoxycytidine

cobitolimod — *todo-P-ambo*-2'-desoxi-*P*-tioguanilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-2'-desoxi-*P*-tioadenilil-(3'→5')-2'-desoxiadenilil-(3'→5')-2'-desoxicitidilil-(3'→5')-2'-desoxiadenilil-(3'→5')-2'-desoxiguanilil-(3'→5')-timidilil-(3'→5')-timidilil-(3'→5')-2'-desoxicitidilil-(3'→5')-2'-desoxiguanilil-(3'→5')-timidilil-(3'→5')-2'-desoxicitidilil-(3'→5')-2'-desoxicitidilil-(3'→5')-2'-desoxiadenilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-2'-desoxicitidina

$C_{185}H_{233}N_{73}O_{106}P_{18}S_6$

(3'-5')-d-(G-G-A-A-C-A-G-T-T-C-G-T-C-C-A-T-G-G-C)

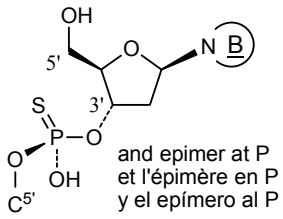
Modified residues / Nucléotides modifiés / Nucleótidos modificados

B = A , G , T

(*P-RS*)-2'-deoxy-*P*-thionucleyl

(*P-RS*)-2'-désoxy-*P*-thionucléyle

(*P-RS*)-2'-deoxi-*P*-thionucleil



and epimer at P
et l'épimère en P
y el epímero al P

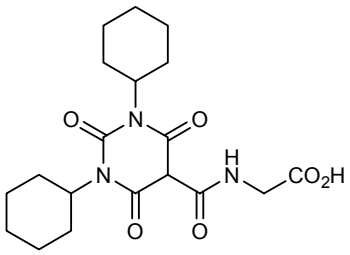
daprodustatum

daprodustat — *N*-[(1,3-dicyclohexylhexahydro-2,4,6-trioxopyrimidin-5-yl)carbonyl]glycine

daprodustat — *N*-[(1,3-dicyclohexylhexahydro-2,4,6-trioxopyrimidin-5-yl)carbonyl]glycine

daprodustat — *N*-[(1,3-diciclohexilhexahidro-2,4,6-trioxopirimidin-5-il)carbonil]glicina

$C_{19}H_{27}N_3O_6$



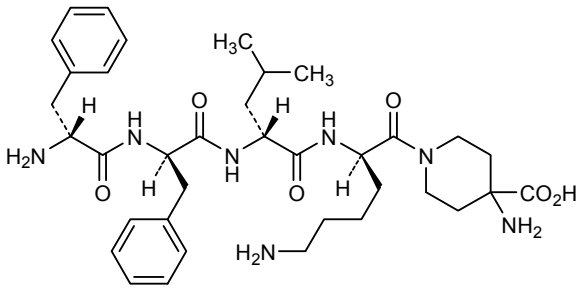
difelikefalinum

difelikefalin — 4-amino-1-(D-phenylalanyl-D-phenylalanyl-D-leucyl-D-lysyl)piperidine-4-carboxylic acid

difélikéfaline — acide 4-amino-1-(D-phénylalanyl-D-phénylalanyl-D-leucyl-D-lysyl)pipéridine-4-carboxylique

difelicefalina — ácido 4-amino-1-(D-fenilalanil-D-fenilalanil-D-leucil-D-lisil)piperidina-4-carboxílico

$C_{36}H_{53}N_7O_6$



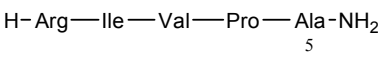
dusquetidum

dusquetide — L-arginyl-L-isoleucyl-L-valyl-L-prolyl-L-alaninamide

dusquétide — L-arginyl-L-isoleucyl-L-valyl-L-prolyl-L-alaninamide

dusquetida — L-arginil-L-isoleucil-L-valil-L-prolil-L-alaninamida

$C_{25}H_{47}N_9O_5$



efpegsomatropinum #

efpegsomatropin — recombinant human growth hormone (somatropin) and human immunoglobulin G4 Fc fragment dimer, produced in *Escherichia coli* (nonglycosylated), linked together with polyethylene glycol derivative linker: $N^{\alpha.1}$,$N^{1.9'}$-[ω-(oxypropane-1,3-diyl)-α-(propane-1,3-diyl)poly(oxyethylene)] human growth hormone, human immunoglobulin G4 Fc fragment (IGHG4*01 H-CH2-CH3)-(9'-229')-peptide dimer (11'-11'')-disulfide

efpègsomatropine — hormone de croissance humaine (somatropine) et dimère du fragment Fc de l'IgG4 humain, recombinants produits par *Escherichia coli* (non glycosylés), liés par un pont dérivé du polyéthylèneglycol : $N^{\alpha.1}$,$N^{1.9'}$- [ω-(oxypropane-1,3-diyl)-α-(propane-1,3-diyl)poly(oxyéthylène)] hormone de croissance humaine, (11'-11'')-disulfure du dimère du fragment Fc de l'immunoglobuline G4 humaine (IGHG4*01 H-CH2-CH3)-(9'-229')-peptide

efpegsomatropina — hormona humana de crecimiento (somatropina) y dímero del fragmento Fc de la IgG4 humana, recombinantes, producidos por *Escherichia coli* (no glicosilados), unidos por un puente derivado del polietilenglicol : $N^{\alpha.1}$,$N^{1.9'}$- [ω-(oxipropano-1,3-diil)-α-(propano-1,3-diil)poli(oxietileno)] hormona humana de crecimiento, (11'-11'')-disulfuro del dímero del fragmento Fc de la inmunoglobulina G4 humana (IGHG4*01 H-CH2-CH3)-(9'-229')-péptido

Growth Hormone / Hormone de croissance humaine / Hormona humana de crecimiento

```
FPTIPLSRLF DNAMLRAHRL HQLAFDTYQE FEEAYIPKEQ KYSFLQNPQT 50
SLCFSESIPT PSNREETQQK SNLELLRISL LLIQSWLEPV QFLRSVFANS 100
LVYGASDSNV YDLLKDLEEG IQTLMGRLED GSPRTGQIFK QTYSKFDTNS 150
HNDDALLKNY GLLYCFRKDM DKVETFLRIV QCRSVEGSCG F         191
```

hIGHG4 Fc monomer / Monomère du Fc de hIGHG4 / Monómero de Fc de hIGHG4

```
        PS CPAPEFLGGP SVFLFPPKPK DTLMISRTPE VTCVVVDVSQ 50'
EDPEVQFNWY VDGVEVHNAK TKPREEQFNS TYRVVSVLTV LHQDWLNGKE 100'
YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM TKNQVSLTCL 150'
VKGFYPSDIA VEWESNGQPE NNYKTTPPVL DSDGSFFLYS RLTVDKSRWQ 200'
EGNVFSCSVM HEALHNHYTQ KSLSLSLGK                       229'
```

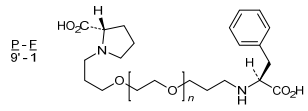
hIGHG4 Fc monomer / Monomère du Fc de hIGHG4 / Monómero de Fc de hIGHG4

```
        PS CPAPEFLGGP SVFLFPPKPK DTLMISRTPE VTCVVVDVSQ 50''
EDPEVQFNWY VDGVEVHNAK TKPREEQFNS TYRVVSVLTV LHQDWLNGKE 100''
YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM TKNQVSLTCL 150''
VKGFYPSDIA VEWESNGQPE NNYKTTPPVL DSDGSFFLYS RLTVDKSRWQ 200''
EGNVFSCSVM HEALHNHYTQ KSLSLSLGK                       229''
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

11'-11'' 43'-103' 43''-103'' 53-165 149'-207' 149''-207'' 182-189

Modified residues / Résidus modifiés / Restos modificados

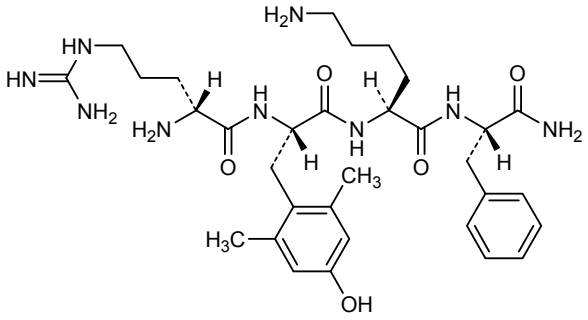


elamipretidum
elamipretide — D-arginyl-2,6-dimethyl-L-tyrosyl-L-lysyl-L-phenylalaninamide

élamiprétide — D-arginyl-2,6-diméthyl-L-tyrosyl-L-lysyl-L-phénylalaninamide

elamipretida — D-arginil-2,6-dimetil-L-tirosil-L-lisil-L-fenilalaninamida

$C_{32}H_{49}N_9O_5$



emicizumabum #
emicizumab — immunoglobulin G4-kappa, bispecific, anti-[*Homo sapiens* F9a (activated coagulation factor F9, activated coagulation factor IX) and anti-[*Homo sapiens* F10 (coagulation factor 10, coagulation factor X)], humanized monoclonal antibody;
gamma4 heavy chain (1-448) [humanized VH (*Homo sapiens* IGHV3-23*04 (87.80%) -(IGHD)-IGHJ4*01 (1-123)), IGHG4*01 (CH1 K100>Q (202) (124-221), hinge S10>P (231) (222-233), CH2 F84.3>Y (299) (234-343), CH3 E12>K (359), R88>K (412), H115>R (438), L125>P (448) (344-448), CHS>del) (124-448)], (137-214')-disulfide with kappa light chain (1'-214') [humanized V-KAPPA (*Homo sapiens* IGKV1-39*01 (80.00%) -IGKJ4*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')];
gamma4 heavy chain (1-444) [VH (*Homo sapiens* IGHV1-2*02 (75.50%) -(IGHD)-IGHJ6*03 Q120>E (111"), T123>L (114") (1"-119")), IGHG4*01 (CH1 A100>Q (198") (120"-217"), hinge S10>P (227") (218"-229"), CH2 F84.3>Y (295"), (230"-339"), CH3 R88>K (408), K119>E (438), L125>P (444) (340"-444"), CHS>del) (120"-444")], (133"-214"')-disulfide with kappa light chain (1"'-214"') [humanized V-KAPPA (*Homo sapiens* IGKV1-39*01 (80.00%) -IGKJ4*01) [6.3.9] (1"'-107"') -*Homo sapiens* IGKC*01, Km3 (108"'-214"')]; dimer (229-225":232-228")-bisdisulfide

émicizumab	immunoglobuline G4-kappa, bispécifique, anti-[*Homo sapiens* F9a (facteur de coagulation F9 activé, facteur de coagulation IX activé) et anti-[*Homo sapiens* F10 (facteur de coagulation 10, facteur de coagulation X)], anticorps monoclonal humanisé; chaîne lourde gamma4 (1-448) [VH humanisé (*Homo sapiens* IGHV3-23*04 (87.80%) -(IGHD)-IGHJ4*01 (1-123)), IGHG4*01 (CH1 K100>Q (202) (124-221), S10>P (231) (222-233), CH2 F84.3>Y (299) (234-343), CH3 E12>K (359), R88>K (412), H115>R (438), L125>P (448) (344-448), CHS>del) (124-448)], (137-214')-disulfure avec la chaîne légère kappa (1'-214') [V-KAPPA humanisé (*Homo sapiens* IGKV1-39*01 (80.00%) -IGKJ4*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; chaîne lourde gamma4 (1-444) [VH humanisé (*Homo sapiens* IGHV1-2*02 (75.50%) -(IGHD)-IGHJ6*03 Q120>E (111"), T123>L (114") (1"-119")), IGHG4*01 (CH1 A100>Q (198") (120"-217"), charnière S10>P (227") (218"-229"), CH2 F84.3>Y (295"), (230"-339"), CH3 R88>K (408), K119>E (438), L125>P (444) (340"-444"), CHS>del) (120"-444")], (133"-214"')-disulfure avec la chaîne légère kappa (1"'-214"') [V-KAPPA humanisé (*Homo sapiens* IGKV1-39*01 (80.00%) -IGKJ4*01) [6.3.9] (1"'-107"') -*Homo sapiens* IGKC*01, Km3 (108"'-214"')]; dimère (229-225":232-228")-bisdisulfure
emicizumab	inmunoglobulina G4-kappa, biespecífica, anti-[*Homo sapiens* F9a (factor de coagulación F9 activado, factor de coagulación IX activado) y anti-[*Homo sapiens* F10 (factor de coagulación 10, factor de coagulación X)], anticuerpo monoclonal humanizado; cadena pesada gamma4 (1-448) [VH humanizado (*Homo sapiens* IGHV3-23*04 (87.80%) -(IGHD)-IGHJ4*01 (1-123)), IGHG4*01 (CH1 K100>Q (202) (124-221), S10>P (231) (222-233), CH2 F84.3>Y (299) (234-343), CH3 E12>K (359), R88>K (412), H115>R (438), L125>P (448) (344-448), CHS>del) (124-448)], (137-214')-disulfuro con la cadena ligera kappa (1'-214') [V-KAPPA humanizado (*Homo sapiens* IGKV1-39*01 (80.00%) -IGKJ4*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; cadena pesada gamma4 (1-444) [VH humanizado (*Homo sapiens* IGHV1-2*02 (75.50%) -(IGHD)-IGHJ6*03 Q120>E (111"), T123>L (114") (1"-119")), IGHG4*01 (CH1 A100>Q (198") (120"-217"),bisagra S10>P (227") (218"-229"), CH2 F84.3>Y (295"), (230"-339"), CH3 R88>K (408), K119>E (438), L125>P (444) (340"-444"), CHS>del) (120"-444")], (133"-214"')-disulfuro con la cadena ligera kappa (1"'-214"') [V-KAPPA humanizado (*Homo sapiens* IGKV1-39*01 (80.00%) -IGKJ4*01) [6.3.9] (1"'-107"') -*Homo sapiens* IGKC*01, Km3 (108"'-214"')]; dímero (229-225":232-228")-bisdisulfuro

Heavy chain anti-F9a/ Chaîne lourde anti-F9a/ Cadena pesada anti-F9a

```
QVQLVESGGG LVQPGGSLRL SCAASGFTFS YYDIQWVRQA PGKGLEWVSS  50
ISPSGQSTYY RREVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARRT 100
GREYGGGWYF DYWGQGTLVT VSSASTKGPS VFPLAPCSRS TSESTAALGC 150
LVKDYFPEPV TVSWNSGALT SGVHTFPAVL QSSGLYSLSS VVTVPSSSLG 200
TQTYTCNVDH KPSNTKVDKR VESKYGPPCP PCPAPEFLGG PSVFLFPPKP 250
KDTLMISRTP EVTCVVVDVS QEDPEVQFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKG LPSSIEKTIS KAKGQPREPQ 350
VYTLPPSQKE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFFLY SKLTVDKSRW QEGNVFSCSV MHEALHNRYT QKSLSLSP   448
```

Heavy chain anti-F10/ Chaîne lourde anti-F10/ Cadena pesada anti-F10

```
QVQLVQSGSE LKKPGASVKV SCKASGYTFT DNNMDWVRQA PGQGLEWMGD  50
INTRSGGSIY NEEFQDRVIM TVDKSTDTAY MELSSLRSED TATYHCARRK 100
SYGYYLDEWG EGTLVTVSSA STKGPSVFPL APCSRSTSES TAALGCLVKD 150
YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY 200
TCNVDHKPSN TKVDKRVESK YGPPCPPCPA PEFLGGPSVF LFPPKPKDTL 250
MISRTPEVTC VVVDVSQEDP EVQFNWYVDG VEVHNAKTKP REEQYNSTYR 300
VVSVLTVLHQ DWLNGKEYKC KVSNKGLPSS IEKTISKAKG QPREPQVYTL 350
PPSQEEMTKN QVSLTCLVKG FYPSDIAVEW ESNGQPENNY KTTPPVLDSD 400
GSFFLYSKLT VDKSRWQEGN VFSCSVMHEA LHNHYTQESL SLSP       444
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS LSASVGDRVT ITCKASRNIE RQLAWYQQKP GQAPELLIYQ  50
ASRKESGVPD RFSGSRYGTD FTLTISSLQP EDIATYYCQQ YSDPPLTFGG 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-96	150-206	264-324	370-428
	22"-96"	146"-202"	260"-320"	366"-424"
Intra-L (C23-C104)	23'-88'	134'-194'		
	23'"-88'"	134'"-194'"		
Inter-H-L (CH1 10-CL 126)	137-214'	133"-214'"		
Inter-H-H (h 8, h 11)	229-225"	232-228"		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
300, 296"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenario complejos fucosilados

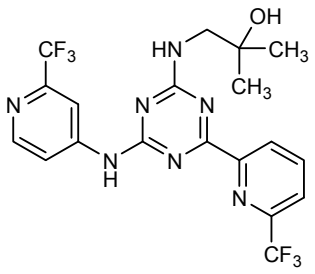
enasidenibum

enasidenib — 2-methyl-1-[(4-[6-(trifluoromethyl)pyridin-2-yl]-6-{[2-(trifluoromethyl)pyridin-4-yl]amino}-1,3,5-triazin-2-yl)amino]propan-2-ol

énasidénib — 2-méthyl-1-[(4-[6-(trifluorométhyl)pyridin-2-yl]-6-{[2-(trifluorométhyl)pyridin-4-yl]amino}-1,3,5-triazin-2-yl)amino]propan-2-ol

enasidenib — 2-metil-1-[(4-[6-(trifluorometil)piridin-2-il]-6-{[2-(trifluorometil)piridin-4-il]amino}-1,3,5-triazin-2-il)amino]propan-2-ol

$C_{19}H_{17}F_6N_7O$



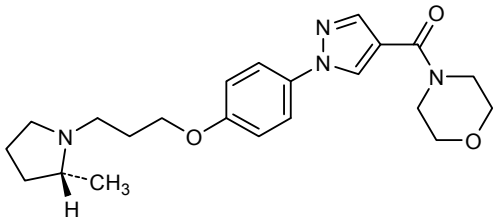
enerisantum

enerisant — [1-(4-{3-[(2*R*)-2-methylpyrrolidin-1-yl]propoxy}phenyl)-1*H*-pyrazol-4-yl](morpholin-4-yl)methanone

énérisant [1-(4-{3-[(2*R*)-2-méthylpyrrolidin-1-yl]propoxy}phényl)-1*H*-pyrazol-4-yl](morpholin-4-yl)méthanone

enerisant 1-(4-{3-[(2*R*)-2-metilpirrolidin-1-il]propoxi}fenil)-1*H*-pirazol-4-il](morfolin-4-il)metanona

$C_{22}H_{30}N_4O_3$



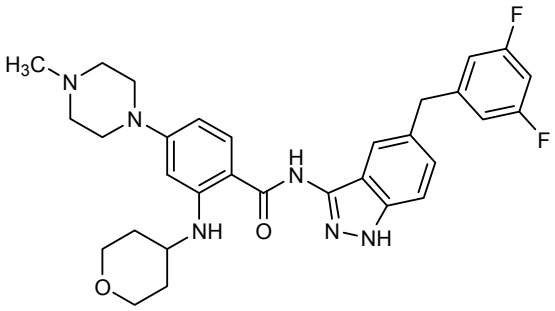
entrectinibum

entrectinib *N*-{5-[(3,5-difluorophenyl)methyl]-1*H*-indazol-3-yl}-4-(4-methylpiperazin-1-yl)-2-[(oxan-4-yl)amino]benzamide

entrectinib *N*-{5-[(3,5-difluorophényl)méthyl]-1*H*-indazol-3-yl}-4-(4-méthylpipérazin-1-yl)-2-[(oxan-4-yl)amino]benzamide

entrectinib *N*-{5-[(3,5-difluorofenil)metil]-1*H*-indazol-3-il}-4-(4-metilpiperazin-1-il)-2-[(oxan-4-il)amino]benzamida

$C_{31}H_{34}F_2N_6O_2$ 1108743-60-7



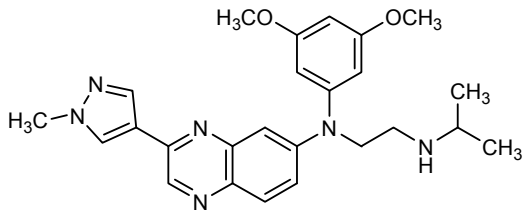
erdafitinibum

erdafitinib N^1-(3,5-dimethoxyphenyl)-N^1-[3-(1-methyl-1*H*-pyrazol-4-yl)quinoxalin-6-yl]-N^2-(propan-2-yl)ethane-1,2-diamine

erdafitinib N^1-(3,5-diméthoxyphényl)-N^1-[3-(1-méthyl-1*H*-pyrazol-4-yl)quinoxalin-6-yl]-N^2-(propan-2-yl)éthane-1,2-diamine

erdafitinib N^1-(3,5-dimetoxifenil)-N^1-[3-(1-metil-1*H*-pirazol-4-il)quinoxalin-6-il]-N^2-(propan-2-il)etano-1,2-diamina

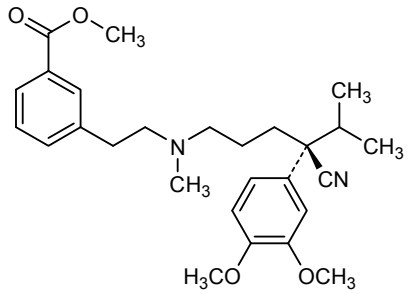
$C_{25}H_{30}N_6O_2$



etripamilum

etripamil	methyl 3-(2-{[(4S)-4-cyano-4-(3,4-dimethoxyphenyl)-5-methylhexyl](methyl)amino}ethyl)benzoate
étripamil	3-(2-{[(4S)-4-cyano-4-(3,4-diméthoxyphényl)-5-méthylhexyl](méthyl)amino}éthyl)benzoate de méthyle
etripamilo	3-(2-{[(4S)-4-ciano-4-(3,4-dimetoxifenil)-5-metilhexil](metil)amino}etil)benzoato de metilo

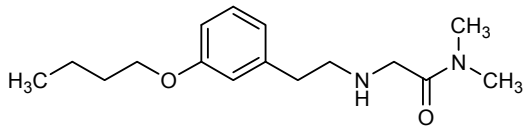
$C_{27}H_{36}N_2O_4$



evenamidum

evenamide	2-{[2-(3-butoxyphenyl)ethyl]amino}-*N*,*N*-dimethylacetamide
événamide	2-{[2-(3-butoxyphényl)éthyl]amino}-*N*,*N*-diméthylacétamide
evenamida	2-{[2-(3-butoxifenil)etil]amino}-*N*,*N*-dimetilacetamida

$C_{16}H_{26}N_2O_2$



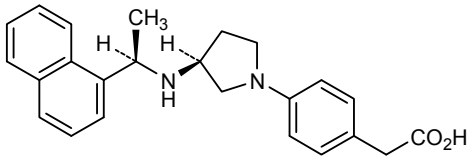
evocalcetum

evocalcet	{4-[(3*S*)-3-{[(1*R*)-1-(naphthalen-1-yl)ethyl]amino}pyrrolidin-1-yl]phenyl}acetic acid
évocalcet	acide {4-[(3*S*)-3-{[(1*R*)-1-(naphtalén-1-yl)éthyl]amino}pyrrolidin-1-yl]phényl}acétique

evocalcet

ácido {4-[(3*S*)-3-{[(1*R*)-1-(naftalen-1-il)etil]amino}pirrolidin-1-il]fenil}acético

$C_{24}H_{26}N_2O_2$



ezutromidum

ezutromid

5-(ethanesulfonyl)-2-(naphthalen-2-yl)-1,3-benzoxazole

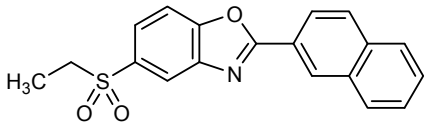
ézutromid

5-(éthanesulfonyl)-2-(naphtalén-2-yl)-1,3-benzoxazole

ezutromid

5-(etanosulfonil)-2-(naftalen-2-il)-1,3-benzoxazol

$C_{19}H_{15}NO_3S$



fitusiranum

fitusiran

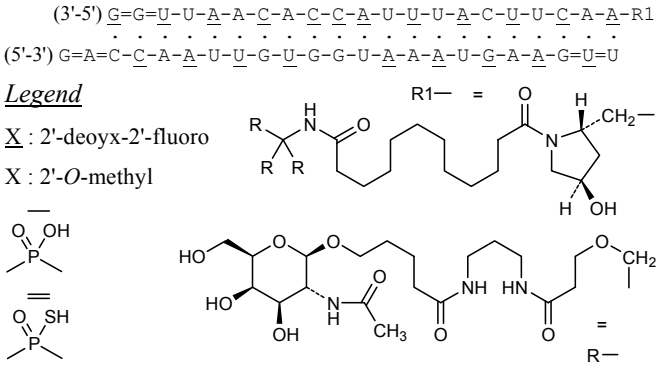
small interfering RNA (siRNA) inhibiting antithrombin liver production:
duplex of [(2*S*,4*R*)-1-{30-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-14,14-bis[16-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-5,11-dioxo-2,16-dioxa-6,10-diazahexadecyl]-12,19,25-trioxo-16,30-dioxa-13,20,24-triazatriacontanoyl}-4-hydroxypyrrolidin-2-yl]methyl hydrogen (*P*-*RS*)-2'-deoxy-2'-fluoro-*P*-thioguanylyl-(3'→5')-(*P*-*RS*)-2'-*O*-methyl-*P*-thioguanylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-deoxy-2'-fluoroadenylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-deoxy-2'-fluoroadenylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-deoxy-2'-fluoroadenylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-deoxy-2'-fluoroadenylate and

	and (*P*-*RS*)-2'-*O*-methyl-*P*-thiouridylyl-(3'→5')-(*P*-*RS*)-2'-deoxy-2'-fluoro-*P*-thiouridylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-deoxy-2'-fluoroadenylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-deoxy-2'-fluoroguanylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-deoxy-2'-fluoroadenylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-deoxy-2'-fluoroadenylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-deoxy-2'-fluoroadenylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-(*P*-*RS*)-2'-*O*-methyl-*P*-thiocytidylyl-(3'→5')-(*P*-*RS*)-2'-*O*-methyl-*P*-thioadenylyl-(3'→5')-2'-*O*-methylguanosine
fitusiran	petit ARN interférant inhibant la production hépatique d'antithrombine: duplex de l'hydrogéno-(*P*-*RS*)-2'-deoxy-2'-fluoro-*P*-thioguanylyl-(3'→5')-(*P*-*RS*)-2'-*O*-méthyl-*P*-thioguanylyl-(3'→5')-2'-désoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-désoxy-2'-fluoroadénylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-désoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-désoxy-2'-fluorocytidylyl-(3'→5')-2'-désoxy-2'-fluorocytidylyl-(3'→5')-2'-désoxy-2'-fluoroadénylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-désoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-désoxy-2'-fluoroadénylyl-(3'→5')-2'-*O*-méthylcytidylyl-(3'→5')-2'-désoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-désoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-désoxy-2'-fluoroadénylate de [(2*S*,4*R*)-1-{30-(2-acétamido-2-désoxy-β-D-galactopyranosyl)-14,14-bis[16-(2-acétamido-2-désoxy-β-D-galactopyranosyl)-5,11-dioxo-2,16-dioxa-6,10-diazahexadécyl]-12,19,25-trioxo-16,30-dioxa-13,20,24-triazatriacontanoyl}-4-hydroxypyrrolidin-2-yl]méthyle et du(*P*-*RS*)-2'-*O*-méthyl-*P*-thiouridylyl-(3'→5')(*P*-*RS*)-2'-désoxy-2'-fluoro-*P*-thiouridylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-désoxy-2'-fluoroadénylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-désoxy-2'-fluoroguanylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-désoxy-2'-fluoroadénylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-désoxy-2'-fluoroadénylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-désoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-désoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-désoxy-2'-fluoroadénylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-désoxy-2'-fluorocytidylyl-(3'→5')-(*P*-*RS*)-2'-*O*-méthyl-*P*-thiocytidylyl-(3'→5')-(*P*-*RS*)-2'-*O*-méthyl-*P*-thioadénylyl-(3'→5')-2'-*O*-méthylguanosine

fitusirán

ARN pequeño de interferencia que inhibe la producción hepática de antitrombina:
dúplex de hidrógeno-(*P*-*RS*)-2'-desoxi-2'-fluoro-*P*-tioguanilil-(3'→5')-(*P*-*RS*)-2'-*O*-metil-*P*-tioguanilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-desoxi-2'-fluoroadenilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-desoxi-2'-fluoroadenilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-desoxi-2'-fluoroadenilil-(3'→5')-2'-*O*-metilcitidill-(3'→5')-2'-desoxi-2'-fluorouridill-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-desoxi-2'-fluoroadenilato de [(2*S*,4*R*)-1-{30-(2-acetamido-2-desoxi-β-D-galactopiranosil)-14,14-bis[16-(2-acetamido-2-desoxi-β-D-galactopiranosil)-5,11-dioxo-2,16-dioxa-6,10-diazahexadecil]-12,19,25-trioxo-16,30-dioxa-13,20,24-triazatriacontanoil}-4-hidroxipirrolidin-2-il]metil y de (*P*-*RS*)-2'-*O*-metil-*P*-tiouridilil-(3'→5') (*P*-*RS*)-2'-desoxi-2'-fluoro-*P*-tiouridilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-desoxi-2'-fluoroadenilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-desoxi-2'-fluoroguanilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-desoxi-2'-fluoroadenilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-desoxi-2'-fluoroadenilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-desoxi-2'-fluoroadenilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-(*P*-*RS*)-2'-*O*-metil-*P*-tiocitidilil-(3'→5')-(*P*-*RS*)-2'-*O*-metil-*P*-tioadenilil-(3'→5')-2'-*O*-metilguanosina

$C_{520}H_{679}F_{21}N_{175}O_{309}P_{43}S_6$



fosnetupitantum

fosnetupitant

{4-[5-{2-[3,5-bis(trifluoromethyl)phenyl]-*N*,2-dimethylpropanamido}-4-(2-methylphenyl)pyridin-2-yl]-1-methylpiperazin-1-ium-1-yl}methyl hydrogen phosphate

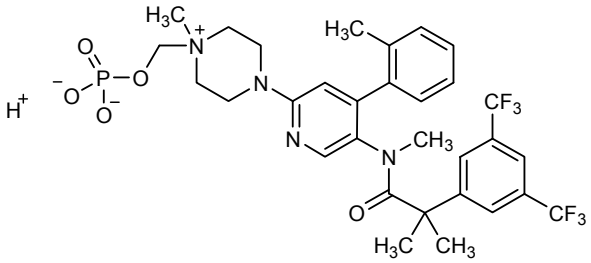
fosnétupitant

hydrogénophosphate de {4-[5-{2-[3,5-bis(trifluorométhyl)phényl]-*N*,2-diméthylpropanamido}-4-(2-méthylphényl)pyridin-2-yl]-1-méthylpipérazin-1-ium-1-yl}méthyle

fosnetupitant

hidrógenofosfato de {4-[5-{2-[3,5-bis(trifluorometil)fenil]-*N*,2-dimetilpropanamido}-4-(2-metilfenil)piridin-2-il]-1-metilpiperazin-1-io-1-il}metilo

$C_{31}H_{35}F_6N_4O_5P$



glembatumumabum vedotinum #

glembatumumab vedotin

immunoglobulin G2-kappa, anti-[*Homo sapiens* GPNMB (glycoprotein (transmembrane) nmb, glycoprotein transmembrane NMB, glycoprotein nonmetastatic melanoma protein B, CG56972, osteoactivin, hematopoietic growth factor inducible neurokinin-1 type, HGFIN) extracellular domain], *Homo sapiens* monoclonal antibody conjugated to auristatin E;
gamma2 heavy chain (1-445) [*Homo sapiens* VH (IGHV4-31*02 (94.90%) -(IGHD)-IGHJ4*01) [10.7.11] (1-119) -IGHG2*01, G2m.. (CH1 (120-217), hinge (218-229), CH2 (230-338), CH3 (339-443), CHS (444-445)) (120-445)], (133-215')-disulfide with kappa light chain (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-15*01 (96.80%) -IGKJ1*01) [6.3.10] (1'-108') -IGKC*01, Km3 (109'-215')]; dimer (221-221'':222-222'':225-225'':228-228'')-tetrakisdisulfide; conjugated, on an average of 5 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker
For the *vedotin* part, please refer to the document *"INN for pharmaceutical substances: Names for radicals, groups and others"*.*

glembatumumab védotine

immunoglobuline G2-kappa, anti-[*Homo sapiens* GPNMB (glycoprotéine (transmembranaire) nmb, glycoprotéine transmembranaire NMB, protéine B glycoprotéine de mélanome non métastatique, CG56972, ostéoactivine, facteur de croissance hématopoïétique inductible type neurokinine-1, HGFIN) domaine extracellulaire], *Homo sapiens* anticorps monoclonal conjugué à l'auristatine E; chaîne lourde gamma2 (1-445) [*Homo sapiens* VH (IGHV4-31*02 (94.90%) -(IGHD)-IGHJ4*01) [10.7.11] (1-119) -IGHG2*01, G2m.. (CH1 (120-217), charnière (218-229), CH2 (230-338), CH3 (339-443), CHS (444-445)) (120-445)], (133-215')-disulfure avec la chaîne légère kappa (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-15*01 (96.80%) -IGKJ1*01) [6.3.10] (1'-108') -IGKC*01, Km3 (109'-215')]; dimère (221-221'':222-222'':225-225'':228-228'')-tétrakisdisulfure; conjugué, sur 5 cystéinyl en moyenne, au monométhylauristatine E (MMAE), via un linker clivable de type maléimidocaproyl-valyl-citrullinyl-*p*-aminobenzyloxycarbonyl (mc-val-cit-PABC)
Pour la partie *védotine*, veuillez-vous référer au document *"INN for pharmaceutical substances: Names for radicals, groups and others"*.*

glembatumumab vedotina

inmunoglobulina G2-kappa, anti-[*Homo sapiens* GPNMB (glicoproteína (transmembrana) nmb, glicoproteina transmembrana NMB, proteína B glicoproteína de melanoma no metastásico, CG56972, osteoactivina, factor de crecimiento hematopoyético inducible tipo neurokinina-1, HGFIN) dominio extracelular], *Homo sapiens* anticuerpo monoclonal conjugado con auristatina E;
cadena pesada gamma2 (1-445) [*Homo sapiens* VH (IGHV4-31*02 (94.90%) -(IGHD)-IGHJ4*01) [10.7.11] (1-119) -IGHG2*01, G2m.. (CH1 (120-217), bisagra (218-229), CH2 (230-338), CH3 (339-443), CHS (444-445)) (120-445)], (133-215')-disulfuro con la cadena ligera kappa (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-15*01 (96.80%) -IGKJ1*01) [6.3.10] (1'-108') -IGKC*01, Km3 (109'-215')]; dímero (221-221":222-222":225-225":228-228")-tetrakisdisulfuro; conjugado, en una media de 5 restos cisteinil, con monometilauristatina E (MMAE), mediante un espaciadorescindible de tipo maleimidocaproil-valil-citrulinil-*p*-aminobenciloxicarbonil (mc-val-cit-PABC)
La fracción *vedotina*, la pueden encontrar en el documento *"INN for pharmaceutical substances: Names for radicals, groups and others"*.*

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLQESGPG LVKPSQTLSL TCTVSGGSIS SFNYYWSWIR HHPGKGLEWI  50
GYIYYSGSTY SNPSLKSRVT ISVDTSKNQF SLTLSSVTAA DTAVYYCARG 100
YNWNYFDYWG QGTLVTVSSA STKGPSVFPL APCSRSTSES TAALGCLVKD 150
YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSNFGTQTY 200
TCNVDHKPSN TKVDKTVERK CCVECPPCPA PPVAGPSVFL FPPKPKDTLM 250
ISRTPEVTCV VVDVSHEDPE VQFNWYVDGV EVHNAKTKPR EEQFNSTFRV 300
VSVLTVVHQD WLNGKEYKCK VSNKGLPAPI EKTISKTKGQ PREPQVYTLP 350
PSREEMTKNQ VSLTCLVKGF YPSDIAVEWE SNGQPENNYK TTPPMLDSDG 400
SFFLYSKLTV DKSRWQQGNV FSCSVMHEAL HNHYTQKSLS LSPGK       445
```

Light chain / Chaîne légère / Cadena ligera

```
EIVMTQSPAT LSVSPGERAT LSCRASQSVD NNLVWYQQKP GQAPRLLIYG  50
ASTRATGIPA RFSGSGSGTE FTLTISSLQS EDFAVYYCQQ YNNWPPWTFG 100
QGTKVEIKRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK 150
VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ 200
GLSSPVTKSF NRGEC                                       215
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-97 146-202 259-319 365-423
22"-97" 146"-202" 259"-319" 365"-423"
Intra-L (C23-C104) 23'-88' 135'-195'
23'"-88'" 135'"-195'"
Inter-H-L (CH1 10-CL 126) 133-215' 133"-215'"
Inter-H-H (h 4, h 5, h 8, h 11) 221-221" 222-222" 225-225" 228-228"
*Two or three of the inter-chain disulfide bridges are not present, an average of 5 cysteinyl being conjugated each via a thioether bond to a drug linker.
*Deux ou trois des ponts disulfures inter-chaînes ne sont pas présents, 5 cystéinyl en moyenne étant chacun conjugué via une liaison thioéther à un linker-principe actif.
*Faltan dos o tres puentes disulfuro inter-catenarios, una media de 5 cisteinil está conjugada a conectores de principio activo.

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
295, 295"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

graunimotidum
graunimotide

L-lysyl-L-arginyl-L-tyrosyl-L-phenylalanyl-L-lysyl-L-leucyl-L-seryl-L-histidyl-L-leucyl-L-glutaminyl-L-methionyl-L-histidyl-L-seryl-L-arginyl-L-lysyl-L-histidine;
human Wilms tumor protein (WT33) (332-347)-peptide

graunimotide

L-lysyl-L-arginyl-L-tyrosyl-L-phénylalanyl-L-lysyl-L-leucyl-L-séryl-L-histidyl-L-leucyl-L-glutaminyl-L-méthionyl-L-histidyl-L-séryl-L-arginyl-L-lysyl-L-histidine;
protéine tumorale Wilms humaine (WT33) (332-347)-peptide

graunimotida

L-lisil-L-arginil-L-tiyrosil-L-fenilalanil-L-lisil-L-leucil-L-seril-L-histidil-L-leucil-L-glutaminil-L-metionyl-L-histidil-L-seril-L-arginil-L-lisil-L-histidina;
proteína de tumor de Wilms humano (WT33) (332-347)-péptido

$C_{94}H_{150}N_{32}O_{21}S$

H−Lys−Arg−Tyr−Phe−Lys−Leu−Ser−His−Leu−
Gln−Met−His−Ser−Arg−Lys−His−OH
10 16

guadecitabinum

guadecitabine

2'-deoxy-5-azacytidylyl-(3'→5')-2'-deoxyguanosine

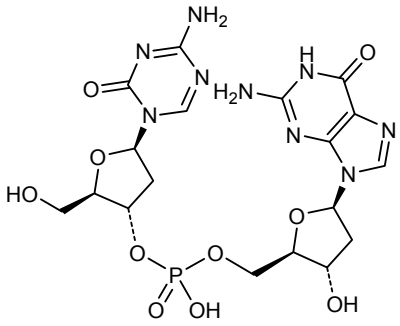
guadécitabine

2'-déoxy-5-azacytidylyl-(3'→5')-2'-déoxyguanosine

guadecitabina

2'-desoxi-5-azacitidilil-(3'→5')-2'-desoxiguanosina

$C_{18}H_{24}N_9O_{10}P$



inebilizumabum

inebilizumab

immunoglobulin G1-kappa, anti-[*Homo sapiens* CD19 (B lymphocyte surface antigen B4, Leu-12)], humanized monoclonal antibody;
gamma1 heavy chain (1-451) [humanized VH (*Homo sapiens* IGHV3-15*06 (83.70%) -(IGHD)-IGHJ4*01) [8.8.14] (1-121) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (122-219), hinge (220-234), CH2 (235-344), CH3 (345-449), CHS (450-451)) (122-451)], (224-218')-disulfide with kappa light chain (1'-218') [humanized V-KAPPA (*Homo sapiens* IGKV6-21*01 (79.80%) -IGKJ4*01) [10.3.9] (1'-111') -*Homo sapiens* IGKC*01, Km3 (112'-218')]; dimer (230-230":233-233")-bisdisulfide

inébilizumab

immunoglobuline G1-kappa, anti-[*Homo sapiens* CD19 (antigène de surface B4 des lymphocytes B, Leu-12)], anticorps monoclonal humanisé;
chaîne lourde gamma1 (1-451) [VH humanisé (*Homo sapiens* IGHV3-15*06 (83.70%) -(IGHD)-IGHJ4*01) [8.8.14] (1-121) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (122-219), charnière (220-234), CH2 (235-344), CH3 (345-449), CHS (450-451)) (122-451)], (224-218')-disulfure avec la chaîne légère kappa (1'-218') [V-KAPPA humanisé (*Homo sapiens* IGKV6-21*01 (79.80%) -IGKJ4*01) [10.3.9] (1'-111') -*Homo sapiens* IGKC*01, Km3 (112'-218')];
dimère (230-230":233-233")-bisdisulfure

inebilizumab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* CD19 (antígeno de superficie B4 de los linfocitos B, Leu-12)], anticuerpo monoclonal humanizado;
cadena pesada gamma1 (1-451) [VH humanizada (*Homo sapiens* IGHV3-15*06 (83.70%) -(IGHD)-IGHJ4*01) [8.8.14] (1-121) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (122-219), bisagra (220-234), CH2 (235-344), CH3 (345-449), CHS (450-451)) (122-451)], (224-218')-disulfuro con la cadena ligera kappa (1'-218') [V-KAPPA humanizada (*Homo sapiens* IGKV6-21*01 (79.80%) -IGKJ4*01) [10.3.9] (1'-111') -*Homo sapiens* IGKC*01, Km3 (112'-218')];
dímero (230-230":233-233")-bisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGGSLRL SCAASGFTFS SSWMNWVRQA PGKGLEWVGR  50
IYPGDGDTNY NVKFKGRFTI SRDDSKNSLY LQMNSLKTED TAVYYCARSG 100
FITTVRDFDY WGQGTLVTVS SASTKGPSVF PLAPSSKSTS GGTAALGCLV 150
KDYFPEPVTV SWNSGALTSG VHTFPAVLQS SGLYSLSSVV TVPSSSLGTQ 200
TYICNVNHKP SNTKVDKRVE PKSCDKTHTC PPCPAPELLG GPSVFLFPPK 250
PKDTLMISRT PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY 300
NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP 350
QVYTLPPSRE EMTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP 400
VLDSDGSFFL YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG 450
K                                                       451
```

Light chain / Chaîne légère / Cadena ligera

```
EIVLTQSPDF QSVTPKEKVT ITCRASESVD TFGISFMNWF QQKPDQSPKL  50
LIHEASNQGS GVPSRFSGSG SGTDFTLTIN SLEAEDAATY YCQQSKEVPF 100
TFGGGTKVEI KRTVAAPSVF IFPPSDEQLK SGTASVVCLL NNFYPREAKV 150
QWKVDNALQS GNSQESVTEQ DSKDSTYSLS STLTLSKADY EKHKVYACEV 200
THQGLSSPVT KSFNRGEC                                    218
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-96	148-204	265-325	371-429
	22"-96"	148"-204"	265"-325"	371"-429"
Intra-L (C23-C104)	23'-92'	138'-198'		
	23'"-92'"	138'"-198'"		
Inter-H-L (h 5-CL 126)	224-218'	224"-218'"		
Inter-H-H (h 11, h 14)	230-230"	233-233"		

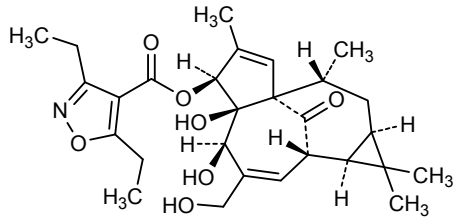
N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
301, 301"
Afucosylated complex bi-antennary CHO-type glycans / Glycanes de type CHO bi-antennaires complexes afucosylés / Glicanos de tipo CHO biantenarios complejos no fucosilados

ingenoli disoxas
ingenol disoxate

(1a*R*,2*S*,3*Z*,5*R*,5a*S*,6*S*,8a*S*,9*R*,10a*R*)-5,5a-dihydroxy-4-(hydroxymethyl)-1,1,7,9-tetramethyl-11-oxo-1a,2,5,5a,6,9,10,10a-octahydro-1*H*-2,8a-methanocyclopenta[*a*]cyclpropa[*e*][10]annulen-6-yl 3,5-diethylisoxazole-4-carboxylate

disoxate d'ingénol	3,5-diéthylisoxazole-4-carboxylate de (1a*R*,2*S*,3*Z*,5*R*,5a*S*,6*S*,8a*S*,9*R*,10a*R*)-5,5a-dihydroxy-4-(hydroxyméthyl)-1,1,7,9-tétraméthyl-11-oxo-1a,2,5,5a,6,9,10,10a-octahydro-1*H*-2,8a-méthanocyclopenta[*a*]cyclpropa[*e*][10]annulén-6-yle
disoxato de ingenol	3,5-dietillisoxazol-4-carboxilato de (1a*R*,2*S*,3*Z*,5*R*,5a*S*,6*S*,8a*S*,9*R*,10a*R*)-5,5a-dihidroxi-4-(hidroximetil)-1,1,7,9-tetrametil-11-oxo-1a,2,5,5a,6,9,10,10a-octahidro-1*H*-2,8a-metanociclopenta[*a*]ciclpropa[*e*][10]anulen-6-ilo

$C_{28}H_{37}NO_7$



iodinum (^{131}I) derlotuximabum biotinum #

iodine (^{131}I) derlotuximab biotin	immunoglobulin G1-kappa, anti-[*Homo sapiens* DNA/histone 1 (H1) complex], chimeric monoclonal antibody radiolabeled with iodine-131 and biotinylated; gamma1 heavy chain (1-450) [*Mus musculus* VH (IGHV2-6-5*01 -(IGHD)-IGHJ4*01) [8.7.14] (1-120) - *Homo sapiens* IGHG1*01, G1m17,1 (CH1 V121>A (218) (121-218), hinge (219-233), CH2 (234-343), CH3 (344-448), CHS (449-450)) (121-450)], (223-215')-disulfide with kappa light chain (1'-215') [*Mus musculus* V-KAPPA (IGKV4-57-1*01 - IGKJ1*01) [7.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (109'-215')]; dimer (229-229'':232-232'')-bisdisulfide; (^{131}I) iodinatedwith iodine-131 covalently linked to tyrosines, and biotinylated
iodine (^{131}I) derlotuximab biotine	immunoglobuline G1-kappa, anti-[*Homo sapiens* complexe ADN/histone 1 (H1)], anticorps monoclonal chimérique biotinylé et marqué à l'iode 131; chaîne lourde gamma1 (1-450) [*Mus musculus* VH (IGHV2-6-5*01 -(IGHD)-IGHJ4*01) [8.7.14] (1-120) - *Homo sapiens* IGHG1*01, G1m17,1 (CH1 V121>A (218) (121-218), charnière (219-233), CH2 (234-343), CH3 (344-448), CHS (449-450)) (121-450)], (223-215')-disulfure avec la chaîne légère kappa (1'-215') [*Mus musculus* V-KAPPA (IGKV4-57-1*01 -IGKJ1*01) [7.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (109'-215')]; dimère (229-229'':232-232'')-bisdisulfure; marqué à l'iode 131 (^{131}I) lié de manière covalente à des tyrosines, et biotinylé

iodo (^{131}I) derlotuximab biotina

inmunoglobulina G1-kappa, anti-[*Homo sapiens* complejo ADN/histona 1 (H1)], anticuerpo monoclonal quimérico biotinilado y marcado con iodo 131;
cadena pesada gamma1 (1-450) [*Mus musculus* VH (IGHV2-6-5*01 -(IGHD)-IGHJ4*01) [8.7.14] (1-120) - *Homo sapiens* IGHG1*01, G1m17,1 (CH1 V121>A (218) (121-218), bisagra(219-233), CH2 (234-343), CH3 (344-448), CHS (449-450)) (121-450)], (223-215')-disulfuro con la cadena ligera kappa (1'-215') [*Mus musculus* V-KAPPA (IGKV4-57-1*01 -IGKJ1*01) [7.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (109'-215')]; dímero (229-229'':232-232'')-bisdisulfuro; marcado con iodo 131 (^{131}I) unido covalentemente a tirosinas, y biotinilado

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLKESGPG LVAPSQSLSI TCTVSGFSLT DYGVRWIRQP PGKGLEWLGV  50
IWGGGSTYYN SALKSRLSIS KDNSKSQVFL KMNSLQTDDT AMYYCAKEKR 100
RGYYYAMDYW GQGTSVTVSS ASTKGPSVFP LAPSSKSTSG GTAALGCLVK 150
DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT 200
YICNVNHKPS NTKVDKKAEP KSCDKTHTCP PCPAPELLGG PSVFLFPPKP 250
KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ 350
VYTLPPSRDE LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPGK 450
```

Light chain / Chaîne légère / Cadena ligera

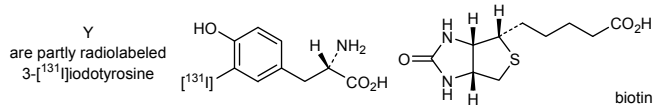
```
ENVLTQSPAI MSASPGEKVT MTCRASSSVS SSYLHWYQQK SGASPKLWIY  50
STSNLASGVP ARFSGSGSGT SYSLTISSVE AEDAATYYCQ QYSGYPLTFG 100
GGTKLEIKRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK 150
VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ 200
GLSSPVTKSF NRGEC                                       215
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-95	147-203	264-324	370-428
	22''-95''	147''-203''	264''-324''	370''-428''
Intra-L (C23-C104)	23'-89'	135'-195'		
	23'''-89'''	135'''-195'''		
Inter-H-L (h 5-CL 126)	223-215'	223''-215'''		
Inter-H-H (h 11, h 14)	229-229''	232-232''		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
300, 300''
Fucosylated complex bi-antennary NS0-type glycans / glycanes de type NS0 bi-antennaires complexes fucosylés / glicanos de tipo NS0 biantenario complejos fucosilados

Modified residues / Résidus modifiés / Restos modificados



isunakinrum #
isunakinra

human interleukin-1 beta-(1-8)-peptide fusion protein with human interleukin-1 receptor antagonist protein-(14-45)-peptide fusion protein with human interleukin-1 beta-(42-120)-peptide fusion protein with human interleukin-1 receptor antagonist protein-(120-147)-peptide fusion protein with human interleukin-1 beta-(148-153)-peptide non-glycosylated

isunakinra

interleukine-1 bêta humaine-(1-8)-peptide protéine de fusion avec l'antagoniste protéique du récepteur de l'interleukine-1 humain-(14-45)-peptide protéine de fusion avec l'interleukine-1 bêta humaine-(42-120)-peptide protéine de fusion avec l'antagoniste protéique du récepteur de l'interleukine-1 humain-(120-147)-peptide protéine de fusion avec l'interleukine-1 bêta humaine-(148-153)-peptide non-glycosylé

isunakinra	interleukina-1 beta humana-(1-8)-péptido proteína de fusión con el antagonista proteíco del receptor de la interleukina-1 humana-(14-45)-péptido proteína de fusión con la interleukina-1 beta humana-(42-120)-péptido proteína de fusión con el antagonista proteíco del receptor de la interleukina-1 humana-(120-147)-péptido proteína de fusión con la interleukina-1 beta humana-(148-153)-péptido no-glicosilado

```
APVRSLNCRI WDVNQKTFYL RNNQLVAGYL QGPNVNLEEK FSMSFVQGEE 50
SNDKIPVALG LKEKNLYLSC VLKDDKPTLQ LESVDPKNYP KKKMEKRFVF 100
NKIEINNKLE FESAQFPNWF LCTAMEADQP VSLTNMPDEG VMVTKFYMQF 150
VSS                                                    153
```

labetuzumabum govitecanum #

labetuzumab govitecan	immunoglobulin G1-kappa, anti-[*Homo sapiens* CEACAM5 (carcinoembryonic antigen-related cell adhesion molecule 5, CEA, CD66e)], monoclonal antibody conjugated to 7-ethyl-10-hydroxycamptothecin (SN-38), active metabolite of irinotecan; gamma1 heavy chain (1-449) [humanized VH (*Homo sapiens* IGHV3-48*01 (75.30%) -(IGHD)-IGHJ5*01) [8.8.12] (1-119) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (120-217), hinge (218-232), CH2 (233-342), CH3 (343-447), CHS (448-449)) (120-449)], (222-213')-disulfide with kappa light chain (1'-213') [humanized V-KAPPA (*Homo sapiens* IGKV1-39*01 (85.70%) -IGKJ1*01) [6.3.8] (1'-106') -*Homo sapiens* IGKC*01, Km3 (107'-213')]; dimer (228-228":231-231")-bisdisulfide; conjugated, on an average of 6 cysteinyl, to 7-ethyl-10-hydroxycamptothecin (SN-38), active metabolite of irinotecan (CPT-11, camptothecin-11), via a maleimide-type cleavable linker (carbonate group, 4-aminobenzyl alcohol and cathepsine-B-cleavable dipeptide Phe-Lys) and containing a triazoline group and a spacer PEG (n=8)
labétuzumab govitécan	immunoglobuline G1-kappa, anti-[*Homo sapiens* CEACAM5 (molécule d'adhésion cellulaire 5 apparentée à l'antigène carcinoembryonaire, CEA, CD66e)], anticorps monoclonal conjugué à la 7-éthyl-10-hydroxycamptothécine (SN-38), métabolite actif de l'irinotécan; chaîne lourde gamma1 (1-449) [humanized VH (*Homo sapiens* IGHV3-48*01 (75.30%) -(IGHD)-IGHJ5*01) [8.8.12] (1-119) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (120-217), charnière (218-232), CH2 (233-342), CH3 (343-447), CHS (448-449)) (120-449)], (222-213')-disulfure avec la chaîne légère kappa (1'-213') [V-KAPPA humanisé (*Homo sapiens* IGKV1-39*01 (85.70%) -IGKJ1*01) [6.3.8] (1'-106') -*Homo sapiens* IGKC*01, Km3 (107'-213')]; dimère (228-228":231-231")-bisdisulfure; conjugué, sur 6 cystéinyl en moyenne, à la 7-éthyl-10-hydroxycamptothécine (SN-38), métabolite actif de l'irinotécan (CPT-11, camptothécine-11), via un linker de type maléimide, clivable (liaison carbonate, 4-aminobenzyl alcool et dipeptide Phe-Lys clivable par la cathepsine B) et comprenant un groupe triazoline et un espaceur PEG (n=8)

labetuzumab govitecán

inmunoglobulina G1-kappa, anti-[*Homo sapiens* CEACAM5 (molècula de adhesión celular 5 relacionada con el antígeno carcinoembrionario, CEA, CD66e)], anticuerpo monoclonal conjugado con la 7-etil-10-hidroxicamptotecina (SN-38), metabolito activo del irinotecán;
cadena pesada gamma1 (1-449) [humanizado VH (*Homo sapiens* IGHV3-48*01 (75.30%) -(IGHD)-IGHJ5*01) [8.8.12] (1-119) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (120-217), bisagra (218-232), CH2 (233-342), CH3 (343-447), CHS (448-449)) (120-449)], (222-213')-disulfuro con la cadena ligera kappa (1'-213') [V-KAPPA humanizado (*Homo sapiens* IGKV1-39*01 (85.70%) -IGKJ1*01) [6.3.8] (1'-106') -*Homo sapiens* IGKC*01, Km3 (107'-213')]; dímero (228-228":231-231")-bisdisulfuro; conjugado, en una media de 6 restos cisteinil, con la 7-etil-10-hidroxicamptotecina (SN-38), metabolito activo del irinotecán (CPT-11, camptotecina-11), mediante un espaciador de tipo maleimida, escindible (enlace carbonato, 4-aminobencil alcohol y dipéptido Phe-Lys escindible por catepsina B) y que comprende un grupo triazolina y un espaciador PEG (n=8)

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG VVQPGRSLRL SCSASGFDFT TYWMSWVRQA PGKGLEWIGE  50
IHPDSSTINY APSLKDRFTI SRDNAKNTLF LQMDSLRPED TGVYFCASLY 100
FGFPWFAYWG QGTPVTVSSA STKGPSVFPL APSSKSTSGG TAALGCLVKD 150
YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY 200
ICNVNHKPSN TKVDKRVEPK SCDKTHTCPP CPAPELLGGP SVFLFPPKPK 250
DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VDGVEVHNAK TKPREEQYNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKAL PAPIEKTISK AKGQPREPQV 350
YTLPPSREEM TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL 400
DSDGSFFLYS KLTVDKSRWQ QGNVFSCSVM HEALHNHYTQ KSLSLSPGK  449
```

Light chain / Chaîne légère / Cadena ligera

```
DIQLTQSPSS LSASVGDRVT ITCKASQDVG TSVAWYQQKP GKAPKLLIYW  50
TSTRHTGVPS RFSGSGSGTD FTFTISSLQP EDIATYYCQQ YSLYRSFGQG 100
TKVEIKRTVA APSVFIFPPS DEQLKSGTAS VVCLLNNFYP REAKVQWKVD 150
NALQSGNSQE SVTEQDSKDS TYSLSSTLTL SKADYEKHKV YACEVTHQGL 200
SSPVTKSFNR GEC                                         213
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104) 22-96 146-202 263-323 369-427
22"-96" 146"-202" 263"-323" 369"-427"
Intra-L (C23-C104) 23'-88' 133'-193'
23'"-88'" 133'"-193'"
Inter-H-L (h 5-CL 126) * 222-213' 222"-213'"
Inter-H-H (h 11, h 14) * 228-228" 231-231"

*Three of the inter-chain disulfide bridges are not present, an average of 6 cysteinyl being conjugated each via a thioether bond to a drug linker.
*Trois des ponts disulfures inter-chaînes ne sont pas présents, 6 cystéinyl en moyenne étant chacun conjugué via une liaison thioéther à un linker-principe actif.
*Faltan tres puentes disulfuro inter-catenarios, una media de 6 cisteinil está conjugada a conectores de principio activo.

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación

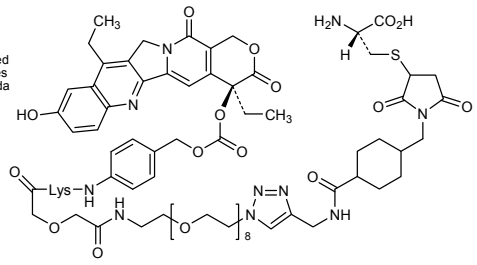
H CH2 N84.4:
299, 299"
Fucosylated complex bi-antennary Sp2/0-type glycans / glycanes de type Sp2/0 bi-antennaires complexes fucosylés / glicanos de tipo Sp2/0 biantenarios complejos fucosilados

Potential modified residues / Résidus modifiés potentiels / Restos modificados potenciales

C*

213'-213'"-222-222"-228-228"-231-231"

* an average of 6 are substituted
* en moyenne, 6 sont substitués
* una media de 6 está sustituída



landogrozumabum #

landogrozumab

immunoglobulin G4-kappa, anti-[*Homo sapiens* MSTN (myostatin, growth differentiation factor 8, GDF8, GDF-8)], humanized monoclonal antibody;
gamma4 heavy chain (1-439) [humanized VH (*Homo sapiens* IGHV3-23*04 (89.80%) -(IGHD)-IGHJ4*01 [8.8.6] (1-113)) , IGHG4*01 (CH1 (114-211), hinge S10>P (221) (212-223), CH2 (224-333), CH3 (334-438), CHS K2>del (439)) (114-439)], (127-215')-disulfide with kappa light chain (1'-215') [humanized V-KAPPA (*Homo sapiens* IGKV3-20*01 (89.10%) -IGKJ4*01) [7.3.9] (1'-108') -*Homo sapiens* IGKC*01 (109'-215')]; dimer (219-219":222-222")-bisdisulfide

landogrozumab

immunoglobuline G4-kappa, anti-[*Homo sapiens* MSTN (myostatine, facteur de croissance et de différenciation 8, GDF8, GDF-8)], anticorps monoclonal humanisé;
chaîne lourde gamma4 (1-441) [VH humanisé (*Homo sapiens* IGHV3-23*04 (89.80%) -(IGHD)-IGHJ4*01 [8.8.6] (1-113)) , IGHG4*01 (CH1 (114-211), charnière S10>P (221) (212-223), CH2 (224-333), CH3 (334-438), CHS K2>del (439)) (114-439)], (127-215')-disulfure avec la chaîne légère kappa (1'-215') [V-KAPPA humanisé (*Homo sapiens* IGKV3-20*01 (89.10%) -IGKJ4*01) [7.3.9] (1'-108') -*Homo sapiens* IGKC*01 (109'-215')]; dimère (219-219":222-222")-bisdisulfure

landogrozumab

inmunoglobulina G4-kappa, anti-[*Homo sapiens* MSTN (miostatina, factor de crecimiento y de diferenciación 8, GDF8, GDF-8)], anticuerpo monoclonal humanizado;
cadena pesada gamma4 (1-441) [VH humanizado (*Homo sapiens* IGHV3-23*04 (89.80%) -(IGHD)-IGHJ4*01 [8.8.6] (1-113)) , IGHG4*01 (CH1 (114-211),bisagra S10>P (221) (212-223), CH2 (224-333), CH3 (334-438), CHS K2>del (439)) (114-439)], (127-215')-disulfuro con la cadena ligera kappa (1'-215') [V-KAPPA humanizado (*Homo sapiens* IGKV3-20*01 (89.10%) -IGKJ4*01) [7.3.9] (1'-108') -*Homo sapiens* IGKC*01 (109'-215')]; dímero (219-219":222-222")-bisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGGSLRL SCAASGLTFS RYPMSWVRQA PGKGLVWVSA  50
ITSSGGSTYY SDTVKGRFTI SRDNAKNTLY LQMNSLRAED TAVYYCARLP 100
DYWGQGTLVT VSSASTKGPS VFPLAPCSRS TSESTAALGC LVKDYFPEPV 150
TVSWNSGALT SGVHTFPAVL QSSGLYSLSS VVTVPSSSLG TKTYTCNVDH 200
KPSNTKVDKR VESKYGPPCP PCPAPEFLGG PSVFLFPPKP KDTLMISRTP 250
EVTCVVVDVS QEDPEVQFNW YVDGVEVHNA KTKPREEQFN STYRVVSVLT 300
VLHQDWLNGK EYKCKVSNKG LPSSIEKTIS KAKGQPREPQ VYTLPPSQEE 350
MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY 400
SRLTVDKSRW QEGNVFSCSV MHEALHNHYT QKSLSLSLG             439
```

Light chain / Chaîne légère / Cadena ligera

```
EIVLTQSPGT LSLSPGERAT LSCRASSSVS SSYLHWYQQK PGQAPRLLIY  50
STSNLVAGIP DRFSGSGSGT DFTLTISRLE PEDFAVYYCQ HHSGYHFTFG 100
GGTKVEIKRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK 150
VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ 200
GLSSPVTKSF NRGEC                                       215
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-96	140-196	254-314	360-418
	22"-96"	140"-196"	254"-314"	360"-418"
Intra-L (C23-C104)	23'-89'	135'-195'		
	23'"-89'"	135'"-195'"		
Inter-H-L (CH1 10-CL 126)	127-215'	127"-215'"		
Inter-H-H (h 8, h 11)	219-219"	222-222"		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
290, 290"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

lefitolimodum

lefitolimod

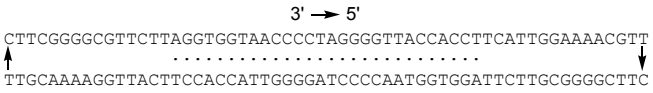
DNA based immunomodulator agent:
cyclo-(3'→5')[2'-deoxy-(A-A-A-A-C-G-T-T-C-T-T-C-G-G-G-G-C-G-T-T-C-T-T-A-G-G-T-G-G-T-A-A-C-C-C-C-T-A-G-G-G-G-T-T-A-C-C-A-C-C-T-T-C-A-T-T-G-G-A-A-A-A-C-G-T-T-C-T-T-C-G-G-G-G-C-G-T-T-C-T-T-A-G-G-T-G-G-T-A-A-C-C-C-C-T-A-G-G-G-G-G-T-T-A-C-C-A-C-C-T-T-C-A-T-T-G-G)]

léfitolimod

immunomodulateur de type ADN:
cyclo-(3'→5')[2'-déoxy-(A-A-A-A-C-G-T-T-C-T-T-C-G-G-G-G-C-G-T-T-C-T-T-A-G-G-T-G-G-T-A-A-C-C-C-C-T-A-G-G-G-G-T-T-A-C-C-A-C-C-T-T-C-A-T-T-G-G-A-A-A-A-C-G-T-T-C-T-T-C-G-G-G-G-C-G-T-T-C-T-T-A-G-G-T-G-G-T-A-A-C-C-C-C-T-A-G-G-G-G-G-T-T-A-C-C-A-C-C-T-T-C-A-T-T-G-G)]

lefitolimod

inmunomodulador de tipo ADN:
ciclo-(3'→5')[2'-desoxi-(A-A-A-A-C-G-T-T-C-T-T-C-G-G-G-G-C-G-T-T-C-T-T-A-G-G-T-G-G-T-A-A-C-C-C-C-T-A-G-G-G-G-T-T-A-C-C-A-C-C-T-T-C-A-T-T-G-G-A-A-A-A-C-G-T-T-C-T-T-C-G-G-G-G-C-G-T-T-C-T-T-A-G-G-T-G-G-T-A-A-C-C-C-C-T-A-G-G-G-G-G-T-T-A-C-C-A-C-C-T-T-C-A-T-T-G-G)]



maralixibati chloridum

maralixibat chloride

1-{[4-({4-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-4-hydroxy-1,1-dioxo-2,3,4,5-tetrahydro-1*H*-1λ^6-benzothiepin-5-yl]phenoxy}methyl)phenyl]methyl}-1,4-diazabicyclo[2.2.2]octan-1-ium chloride

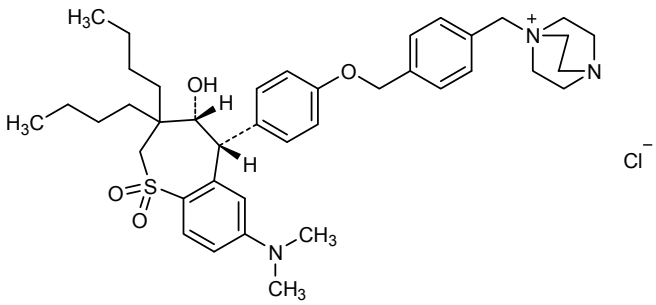
chlorure de maralixibat

chlorure de 1-{[4-({4-[(4*R*,5*R*)-3,3-dibutyl-7-(diméthylamino)-4-hydroxy-1,1-dioxo-2,3,4,5-tétrahydro-1*H*-1λ^6-benzothiépin-5-yl]phénoxy}méthyl)phényl]méthyl}-1,4-diazabicyclo[2.2.2]octan-1-ium

cloruro de maralixibat

cloruro de 1-{[4-({4-[(4*R*,5*R*)-3,3-dibutil-7-(dimetilamino)-4-hidroxi-1,1-dioxo-2,3,4,5-tetrahidro-1*H*-1λ^6-benzotiepin-5-il]fenoxi}metil)fenil]metil}-1,4-diazabiciclo[2.2.2]octan-1-io

$C_{40}H_{56}ClN_3O_4S$



marzeptacogum alfa (activatum) #

marzeptacog alfa (activated)

recombinant DNA derived human blood coagulation factor VIIa analogue:
[128-L-asparagine(T>N),129-L-alanine(P>A),286-L-arginine(Q>R),298-L-glutamine(M>Q)]activated human coagulation factor VII (proconvertine, SPCA), produced in Chinese hamster ovary (CHO) cells, glycoform alfa

marzeptacog alfa (activé)

analogue du facteur VIIa de coagulation sanguine humain produit à partir d'ADN recombinant :
[128-L-asparagine(T>N),129-L-alanine(P>A),286-L-arginine(Q>R),298-L-glutamine(M>Q)]facteur VII de coagulation humain activé (proconvertine, SPCA), produite par des cellules ovariennes de hamster chinois (CHO), forme glycosylée alfa

marzeptacog alfa (activado)

análogo del factor VIIa de coagulación sanguínea humano producido a partir de ADN recombinante :
[128-L-asparagina(T>N),129-L-alanina(P>A),286-L-arginina(Q>R),298-L-glutamina(M>Q)]factor VII de coagulación humano activado (proconvertina, SPCA), producida por células ováricas de hamster chino (CHO), forma glicosilada alfa

Light chain / Chaîne légère / Cadena ligera

```
ANAFLEELRP GSLERECKEE QCSFEEAREI FKDAERTKLF WISYSDGDQC 50
ASSPCQNGGS CKDQLQSYIC FCLPAFEGRN CETHKDDQLI CVNENGGCEQ 100
YCSDHTGTKR SCRCHEGYSL LADGVSCNAT VEYPCGKIPI LEKRNASKPQ 150
GR                                                    152
```

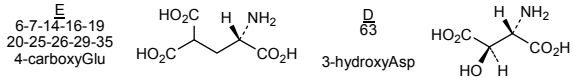
Heavy chain / Chaîne lourde / Cadena pesada

```
  IVGGKVCP KGECPWQVLL LVNGAQLCGG TLINTIWVVS AAHCFDKIKN 200
WRNLIAVLGE HDLSEHDGDE QSRRVAQVII PSTYVPGTTN HDIALLRLHQ 250
PVVLTDHVVP LCLPERTFSE RTLAFVRFSL VSGWGRLLDR GATALELQVL 300
NVPRLMTQDC LQQSRKVGDS PNITEYMFCA GYSDGSKDSC KGDSGGPHAT 350
HYRGTWYLTG IVSWGQGCAT VGHFGVYTRV SQYIEWLQKL MRSEPRPGVL 400
LRAPFP                                                406
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

17-22 50-61 55-70 72-81 91-102 98-112
114-127 135-262 159-164 178-194 310-329 340-368

Modified residues / Résidus modifiés / Restos modificados



Glycosylation sites (S or N) / Sites de glycosylation (S ou N) / Posiciones de glicosilación (S o N)

Ser-52 Ser-60 Asn-128 Asn-145 Asn-322

mecapegfilgrastimum #

mecapegfilgrastim

[1-[*N*-(3-{[(3*RS*)-1-{3-[(2-{[ω-methoxypoly(oxyethane-1,2-diyl)]formamido}ethyl)amino]-3-oxopropyl}-2,5-dioxopyrrolidin-3-yl]sulfanyl}propyl)-L-methionine]]human granulocyte colony-stimulating factor (pluripoietin) isoform Short

mécapegfilgrastim

[1-[*N*-(3-{[(3*RS*)-1-{3-[(2-{[ω-méthoxypoly(oxyéthane-1,2-diyl)]formamido}éthyl)amino]-3-oxopropyl}-2,5-dioxopyrrolidin-3-yl]sulfanyl}propyl)-L-méthionine]]isoforme court (*Short*) du facteur de stimulation des colonies de granulocytes humain (pluripoiétine)

mecapegfilgrastim

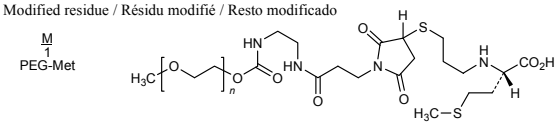
[1-[*N*-(3-{[(3*RS*)-1-{3-[(2-{[ω-metoxipoli(oxietano-1,2-diil)]formamido}etil)amino]-3-oxopropil}-2,5-dioxopirrolidin-3-il]sulfanil}propil)-L-metionina]]isoforma corta (*Short*) del factor humano de estimulación de colonias de granulocitos (pluripoyetina)

Sequence / Séquence / Secuencia

```
MTPLGPASSL PQSFLLKCLE QVRKIQGDGA ALQEKLCATY KLCHPEELVL 50
LGHSLGIPWA PLSSCPSQAL QLAGCLSQLH SGLFLYQGLL QALEGISPEL 100
GPTLDTLQLD VADFATTIWQ QMEELGMAPA LQPTQGAMPA FASAFQRRAG 150
GVLVASHLQS FLEVSYRVLR HLAQP   175
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
37-43 65-75

Modified residue / Résidu modifié / Resto modificado



merestinibum

merestinib

N-(3-fluoro-4-{[1-methyl-6-(1*H*-pyrazol-4-yl)-1*H*-indazol-5-yl]oxy}phenyl)-1-(4-fluorophenyl)-6-methyl-2-oxo-1,2-dihydropyridine-3-carboxamide

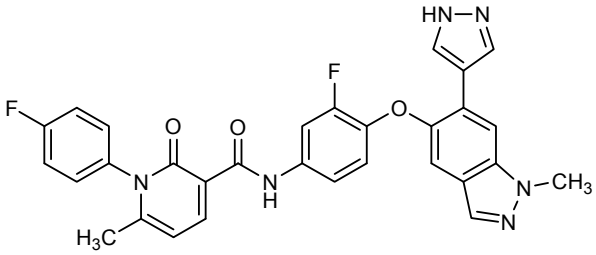
mérestinib

N-(3-fluoro-4-{[1-méthyl-6-(1*H*-pyrazol-4-yl)-1*H*-indazol-5-yl]oxy}phényl)-1-(4-fluorophényl)-6-méthyl-2-oxo-1,2-dihydropyridine-3-carboxamide

merestinib

N-(3-fluoro-4-{[1-metil-6-(1*H*-pirazol-4-il)-1*H*-indazol-5-il]oxi}fenil)-1-(4-fluorofenil)-6-metil-2-oxo-1,2-dihidropiridina-3-carboxamida

$C_{30}H_{22}F_2N_6O_3$



mirvetuximabum soravtansinum #

mirvetuximab soravtansine

immunoglobulin G1-kappa, anti-[*Homo sapiens* FOLR1 (folate receptor 1, folate receptor alpha, FR-alpha, adult folate-binding protein, FBP, ovarian tumor-associated antigen MOv18)], chimeric monoclonal antibody conjugated to maytansinoid DM4;

	gamma1 heavy chain (1-447) [*Mus musculus* VH (IGHV1-37*01 -(IGHD)-IGHJ4*01) [8.8.11] (1-118) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (119-216), hinge (217-231), CH2 (232-341), CH3 (342-446), CHS K2>del (447)) (119-447)], (221-218')-disulfide with kappa light chain (1'-218') [*Mus musculus* V-KAPPA (IGKV3-9*01 -IGKJ2*01) [10.3.9] (1'-111') -*Homo sapiens* IGKC*01, Km3 (112'-218')]; dimer (227-227'':230-230'')-bisdisulfide;conjugated, on an average of 3 or 4 lysyl, to maytansinoid DM4 [*N*2'-deacetyl-*N*2'-(4-mercapto-4-methyl-1-oxopentyl)-maytansine] via the reducible sulfo-SPDB linker [*N*-succinimidyl 4-(2-pyridyldithio)-2-sulfobutanoate]
mirvétuximab soravtansine	immunoglobuline G1-kappa, anti-[*Homo sapiens* FOLR1 (réceptor 1 du folate, récepteur alpha du folate, FR-alpha, protéine de l'adulte liant le folate, FBP, antigène MOv18 associé à des tumeurs ovariennes)], anticorps monoclonal chimérique conjugué au maytansinoïde DM4; chaîne lourde gamma1 (1-447) [*Mus musculus* VH (IGHV1-37*01 -(IGHD)-IGHJ4*01) [8.8.11] (1-118) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (119-216), charnière (217-231), CH2 (232-341), CH3 (342-446), CHS K2>del (447)) (119-447)], (221-218')-disulfure avec la chaîne légère kappa (1'-218') [*Mus musculus* V-KAPPA (IGKV3-9*01 -IGKJ2*01) [10.3.9] (1'-111') -*Homo sapiens* IGKC*01, Km3 (112'-218')]; dimère (227-227'':230-230'')-bisdisulfure; conjugué, sur 3 ou 4 lysyl en moyenne, au maytansinoïde DM4 [*N*2'-déacétyl-*N*2'-(4-mercapto-4-méthyl-1-oxopentyl)-maytansine] via le linker sulfo-SPDB réductible [4-(2-pyridyldithio)-2-sulfobutanoate de *N*-succinimidyle]
mirvetuximab soravtansina	inmunoglobulina G1-kappa, anti-[*Homo sapiens* FOLR1 (receptor 1 de folato, receptor alfa de folato, FR-alfa, proteína del adulto que liga el folato, FBP, antígeno MOv18 asociado a tumores ováricos)], anticuerpo monoclonal quimérico conjugado con el maitansinoide DM4; cadena pesada gamma1 (1-447) [*Mus musculus* VH (IGHV1-37*01 -(IGHD)-IGHJ4*01) [8.8.11] (1-118) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (119-216), cbisagra (217-231), CH2 (232-341), CH3 (342-446), CHS K2>del (447)) (119-447)], (221-218')-disulfuro con la cadena ligera-*Homo sapiens* IGKC*01, Km3 (112'-218')]; dímero (227-227'':230-230'')-bisdisulfuro; conjugado en 3-4 grupos lisil por término medio con el maitansinoide DM4 [*N*2'-desacetil-*N*2'-(4-mercapto-4-metil-1-oxopentil)-maitansina] mediante el espaciador sulfo-SPDB reducible [4-(2-piridilditio)butanoato de *N*-succinimidilo]

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VVKPGASVKI SCKASGYTFT GYFMNWVKQS PGQSLEWIGR  50
IHPYDGDTFY NQKFQGKATL TVDKSSNTAH MELLSLTSED FAVYYCTRYD 100
GSRAMDYWGQ GTTVTVSSAS TKGPSVFPLA PSSKSTSGGT AALGCLVKDY 150
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTQTYI 200
CNVNHKPSNT KVDKKVEPKS CDKTHTCPPC PAPELLGGPS VFLFPPKPKD 250
TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY 350
TLPPSRDELT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD 400
SDGSFFLYSK LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPG    447
```

Light chain / Chaîne légère / Cadena ligera

```
DIVLTQSPLS LAVSLGQPAI ISCKASQSVS FAGTSLMHWY HQKPGQQPRL  50
LIYRASNLEA GVPDRFSGSG SKTDFTLTIS PVEAEDAATY YCQQSREYPY 100
TFGGGTKLEI KRTVAAPSVF IFPPSDEQLK SGTASVVCLL NNFYPREAKV 150
QWKVDNALQS GNSQESVTEQ DSKDSTYSLS STLTLSKADY EKHKVYACEV 200
THQGLSSPVT KSFNRGEC                                    218
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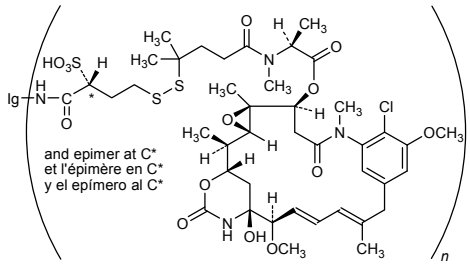
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104) 22-96 145-201 262-322 368-426
22"-96" 145"-201" 262"-322" 368"-426"
Intra-L (C23-C104) 23'-92' 138'-198'
23'"-92'" 138'"-198'"
Inter-H-L (h 5-CL 126) 221-218' 221"-218'"
Inter-H-H (h 11, h 14) 227-227" 230-230"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
298, 298"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

soravtansine / soravtansine / soravtansina

$Ig(NH_2)_n$ = Immunoglobulin



monalizumabum #

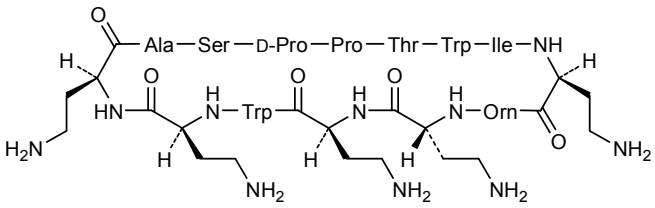
monalizumab	immunoglobulin G4-kappa, anti-[*Homo sapiens* KLRC1 (killer cell lectin-like receptor subfamily C member 1, NKG2-A, NKG2A, CD159a, CD94)],humanized monoclonal antibody; gamma4 heavy chain (1-452) [humanized VH (*Homo sapiens* IGHV1-18*01 (89.80%) -(IGHD)-IGHJ2*01 R120>Q (117), L123>T (130)) [8.8.18] (1-125)), IGHG4*01 (CH1 (126-223), hinge S10>P (233) (224-235), CH2 (236-345), CH3 (346-450), CHS (451-452)) (126-452)], (139-214')-disulfide with kappa light chain (1'-214') [humanized V-KAPPA (*Homo sapiens* IGKV1-39*01 (87.40%) -IGKJ4*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimer (231-231":234-234")-bisdisulfide
monalizumab	immunoglobuline G4-kappa, anti-[*Homo sapiens* KLRC1 (membre 1 de la sous-famille C des récepteurs de type lectine des cellules NK, NKG2-A, NKG2A, CD159a, CD94)], anticorps monoclonal humanisé;

	chaîne lourde gamma4 (1-452) [VH humanisé (*Homo sapiens* IGHV1-18*01 (89.80%) -(IGHD)-IGHJ2*01 R120>Q (117), L123>T (130)) [8.8.18] (1-125)), IGHG4*01 (CH1 (126-223), charnière S10>P (233) (224-235), CH2 (236-345), CH3 (346-450), CHS (451-452)) (126-452)], (139-214')-disulfure avec la chaîne légère kappa (1'-214') [V-KAPPA humanisé (*Homo sapiens* IGKV1-39*01 (87.40%) -IGKJ4*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimère (231-231":234-234")-bisdisulfure
monalizumab	inmunoglobulina G4-kappa, anti-[*Homo sapiens* KLRC1 (miembro 1 de la subfamilia C de receptores de tipo lectina de las células NK, NKG2-A, NKG2A, CD159a, CD94)], anticuerpo monoclonal humanizado; cadena pesada gamma4 (1-452) [VH humanizado (*Homo sapiens* IGHV1-18*01 (89.80%) -(IGHD)-IGHJ2*01 R120>Q (117), L123>T (130)) [8.8.18] (1-125)), IGHG4*01 (CH1 (126-223), bisagra S10>P (233) (224-235), CH2 (236-345), CH3 (346-450), CHS (451-452)) (126-452)], (139-214')-disulfuro con la cadena ligera kappa (1'-214') [V-KAPPA humanizado (*Homo sapiens* IGKV1-39*01 (87.40%) -IGKJ4*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dímero (231-231":234-234")-bisdisulfuro Heavy chain / Chaîne lourde / Cadena pesada QVQLVQSGAE VKKPGASVKV SCKASGYTFT SYWMNWVRQA PGQGLEWMGR 50 IDPYDSETHY AQKLQGRVTM TTDTSTSTAY MELRSLRSDD TAVYYCARGG 100 YDFDVGTLYW FFDVWGQGTT VTVSSASTKG PSVFPLAPCS RSTSESTAAL 150 GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL SSVVTVPSSS 200 LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 250 KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEVH NAKTKPREEQ 300 FNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE 350 PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP 400 PVLDSDGSFF LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL 450 GK 452 Light chain / Chaîne légère / Cadena ligera DIQMTQSPSS LSASVGDRVT ITCRASENIY SYLAWYQQKP GKAPKLLIYN 50 AKTLAEGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQH HYGTPRTFGG 100 GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150 DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200 LSSPVTKSFN RGEC 214 Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro Intra-H (C23-C104) 22-96 152-208 266-326 372-430 22"-96" 152"-208" 266"-326" 372"-430" Intra-L (C23-C104) 23'-88' 134'-194' 23'"-88'" 134'"-194'" Inter-H-L (CH1 10-CL 126) 139-214' 139"-214'" Inter-H-H (h 8, h 11) 231-231" 234-234" N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación H CH2 N84.4: 302, 302" Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados
murepavadinum murepavadin	cyclo[L-alanyl-L-seryl-D-prolyl-L-prolyl-L-threonyl-L-tryptophyl-L-isoleucyl-(2*S*)-2,4-diaminobutanoyl-L-ornithyl-(2*R*)-2,4-diaminobutanoyl-(2*S*)-2,4-diaminobutanoyl-L-tryptophyl-(2*S*)-2,4-diaminobutanoyl-(2*S*)-2,4-diaminobutanoyl]
murépavadine	cyclo[L-alanyl-L-séryl-D-prolyl-L-prolyl-L-thréonyl-L-tryptophyl-L-isoleucyl-(2*S*)-2,4-diaminobutanoyl-L-ornithyl-(2*R*)-2,4-diaminobutanoyl-(2*S*)-2,4-diaminobutanoyl-L-tryptophyl-(2*S*)-2,4-diaminobutanoyl-(2*S*)-2,4-diaminobutanoyl]

murepavadina

ciclo[L-alanil-L-seril-D-prolil-L-prolil-L-treonil-L-triptofil-L-isoleucil-(2*S*)-2,4-diaminobutanoil-L-ornitil-(2*R*)-2,4-diaminobutanoil-(2*S*)-2,4-diaminobutanoil-L-triptofil-(2*S*)-2,4-diaminobutanoil-(2*S*)-2,4-diaminobutanoil]

$C_{73}H_{112}N_{22}O_{16}$



nadorameranum #

nadorameran

an mRNA molecule encoding the rabies virus glycoprotein RAV-G containing elements for expression within eukaryotic cells; manufactured by enzymatic *in vitro* transcription from linearized plasmid DNA

nadoraméran

ARN messager codant la glycoprotéine G du virus de la rage contenant les éléments pour son expression dans des cellules eucaryotes; obtenu par transcription enzymatique *in vitro* à partir d'ADN de plasmide linéarisé

nadoramerán

ARN mensajero que codifica la glicoproteína G del virus de la rabia y contiene los elementos para su expresión en células eucariotas; obtenido por transcripción enzimática *in vitro* a partir de ADN de plásmido transformado en lineal

nastorazepidum

nastorazepide

3-({[(3*R*)-5-cyclohexyl-1-(3,3-dimethyl-2-oxobutyl)-2-oxo-2,3,4,5-tetrahydro-1*H*-1,5-benzodiazepin-3-yl]carbamoyl}amino)benzoic acid

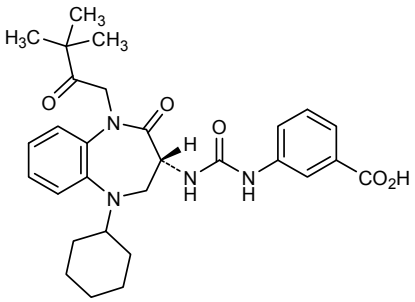
nastorazépide

acide 3-({[(3*R*)-5-cyclohexyl-1-(3,3-diméthyl-2-oxobutyl)-2-oxo-2,3,4,5-tétrahydro-1*H*-1,5-benzodiazépin-3-yl]carbamoyl}amino)benzoïque

nastorazepida

ácido 3-({[(3*R*)-5-cyclohexyl-1-(3,3-dimetil-2-oxobutil)-2-oxo-2,3,4,5-tetrahidro-1*H*-1,5-benzodiazepin-3-il]carbamoil}amino)benzoico

$C_{29}H_{36}N_4O_5$



natrii cinhyaluronas
cinhyaluronate sodium

sodium salt of hyaluronic acid partly amidified with 3-{[(2*E*)-3-phenylprop-2-enoyl]oxy}propan-1-amine

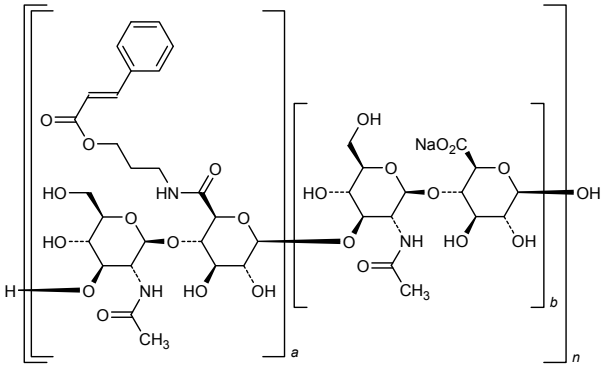
cinhyaluronate de sodium

sel sodique de l'acide hyaluronique partiellement amidifié par la 3-{[(2*E*)-3-phénylprop-2-énoyl]oxy}propan-1-amine

cinhialuronato de sodio

sal sódica del ácido hialurónico parcialmente amidificado por la 3-{[(2*E*)-3-fenilprop-2-enoil]oxi}propan-1-amina

$[(C_{26}H_{34}N_2O_{12})_a(C_{14}H_{20}NNaO_{11})_b]_nH_2O$



navivumabum #
navivumab

immunoglobulin G1-kappa, anti-[influenza A virus hemagglutinin HA], *Homo sapiens* monoclonal antibody; gamma1 heavy chain (1-456) [*Homo sapiens* VH (IGHV1-18*01 (78.60%) -(IGHD)-IGHJ4*01) [8.8.19] (1-126) -IGHG1*07, G1m17,1,2 (CH1 (127-224), hinge (225-239), CH2 (240-349), CH3 (350-454), CHS (455-456)) (127-456)], (229-215')-disulfide with kappa light chain (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-20*01 (82.30%) -IGKJ1*01) [7.3.9] (1'-108') -IGKC*01, Km3 (109'-215')]; dimer (235-235":238-238")-bisdisulfide

navivumab

immunoglobuline G1-kappa, anti-[hémagglutinine HA du virus de la grippe A], *Homo sapiens* anticorps monoclonal; chaîne lourde gamma1 (1-456) [*Homo sapiens* VH (IGHV1-18*01 (78.60%) -(IGHD)-IGHJ4*01) [8.8.19] (1-126) -IGHG1*07, G1m17,1,2 (CH1 (127-224), charnière (225-239), CH2 (240-349), CH3 (350-454), CHS (455-456)) (127-456)], (229-215')-disulfure avec la chaîne légère kappa (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-20*01 (82.30%) -IGKJ1*01) [7.3.9] (1'-108') -IGKC*01, Km3 (109'-215')]; dimère (235-235":238-238")-bisdisulfure

navivumab

inmunoglobulina G1-kappa, anti-[hemaglutinina HA del virus de la gripe A], anticuerpo monoclonal *Homo sapiens*; cadena pesada gamma1 (1-456) [*Homo sapiens* VH (IGHV1-18*01 (78.60%) -(IGHD)-IGHJ4*01) [8.8.19] (1-126) -IGHG1*07, G1m17,1,2 (CH1 (127-224), bisagra (225-239), CH2 (240-349), CH3 (350-454), CHS (455-456)) (127-456)], (229-215')-disulfuro con la cadena ligera kappa (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-20*01 (82.30%) -IGKJ1*01) [7.3.9] (1'-108') -IGKC*01, Km3 (109'-215')]; dímero (235-235'':238-238'')-bisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGASVKV SCKTSGYSFS TYGVSWVRQA PGQGPEWVGW  50
ISAYTGITDY AQKFQGRVTL TTDATTATAF LDLRSLRPDD TATYFCARDK 100
VQGRVEVGSG GRHDYWGQGT LVIVSSASTK GPSVFPLAPS SKSTSGGTAA 150
LGCLVKDYFP EPVTVSWNSG ALTSGVHTFP AVLQSSGLYS LSSVVTVPSS 200
SLGTQTYICN VNHKPSNTKV DKKVEPKSCD KTHTCPPCPA PELLGGPSVF 250
LFPPKPKDTL MISRTPEVTC VVVDVSHEDP EVKFNWYVDG VEVHNAKTKP 300
REEQYNSTYR VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP IEKTISKAKG 350
QPREPQVYTL PPSRDELTKN QVSLTCLVKG FYPSDIAVEW ESNGQPENNY 400
KTTPPVLDSD GSFFLYSKLT VDKSRWQQGN VFSCSVMHEG LHNHYTQKSL 450
SLSPGK                                                 456
```

Light chain / Chaîne légère / Cadena ligera

```
EVVLTQSPGT LALPPGERAT LSCRASHRVG STYIAWYQQK SGQAPRRLIY  50
GASNRATDIP DRFSGSGSGT DFTLTIRRLE PEDSAVYYCQ QFSVSPWTFG 100
QGTRVEIKRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK 150
VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ 200
GLSSPVTKSF NRGEC                                       215
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-96	153-209	270-330	376-434
	22"-96"	153"-209"	270"-330"	376"-434"
Intra-L (C23-C104)	23'-89'	135'-195'		
	23'"-89'"	135'"-195'"		
Inter-H-L (h 5-CL 126)	229-215'	229"-215'"		
Inter-H-H (h 11, h 14)	235-235"	238-238"		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
306, 306"

Other post-translational modifications / Autres modifications post-traductionnelles / Otras modificaciones post-traduccionales
H CHS K2 C-terminal lysine clipping:
456, 456"

neladenosoni bialanas
neladenoson bialanate

2-{4-[2-({[2-(4-chlorophenyl)-1,3-thiazol-4-yl]methyl}sulfanyl)-3,5-dicyano-6-(pyrrolidin-1-yl)pyridin-4-yl]phenoxy}ethyl L-alanyl-L-alaninate

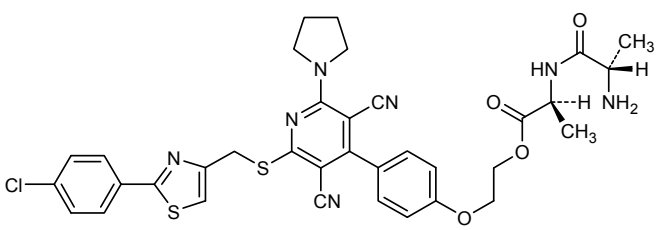
bialanate de néladénoson

L-alanyl-L-alaninate de 2-{4-[2-({[2-(4-chlorophényl)-1,3-thiazol-4-yl]méthyl}sulfanyl)-3,5-dicyano-6-(pyrrolidin-1-yl)pyridin-4-yl]phénoxy}éthyle

bialanato de neladenosón

L-alanil-L-alaninato de 2-{4-[2-({[2-(4-clorofenil)-1,3-tiazol-4-il]metil}sulfanil)-3,5-diciano-6-(pirrolidin-1-il)piridin-4-il]fenoxi}etilo

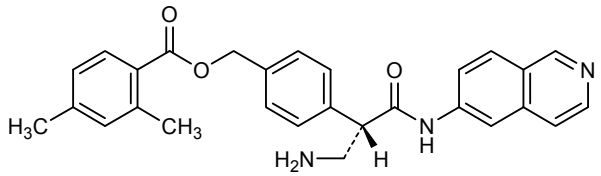
$C_{35}H_{34}ClN_7O_4S_2$



netarsudilum

netarsudil	{4-[(2*S*)-3-amino-1-(isoquinolin-6-ylamino)-1-oxopropan-2-yl]phenyl}methyl 2,4-dimethylbenzoate
nétarsudil	2,4-diméthylbenzoate de {4-[(2*S*)-3-amino-1-(isoquinoléin-6-ylamino)-1-oxopropan-2-yl]phényl}méthyle
netarsudil	2,4-dimetilbenzoato de {4-[(2*S*)-3-amino-1-(isoquinolein-6-ilamino)-1-oxopropan-2-il]fenil}metilo

$C_{28}H_{27}N_3O_3$



obiltoxaximabum #

obiltoxaximab	immunoglobulin G1-kappa, anti-[*Bacillus anthracis* anthrax toxin protective antigen (PA)], chimeric monoclonal antibody; gamma1 heavy chain (1-449) [*Mus musculus* VH (IGHV1-82*01 -(IGHD)-*Homo sapiens* IGHJ4*01) [8.8.12] (1-119) -*Homo sapiens* IGHG1*01, Gm17,1 (CH1 (120-217), hinge (218-232), CH2 (233-342), CH3 (343-447), CHS (448-449)) (120-449)], (222-214')-disulfide with kappa light chain (1'-214') [*Mus musculus* V-KAPPA (IGKV10-96*01 -*Homo sapiens* IGKJ1*01 K127>R (107) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimer (228-228'':231-231'')-bisdisulfide
obiltoxaximab	immunoglobuline G1-kappa, anti-[antigène protecteur (AP) de la toxine de *Bacillus anthracis* de la maladie du charbon], anticorps monoclonal chimérique; chaîne lourde gamma1 (1-449) [*Mus musculus* VH (IGHV1-82*01 -(IGHD)-*Homo sapiens* IGHJ4*01) [8.8.12] (1-119) -*Homo sapiens* IGHG1*01, Gm17,1 (CH1 (120-217), charnière (218-232), CH2 (233-342), CH3 (343-447), CHS (448-449)) (120-449)], (222-214')-disulfure avec la chaîne légère kappa (1'-214') [*Mus musculus* V-KAPPA (IGKV10-96*01 -*Homo sapiens* IGKJ1*01 K127>R (107) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimère (228-228'':231-231'')-bisdisulfure
obiltoxaximab	inmunoglobulina G1-kappa, anti-[antigeno protector (AP) de la toxina de *Bacillus anthracis*, del carbunco], anticuerpo monoclonal quimérico; cadena pesada gamma1 (1-449) [*Mus musculus* VH (IGHV1-82*01 -(IGHD)-*Homo sapiens* IGHJ4*01) [8.8.12] (1-119) -*Homo sapiens* IGHG1*01, Gm17,1 (CH1 (120-217), bisagra (218-232), CH2 (233-342), CH3 (343-447), CHS (448-449)) (120-449)], (222-214')-disulfuro con la cadena ligera kappa (1'-214') [*Mus musculus* V-KAPPA (IGKV10-96*01 -*Homo sapiens* IGKJ1*01 K127>R (107) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimero (228-228'':231-231'')-bisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLQQSGPE LKKPGASVKV SCKDSGYAFS SSWMNWVRQA PGQGLEWIGR  50
IYPGDGDTNY NGKFQGRVTI TADKSSSTAY MELSSLRSED TAVYFCARSG 100
LLRYAMDYWG QGTLVTVSSA STKGPSVFPL APSSKSTSGG TAALGCLVKD 150
YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY 200
ICNVNHKPSN TKVDKKVEPK SCDKTHTCPP CPAPELLGGP SVFLFPPKPK 250
DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VDGVEVHNAK TKPREEQYNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKAL PAPIEKTISK AKGQPREPQV 350
YTLPPSRDEL TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL 400
DSDGSFFLYS KLTVDKSRWQ QGNVFSCSVM HEALHNHYTQ KSLSLSPGK  449
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS LSASVGDRVT ITCRASQDIR NYLNWYQQKP GKAVKLLIYY  50
TSRLLPGVPS RFSGSGSGTD YSLTISSQEQ EDIGTYFCQQ GNTLPWTFGQ 100
GTKVEIRRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-96	146-202	263-323	369-427
	22"-96"	146"-202"	263"-323"	369"-427"
Intra-L (C23-C104)	23'-88'	134'-194'		
	23'"-88'"	134'"-194'"		
Inter-H-L (h 5-CL 126)	222-214'	222"-214'"		
Inter-H-H (h 11, h 14)	228-228"	231-231"		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
299, 299"

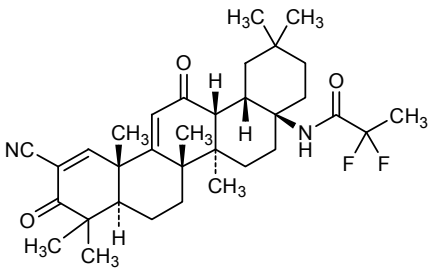
omaveloxolonum

omaveloxolone — *N*-(2-cyano-3,12-dioxo-28-noroleana-1,9(11)-dien-17-yl)-2,2-difluoropropanamide

omavéloxolone — *N*-(2-cyano-3,12-dioxo-28-noroléana-1,9(11)-dién-17-yl)-2,2-difluoropropanamide

omaveloxolona — *N*-(2-ciano-3,12-dioxo-28-noroleana-1,9(11)-dien-17-il)-2,2-difluoropropanamida

$C_{33}H_{44}F_2N_2O_3$



opicinumabum #

opicinumab — immunoglobulin G1-kappa, anti-[*Homo sapiens* LINGO1 (leucine-rich repeat and Ig-like domain-containing nogo receptor-interacting protein 1, LINGO-1, leucine-rich repeat neuronal protein 1, LERN1, leucine-rich repeat neuronal protein 6A, LRRN6A)], *Homo sapiens* monoclonal antibody;
gamma1 heavy chain (1-447) [*Homo sapiens* VH (IGHV3-23*01 (91.80%) -(IGHD)-IGHJ3*02) [8.8.11] (1-118) -IGHG1*01, G1m17,1 (CH1 (119-216), hinge (217-231), CH2 T85.3>A (300) (232-341), CH3 (342-446), CHS K2>del (447)) (119-447)], (221-215')-disulfide with kappa light chain (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-11*01 (96.80%) -IGKJ2*01) [6.3.10] (1'-108') -IGKC*01, Km3 (109'-215')]; dimer (227-227":230-230")-bisdisulfide

opicinumab

immunoglobuline G1-kappa, anti-[*Homo sapiens* LINGO1 (protéine 1 interagissant avec le récepteur de nogo et contenant des répétitions riches en leucine et un domaine Ig-like, LINGO-1, protéine neuronale 1 contenant des répétitions riches en leucine, LERN1, protéine neuronale 6A contenant des répétitions riches en leucine, LRRN6A)], *Homo sapiens* anticorps monoclonal;
chaîne lourde gamma1 (1-447) [*Homo sapiens* VH (IGHV3-23*01 (91.80%) -(IGHD)-IGHJ3*02) [8.8.11] (1-118) -IGHG1*01, G1m17,1 (CH1 (119-216), charnière (217-231), CH2 T85.3>A (300) (232-341), CH3 (342-446), CHS K2>del (447)) (119-447)], (221-215')-disulfure avec la chaîne légère kappa (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-11*01 (96.80%) -IGKJ2*01) [6.3.10] (1'-108') -IGKC*01, Km3 (109'-215')]; dimère (227-227''':230-230''')-bisdisulfure

opicinumab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* LINGO1 (proteína 1 que interacciona con el receptor de nogo y contiene repeticiones ricas en leucina y un dominio Ig-like, LINGO-1, proteína neuronal 1, que contiene repeticiones ricas en leucina,LERN1, proteína neuronal 6A que contiene repeticiones ricas en leucina, LRRN6A)], anticuerpo monoclonal de *Homo sapiens* ;
cadena pesada gamma1 (1-447) [*Homo sapiens* VH (IGHV3-23*01 (91.80%) -(IGHD)-IGHJ3*02) [8.8.11] (1-118) -IGHG1*01, G1m17,1 (CH1 (119-216), bisagra (217-231), CH2 T85.3>A (300) (232-341), CH3 (342-446), CHS K2>del (447)) (119-447)], (221-215')-disulfuro con la cadena ligera kappa (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-11*01 (96.80%) -IGKJ2*01) [6.3.10] (1'-108') -IGKC*01, Km3 (109'-215')]; dímero (227-227''':230-230''')-bisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLLESGGG LVQPGGSLRL SCAASGFTFS AYEMKWVRQA PGKGLEWVSV  50
IGPSGGFTFY ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCATEG 100
DNDAFDIWGQ GTTVTVSSAS TKGPSVFPLA PSSKSTSGGT AALGCLVKDY 150
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTQTYI 200
CNVNHKPSNT KVDKKVEPKS CDKTHTCPPC PAPELLGGPS VFLFPPKPKD 250
TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYNSA 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY 350
TLPPSRDELT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD 400
SDGSFFLYSK LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPG    447
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQQKP GQAPRLLIYD  50
ASNRATGIPA RFSGSGSGTD FTLTISSLEP EDFAVYYCQQ RSNWPMYTFG 100
QGTKLEIKRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK 150
VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ 200
GLSSPVTKSF NRGEC                                       215
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-96	145-201	262-322	368-426
	22''-96''	145''-201''	262''-322''	368''-426''
Intra-L (C23-C104)	23'-88'	135'-195'		
	23'''-88'''	135'''-195'''		
Inter-H-L (h 5-CL 126)	221-215'	221''-215'''		
Inter-H-H (h 11, h 14)	227-227''	230-230''		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
298, 298'' but no glycosylation owing to / mais pas de glycosylation dû à / pero ningún glicosilación debida a H CH2 T85.3>A (300, 300'')

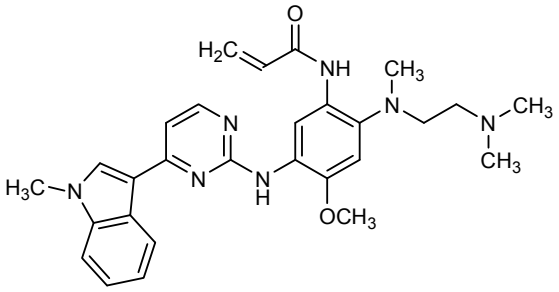
osimertinibum

osimertinib — *N*-(2-{[2-(dimethylamino)ethyl](methyl)amino}-4-methoxy-5-{[4-(1-methyl-1*H*-indol-3-yl)pyrimidin-2-yl]amino}phenyl)prop-2-enamide

osimertinib — *N*-(2-{[2-(diméthylamino)éthyl](méthyl)amino}-4-méthoxy-5-{[4-(1-méthyl-1*H*-indol-3-yl)pyrimidin-2-yl]amino}phényl)prop-2-énamide

osimertinib — *N*-(2-{[2-(dimetilamino)etil](metil)amino}-4-metoxi-5-{[4-(1-metil-1*H*-indol-3-il)pirimidin-2-il]amino}fenil)prop-2-enamida

$C_{28}H_{33}N_7O_2$



pamrevlumabum #

pamrevlumab — immunoglobulin G1-kappa, anti-[*Homo sapiens* CTGF (connective tissue growth factor, CCN family member 2, CCN2, hypertrophic chondrocyte-specific protein 24, HCS24, insulin-like growth factor-binding protein 8, IGFBP-8)], *Homo sapiens* monoclonal antibody;
gamma1 heavy chain (1-449) [*Homo sapiens* VH (IGHV3-48*03 (84.70%) -(IGHD)-IGHJ4*01) [8.7.14] (1-120) -IGHG1*03, G1m3 (CH1 (121-218), hinge (219-233), CH2 (234-343), CH3 (344-448), CHS K2>del (449)) (121-449)], (223-214')-disulfide with kappa light chain (1'-214') [*Homo sapiens* V-KAPPA (IGKV1D-16*01 (100.00%) -IGKJ2*01) [6.3.9] (1'-107') -IGKC*01, Km3 (108'-214')]; dimer(229-229'':232-232'')-bisdisulfide

pamrevlumab — immunoglobuline G1-kappa, anti-[*Homo sapiens* CTGF (facteur de croissance du tissu conjonctif, membre 2 de la famille CCN, CCN2, protéine 24 spécifique de l'hypertrophie des chondrocytes, HCS24, protéine 8 liant le facteur de croissance analogue à l'insuline, IGFBP-8)], *Homo sapiens* anticorps monoclonal;
chaîne lourde gamma1 (1-449) [*Homo sapiens* VH (IGHV3-48*03 (84.70%) -(IGHD)-IGHJ4*01) [8.7.14] (1-120) -IGHG1*03, G1m3 (CH1 (121-218), charnière (219-233), CH2 (234-343), CH3 (344-448), CHS K2>del (449)) (121-449)], (223-214')-disulfure avec la chaîne légère kappa (1'-214') [*Homo sapiens* V-KAPPA (IGKV1D-16*01 (100.00%) -IGKJ2*01) [6.3.9] (1'-107') -IGKC*01, Km3 (108'-214')]; dimère (229-229'':232-232'')-bisdisulfure

pamrevlumab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* CTGF (factor de crecimiento de tejido conjunctivo, miembro 2 de la familia CCN, CCN2, proteína 24 específica de la hipertrofia de condrocitos, HCS24, proteína 8 que ligada el factor de crecimiento análogo a la insulina, IGFBP-8)], *Homo sapiens* anticuerpo monoclonal;
cadena pesada gamma1 (1-449) [*Homo sapiens* VH (IGHV3-48*03 (84.70%) -(IGHD)-IGHJ4*01) [8.7.14] (1-120) -IGHG1*03, G1m3 (CH1 (121-218), bisagra (219-233), CH2 (234-343), CH3 (344-448), CHS K2>del (449)) (121-449)], (223-214')-disulfuro con la cadena ligera kappa (1'-214') [*Homo sapiens* V-KAPPA (IGKV1D-16*01 (100.00%) -IGKJ2*01) [6.3.9] (1'-107') -IGKC*01, Km3 (108'-214')]; dímero (229-229":232-232")-bisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
EGQLVQSGGG LVHPGGSLRL SCAGSGFTFS SYGMHWVRQA PGKGLEWVSG  50
IGTGGGTYST DSVKGRFTIS RDNAKNSLYL QMNSLRAEDM AVYYCARGDY 100
YGSGSFFDCW GQGTLVTVSS ASTKGPSVFP LAPSSKSTSG GTAALGCLVK 150
DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT 200
YICNVNHKPS NTKVDKRVEP KSCDKTHTCP PCPAPELLGG PSVFLFPPKP 250
KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ 350
VYTLPPSREE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPG  449
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS LSASVGDRVT ITCRASQGIS SWLAWYQQKP EKAPKSLIYA  50
ASSLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ YNSYPPTFGQ 100
GTKLEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-95	147-203	264-324	370-428
	22"-95"	147"-203"	264"-324"	370"-428"
Intra-L (C23-C104)	23'-88'	134'-194'		
	23'"-88'"	134'"-194'"		
Inter-H-L (h 5-CL 126)	223-214'	223"-214'"		
Inter-H-H (h 11, h 14)	229-229"	232-232"		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
300, 300"
Fucosylated complex bi-antennary CHO-type glycans/ glycanes de type CHO bi-antennaires complexes fucosylés/ glicanos de tipo CHO biantenarios complejos fucosilados

Other post-translational modifications / Autres modifications post-traductionnelles / Otras modificaciones post-traduccionales
H VH CDR3 C117 (109, 109"): cysteinylation with either Cys, Cys-Gly, glutathione, or no cysteinylation
cystéinylation avec soit Cys, Cys-Gly, glutathion, ou absence de cystéinylation / cisteinilación con Cis, o Cis-Gli, o glutatión, o ausencia de cisteinilación

pegcantratinibum

pegcantratinib

(5'*R*,9*S*,12*R*)-9-methyl-3'-[α-methylpoly(oxyethane-1,2-diyl)]-2,3,11,12-tetrahydro-1*H*,9*H*-spiro[9,12-epoxydiindolo[1,2,3-*fg*:3',2',1'-*kl*]pyrrolo[3,4-*i*][1,6]benzodiazocine-10,5'-oxazolidine]-1,2',4'-trione

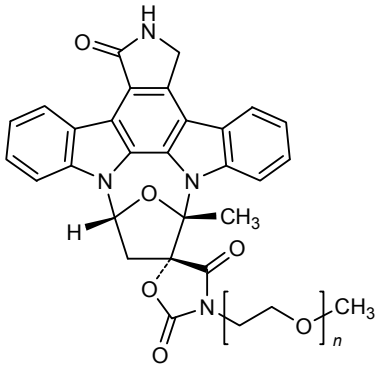
pegcantratinib

(5'*R*,9*S*,12*R*)-9-méthyl-3'-[α-méthylpoly(oxyéthane-1,2-diyl)]-2,3,11,12-tétrahydro-1*H*,9*H*-spiro[9,12-époxydiindolo[1,2,3-*fg*:3',2',1'-*kl*]pyrrolo[3,4-*i*][1,6]benzodiazocine-10,5'-oxazolidine]-1,2',4'-trione

pegcantratinib

(5'*R*,9*S*,12*R*)-9-metil-3'-[α-metilpoli(oxietano-1,2-diil)]-2,3,11,12-tetrahidro-1*H*,9*H*-espiro[9,12-epoxidiindolo[1,2,3-*fg*:3',2',1'-*kl*]pirrolo[3,4-*i*][1,6]benzodiazocina-10,5'-oxazolidina]-1,2',4'-triona

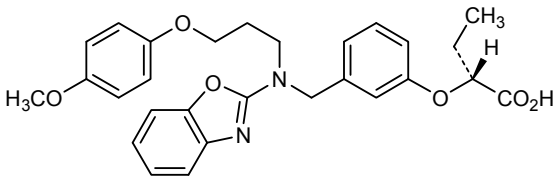
$C_{28}H_{20}N_4O_5[C_2H_4O]_n$



pemafibratum

pemafibrate	(2*R*)-2-[3-({(1,3-benzoxazol-2-yl)[3-(4-methoxyphenoxy) propyl]amino}methyl)phenoxy]butanoic acid
pémafibrate	acide (2*R*)-2-[3-({(1,3-benzoxazol-2-yl)[3-(4-méthoxyphénoxy)propyl]amino}méthyl)phénoxy] butanoïque
pemafibrato	ácido (2*R*)-2-[3-({(benzoxazol-2-il)[3-(4-metoxifenoxi) propil]amino}metil)fenoxi]butanoico

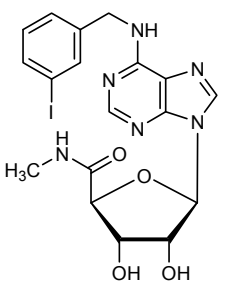
$C_{28}H_{30}N_2O_6$



piclidenosonum

piclidenoson	1-deoxy-1-(6-{[(3-iodophenyl)methyl]amino}-9*H*-purin-9-yl)-*N*-methyl-β-D-ribofuranuronamide
piclidénoson	1-déoxy-1-(6-{[(3-iodophényl)méthyl]amino}-9*H*-purin-9-yl)-*N*-méthyl-β-D-ribofuranuronamide
piclidenosón	1-desoxi-1-(6-{[(3-iodofenil)metil]amino}-9*H*-purin-9-il)-*N*-metil-β-D-ribofuranuronamida

$C_{18}H_{19}IN_6O_4$



plozalizumabum #

plozalizumab	immunoglobulin G1-kappa, anti-[*Homo sapiens* CCR2 (chemokine (C-C motif) receptor 2, C-C chemokine receptor 2, CC-CKR-2, CKR-2, monocyte chemoattractant protein 1 receptor, MCP-1-R, CD192)], humanized monoclonal antibody; gamma1 heavy chain (1-447) [humanized VH (*Homo sapiens* IGHV3-73*01 (86.90%) -(IGHD)-IGHJ1*01) [8.10.8] (1-117) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (118-215), hinge (216-230), CH2 L1.2>A (235), G1>A (237) (231-340), CH3 (341-445), CHS (446-447)) (118-447)], (220-219')-disulfide with kappa light chain (1'-219') [humanized V-KAPPA (*Homo sapiens* IGKV2-30*01 (90.00%) -IGKJ2*01) [11.3.9] (1'-112') -*Homo sapiens* IGKC*01 (113'-219')]; dimer (226-226":229-229")-bisdisulfide
plozalizumab	immunoglobuline G1-kappa, anti-[*Homo sapiens* CCR2 (récepteur 2 de chimiokine (C-C motif), récepteur 2 de chimiokine C-C, CC-CKR-2, CKR-2, récepteur de la protéine 1 chimio-attractive du monocyte, MCP-1-R, CD192)], anticorps monoclonal humanisé; chaîne lourde gamma1 (1-447) [VH humanisé (*Homo sapiens* IGHV3-73*01 (86.90%) -(IGHD)-IGHJ1*01) [8.10.8] (1-117) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (118-215), charnière (216-230), CH2 L1.2>A (235), G1>A (237) (231-340), CH3 (341-445), CHS (446-447)) (118-447)], (220-219')-disulfure avec la chaîne légère kappa (1'-219') [V-KAPPA humanisé (*Homo sapiens* IGKV2-30*01 (90.00%) -IGKJ2*01) [11.3.9] (1'-112') -*Homo sapiens* IGKC*01 (113'-219')]; dimère (226-226":229-229")-bisdisulfure
plozalizumab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* CCR2 (receptor 2 de quimiokina (C-C motif), receptor 2 de quimiokina C-C, CC-CKR-2, CKR-2, receptor de la proteína 1 quimioatrayente de monocitos, MCP-1-R, CD192)], anticuerpo monoclonal humanizado; cadena pesada gamma1 (1-447) [VH humanizada (*Homo sapiens* IGHV3-73*01 (86.90%) -(IGHD)-IGHJ1*01) [8.10.8] (1-117) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (118-215), bisagra (216-230), CH2 L1.2>A (235), G1>A (237) (231-340), CH3 (341-445), CHS (446-447)) (118-447)], (220-219')-disulfuro con la cadena ligera kappa (1'-219') [V-KAPPA humanizado (*Homo sapiens* IGKV2-30*01 (90.00%) -IGKJ2*01) [11.3.9] (1'-112') -*Homo sapiens* IGKC*01 (113'-219')]; dímero (226-226":229-229")-bisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVKPGGSLRL SCAASGFTFS AYAMNWVRQA PGKGLEWVGR  50
IRTKNNNYAT YYADSVKDRF TISRDDSKNT LYLQMNSLKT EDTAVYYCTT 100
FYGNGVWGQG TLVTVSSAST KGPSVFPLAP SSKSTSGGTA ALGCLVKDYF 150
PEPVTVSWNS GALTSGVHTF PAVLQSSGLY SLSSVVTVPS SSLGTQTYIC 200
NVNHKPSNTK VDKKVEPKSC DKTHTCPPCP APELAGAPSV FLFPPKPKDT 250
LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT 350
LPPSRDELTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTPPVLDS 400
DGSFFLYSKL TVDKSRWQQG NVFSCSVMHE ALHNHYTQKS LSLSPGK    447
```

Light chain / Chaîne légère / Cadena ligera

```
DVVMTQSPLS LPVTLGQPAS ISCKSSQSLL DSDGKTFLNW FQQRPGQSPR  50
RLIYLVSKLD SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCWQGTHFP 100
YTFGQGTRLE IKRTVAAPSV FIFPPSDEQL KSGTASVVCL LNNFYPREAK 150
VQWKVDNALQ SGNSQESVTE QDSKDSTYSL SSTLTLSKAD YEKHKVYACE 200
VTHQGLSSPV TKSFNRGEC                                   219
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-98	144-200	261-321	367-425
	22"-98"	144"-200"	261"-321"	367"-425"
Intra-L (C23-C104)	23'-93'	139'-199'		
	23'"-93'"	139'"-199'"		
Inter-H-L (h 5-CL 126)	220-219'	220"-219'"		
Inter-H-H (h 11, h 14)	226-226"	229-229"		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
297, 297"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

ravidasvirum

ravidasvir

methyl *N*-[(2*S*)-1-{(2*S*)-2-[5-(6-{2-[(2*S*)-1-{(2*S*)-2-[(methoxycarbonyl)amino]-3-methylbutanoyl}pyrrolidin-2-yl]-1*H*-imidazol-4-yl}naphthalen-2-yl)-1*H*-benzimidazol-2-yl]pyrrolidin-1-yl}-3-methyl-1-oxobutan-2-yl]carbamate

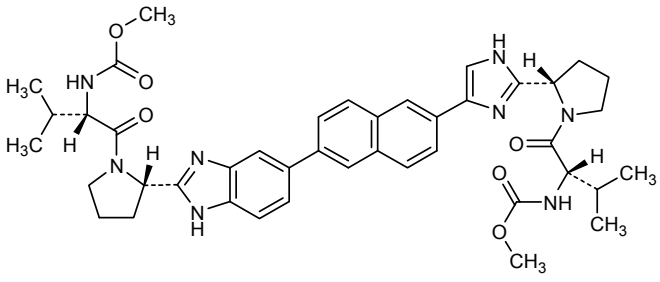
ravidasvir

N-[(2*S*)-1-{(2*S*)-2-[5-(6-{2-[(2*S*)-1-{(2*S*)-2-[(méthoxycarbonyl)amino]-3-méthylbutanoyl}pyrrolidin-2-yl]-1*H*-imidazol-4-yl}naphtalén-2-yl)-1*H*-benzimidazol-2-yl]pyrrolidin-1-yl}-3-méthyl-1-oxobutan-2-yl]carbamate de méthyle

ravidasvir

N-[(2*S*)-1-{(2*S*)-2-[5-(6-{2-[(2*S*)-1-{(2*S*)-2-[(metoxicarbonil)amino]-3-metilbutanoil}pirrolidin-2-il]-1*H*-imidazol-4-il}naftalen-2-il)-1*H*-benzoimidazol-2-il]pirrolidin-1-il}-3-metil-1-oxobutan-2-il]carbamato de metilo

$C_{42}H_{50}N_8O_6$



rinucumabum #

rinucumab — immunoglobulin G4-kappa, anti-[*Homo sapiens* PDGFRB (platelet-derived growth factor receptor beta subunit, PDGFR-1, CD140b)], human monoclonal antibody; gamma4 heavy chain (1-449) [*Homo sapiens* VH (IGHV4-39*01 (92.90%) -(IGHD)-IGHJ5*01) [10.7.14] (1-122) -IGHG4*01 (CH1 (123-220), hinge S10>P (230) (221-232), CH2 (233-342), CH3 (343-447), CHS (448-449)) (123-449)], (136-215')-disulfide with kappa light chain (1'-215') [*Homo sapiens* (V-KAPPA (IGKV3-20*01 (91.70%) -IGKJ3*01) [7.3.9] (1'-108') -IGKC*01, Km3 (109'-215')]; dimer (228-228":231-231")-bisdisulfide

rinucumab — immunoglobuline G4-kappa, anti-[*Homo sapiens* PDGFRB (sous-unité bêta du récepteur du facteur de croissance dérivé des plaquettes, PDGFR-1, CD140b)], anticorps monoclonal humain;
chaîne lourde gamma4 (1-449) [*Homo sapiens* VH (IGHV4-39*01 (92.90%) -(IGHD)-IGHJ5*01) [10.7.14] (1-122) -IGHG4*01 (CH1 (123-220), charnière S10>P (230) (221-232), CH2 (233-342), CH3 (343-447), CHS (448-449) (123-449)], (136-215')-disulfure avec la chaîne légère kappa (1'-215') [*Homo sapiens* (V-KAPPA (IGKV3-20*01 (91.70%) -IGKJ3*01) [7.3.9] (1'-108') -IGKC*01, Km3 (109'-215')]; dimère (228-228":231-231")-bisdisulfure

rinucumab — inmunoglobulina G4-kappa, anti-[*Homo sapiens* PDGFRB (subunidad beta del receptor del factor de crecimiento derivado de plaquetas, PDGFR-1, CD140b)], anticuerpo monoclonal humano;
cadena pesada gamma4 (1-449) [*Homo sapiens* VH (IGHV4-39*01 (92.90%) -(IGHD)-IGHJ5*01) [10.7.14] (1-122) -IGHG4*01 (CH1 (123-220), bisagra S10>P (230) (221-232), CH2 (233-342), CH3 (343-447), CHS (448-449) (123-449)], (136-215')-disulfuro con la cadena ligera kappa (1'-215') [*Homo sapiens* (V-KAPPA (IGKV3-20*01 (91.70%) -IGKJ3*01) [7.3.9] (1'-108') -IGKC*01, Km3 (109'-215')]; dímero (228-228":231-231")-bisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
QLQLQESGPG LVKPSETLSL TCTVSGGSIT SSSYYWGWIR QPPGKGLEWI  50
GSIYYRGSTN YNPSLKSRVT ISVDSSKNQF YLKVSSVTAV DTAVYYCARQ 100
NGAARPSWFD PWGQGTLVTV SSASTKGPSV FPLAPCSRST SESTAALGCL 150
VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ SSGLYSLSSV VTVPSSSLGT 200
KTYTCNVDHK PSNTKVDKRV ESKYGPPCPP CPAPEFLGGP SVFLFPPKPK 250
DTLMISRTPE VTCVVVDVSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV 350
YTLPPSQEEM TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL 400
DSDGSFFLYS RLTVDKSRWQ EGNVFSCSVM HEALHNHYTQ KSLSLSLGK  449
```

Light chain / Chaîne légère / Cadena ligera

```
EIVLTQSPDT ISLSPGERAT LSCRASQSIS SIYLAWYQQK PGQAPRLLIY  50
GASSRVTGIP DRFSVSGSGT DFTLTISRLE PEDFAVYYCQ HYGISPFTFG 100
PGTKVDIRRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK 150
VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ 200
GLSSPVTKSF NRGEC                                       215
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-97	149-205	263-323	369-427
	22"-97"	149"-205"	263"-323"	369"-427"
Intra-L (C23-C104)	23'-89'	135'-195'		
	23'"-89'"	135'"-195'"		
Inter-H-L (CH1 10-CL 126)	136-215'	136"-215'"		
Inter-H-H (h 8, h 11)	228-228"	231-231"		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
299, 299"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

Other post-translational modifications / Autres modifications post-traductionnelles / Otras modificaciones post-traduccionales
H CHS K2 C-terminal lysine clipping:
449, 449"

risankizumabum #

risankizumab

immunoglobulin G1-kappa, anti-[*Homo sapiens* IL23A (interleukin 23 subunit alpha, IL-23A, IL23 subunit p19, IL23p19)], humanized monoclonal antibody; gamma1 heavy chain (1-449) [humanized VH (*Homo sapiens* IGHV1-69*02 (79.40%) -(IGHD)-IGHJ5*01) [8.8.13] (1-120) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (121-218), hinge (219-233), CH2 L1.3>A (237), L1.2>A (238) (234-343), CH3 (344-448), CHS K2>del (449)) (121-449)], (223-214')-disulfide with kappa light chain (1'-214') [humanized V-KAPPA (*Homo sapiens* IGKV1-27*01 (80.00%) -IGKJ2*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimer (229-229":232-232")-bisdisulfide

risankizumab

immunoglobuline G1-kappa, anti-[*Homo sapiens* IL23A (interleukine 23 sous-unité alpha, IL-23A, IL23 sous-unité p19, IL23p19)], anticorps monoclonal humanisé; chaîne lourde gamma1 (1-449) [VH humanisé (*Homo sapiens* IGHV1-69*02 (79.40%) -(IGHD)-IGHJ5*01) [8.8.13] (1-120) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (121-218), charnière (219-233), CH2 L1.3>A (237), L1.2>A (238) (234-343), CH3 (344-448), CHS K2>del (449)) (121-449)], (223-214')-disulfure avec la chaîne légère kappa (1'-214') [V-KAPPA humanisé (*Homo sapiens* IGKV1-27*01 (80.00%) -IGKJ2*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimère (229-229":232-232")-bisdisulfure

risankizumab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* IL23A (interleukina 23 subunidad alfa, IL-23A, IL23 subunidad p19, IL23p19)], anticuerpo monoclonal humanizado; cadena pesada gamma1 (1-449) [VH humanizado (*Homo sapiens* IGHV1-69*02 (79.40%) -(IGHD)-IGHJ5*01) [8.8.13] (1-120) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (121-218), bisagra (219-233), CH2 L1.3>A (237), L1.2>A (238) (234-343), CH3 (344-448), CHS K2>del (449)) (121-449)], (223-214')-disulfuro con la cadena ligera kappa (1'-214') [V-KAPPA humanizado (*Homo sapiens* IGKV1-27*01 (80.00%) -IGKJ2*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dímero (229-229":232-232")-bisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGSSVKV SCKASGYTFT DQTIHWMRQA PGQGLEWIGY  50
IYPRDDSPKY NENFKGKVTI TADKSTSTAY MELSSLRSED TAVYYCAIPD 100
RSGYAWFIYW GQGTLVTVSS ASTKGPSVFP LAPSSKSTSG GTAALGCLVK 150
DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT 200
YICNVNHKPS NTKVDKRVEP KSCDKTHTCP PCPAPEAAGG PSVFLFPPKP 250
KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ 350
VYTLPPSREE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPG  449
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS LSASVGDRVT ITCKASRDVA IAVAWYQQKP GKVPKLLIYW  50
ASTRHTGVPS RFSGSGSRTD FTLTISSLQP EDVADYFCHQ YSSYPFTFGS 100
GTKLEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-96	147-203	264-324	370-428
	22"-96"	147"-203"	264"-324"	370"-428"
Intra-L (C23-C104)	23'-88'	134'-194'		
	23'"-88'"	134'"-194'"		
Inter-H-L (h 5-CL 126)	223-214'	223"-214'"		
Inter-H-H (h 11, h 14)	229-229"	232-232"		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
300, 300"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

rivabazumabum pegolum #

rivabazumab pegol	immunoglobulin Fab' G1-kappa pegylated, anti-[*Pseudomonas aeruginosa* type III secretion system (TTSS) PcrV protein], pegylated humanized monoclonal antibody; gamma1 heavy chain fragment VH-(CH1-hinge) (1-238) [humanized VH (*Homo sapiens* IGHV3-30*06 (92.90%) -(IGHD)-IGHJ6*01) [8.8.17] (1-124) -*Homo sapiens* IGHG1*01 (CH1 (125-222), hinge C5>S (227) (223-237), CH2 (238)) (125-238)], noncovalently associated with kappa light chain (1'-214') [humanized V-KAPPA (*Homo sapiens* IGKV1-5*01 (84.60%) -IGKJ2*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01 C126>S (214') (108'-214')]; conjugated via a linker of the maleimide group (thioether bond with cysteinyl H h 11 (C233) and H h 14 (236)) to two linear chains of methoxy polyethylene glycol 30 (mPEG30).
rivabazumab pégol	immunoglobuline Fab' G1-kappa pégylé, anti-[protéine PcrV du système de sécrétion type III (TTSS) de *Pseudomonas aeruginosa*], anticorps monoclonal humanisé pégylé; fragment VH-(CH1-charnière) de la chaîne lourde gamma1 (1-238) [VH humanisé (*Homo sapiens* IGHV3-30*06 (92.90%) -(IGHD)-IGHJ6*01) [8.8.17] (1-124) -*Homo sapiens* IGHG1*01 (CH1 (125-222), charnière C5>S (227) (223-237), CH2 (238)) (125-238)], associé de manière non covalente avec la chaîne légère kappa (1'-214') [V-KAPPA humanisé (*Homo sapiens* IGKV1-5*01 (84.60%) -IGKJ2*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01 C126>S (214') (108'-214')]; conjugué via un linker du groupe maléimide (liaison thioéther avec les cystéinyl H h 11 (C233) et H h 14 (C236)) à deux chaînes linéaires de méthoxy polyéthylène glycol 30 (mPEG30).
rivabazumab pegol	inmunoglobulina Fab' G1-kappa pegilada, anti-[proteína PcrV del sistema de secreción tipo III (TTSS) de *Pseudomonas aeruginosa*], anticuerpo monoclonal humanizado pegilado; fragmento VH-(CH1-bisagra) de la cadena ligera gamma1 (1-238) [VH humanizado (*Homo sapiens* IGHV3-30*06 (92.90%) -(IGHD)-IGHJ6*01) [8.8.117] (1-124) -*Homo sapiens* IGHG1*01 (CH1(125-222), bisagra C5>S (227) (223-237), CH2 (238)) (125-238)], asociado de modo no covalente con la cadena ligera kappa (1'-214') [V-KAPPA humanizado (*Homo sapiens* IGKV1-5*01 (84.60%) -IGKJ2*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01 C126>S (214') (108'-214')]; conjugado mediante un espaciador del grupo maleimida (unión tioéter con los cisteinil H h 11 (C233) et H h 14 (C236)) con dos cadenas lineales de metoxi polietilen glicol 30 (mPEG30).

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG VVQPGRSLRL SCAASGFTFS NYPMHWVRQA PGKGLEWVAV  50
ISYDGSEKWY ADSVKGRFTI SRDNSKNTLY LEMNSLRPED TAVYYCARNR 100
GDIYYDFTYA MDIWGQGTTV TVSSASTKGP SVFPLAPSSK STSGGTAALG 150
CLVKDYFPEP VTVSWNSGAL TSGVHTFPAV LQSSGLYSLS SVVTVPSSSL 200
GTQTYICNVN HKPSNTKVDK KVEPKSSDKT HTCPPCPA              238
```

Light chain / Chaîne légère / Cadena ligera

```
DIQLTQSPST LSASVGDSVT ITCRASEGVD RWLAWYQQKP GRAPKLLIYD  50
ASTLQSGVPS RFSGSGSGTE FSLTISSLQP DDVATYYCQH FWGTPYTFGQ 100
GTKLEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGES                                       214
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 151-207
Intra-L (C23-C104) 23'-88' 134'-194'

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
None

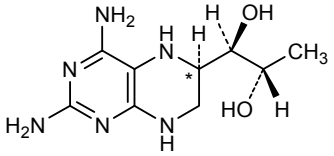
Pegylation site / Site de pegylation / Posiciones de pegilación
H hinge h 11, h 14
C233, C236

ronopterinum
ronopterin — (1*R*,2*S*)-1-[(6*RS*)-2,4-diamino-5,6,7,8-tetrahydropteridin-6-yl]propane-1,2-diol

ronoptérine — (1*R*,2*S*)-1-[(6*RS*)-2,4-diamino-5,6,7,8-tétrahydroptéridin-6-yl]propane-1,2-diol

ronopterina — (1*R*,2*S*)-1-[(6*RS*)-2,4-diamino-5,6,7,8-tetrahidropteridin-6-il]propano-1,2-diol

$C_9H_{16}N_6O_2$



and epimer at C*
et l'épimère en C*
y el epímero al C*

rovalpituzumabum #
rovalpituzumab — immunoglobulin G1-kappa, anti-[*Homo sapiens* DLL3 (delta-like ligand 3)], humanized monoclonal antibody; gamma1 heavy chain (1-447) [humanized VH (*Homo sapiens* IGHV1-18*01 (86.700%) -(IGHD)-IGHJ4*01) [8.8.11] (1-118) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (119-216), hinge (217-231), CH2 (232-341), CH3 (342-446), CHS K2>del (447)) (119-447)], (221-214')-disulfide with kappa light chain (1'-214') [humanized V-KAPPA (*Homo sapiens* IGKV3-15*01 (87.40%) -IGKJ2*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimer (227-227":230-230")-bisdisulfide

rovalpituzumab	immunoglobuline G1-kappa, anti-[*Homo sapiens* DLL3 (delta-like ligand 3)], anticorps monoclonal humanisé; chaîne lourde gamma1 (1-447) [VH humanisé (*Homo sapiens* IGHV1-18*01 (86.700%) -(IGHD)-IGHJ4*01) [8.8.11] (1-118) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (119-216), charnière (217-231), CH2 (232-341), CH3 (342-446), CHS K2>del (447)) (119-447)], (221-214')-disulfure avec la chaîne légère kappa (1'-214') [V-KAPPA humanisé (*Homo sapiens* IGKV3-15*01 (87.40%) -IGKJ2*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimère (227-227":230-230")-bisdisulfure
rovalpituzumab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* DLL3 (delta-like ligando 3)], anticuerpo monoclonal humanizado; cadena pesada gamma1 (1-447) [VH humanizado (*Homo sapiens* IGHV1-18*01 (86.700%) -(IGHD)-IGHJ4*01) [8.8.11] (1-118) -*Homo sapiens* IGHG1*01 G1m17,1 (CH1 (119-216), bisagra(217-231), CH2 (232-341), CH3 (342-446), CHS K2>del (447)) (119-447)], (221-214')-disulfuro con la cadena ligera kappa (1'-214') [V-KAPPA humanizado (*Homo sapiens* IGKV3-15*01 (87.40%) -IGKJ2*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dímero (227-227":230-230")-bisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGASVKV SCKASGYTFT NYGMNWVRQA PGQGLEWMGW  50
INTYTGEPTY ADDFKGRVTM TTDTSTSTAY MELRSLRSDD TAVYYCARIG 100
DSSPSDYWGQ GTLVTVSSAS TKGPSVFPLA PSSKSTSGGT AALGCLVKDY 150
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTQTYI 200
CNVNHKPSNT KVDKKVEPKS CDKTHTCPPC PAPELLGGPS VFLFPPKPKD 250
TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY 350
TLPPSRDELT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD 400
SDGSFFLYSK LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPG    447
```

Light chain / Chaîne légère / Cadena ligera

```
EIVMTQSPAT LSVSPGERAT LSCKASQSVS NDVVWYQQKP GQAPRLLIYY  50
ASNRYTGIPA RFSGSGSGTE FTLTISSLQS EDFAVYYCQQ DYTSPWTFGQ 100
GTKLEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-96	145-201	262-322	368-426
	22"-96"	145"-201"	262"-322"	368"-426"
Intra-L (C23-C104)	23'-88'	134'-194'		
	23'"-88'"	134'"-194'"		
Inter-H-L (h 5-CL 126)	221-214'	221"-214'"		
Inter-H-H (h 11, h 14)	227-227"	230-230"		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación

H CH2 N84.4:
298, 298"

Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

rovalpituzumabum tesirinum #

rovalpituzumab tesirine	immunoglobulin G1-kappa, anti-[*Homo sapiens* DLL3 (delta-like ligand 3)], humanized monoclonal antibody conjugated to the pyrrolobenzodiazepine (PBD) dimer SCX; gamma1 heavy chain (1-447) [humanized VH (*Homo sapiens* IGHV1-18*01 (86.700%) -(IGHD)-IGHJ4*01) [8.8.11] (1-118) -*Homo sapiens* IGHG1*01 G1m17,1 (CH1 (119-216), hinge (217-231), CH2 (232-341), CH3 (342-446), CHS K2>del (447)) (119-447)], (221-214')-disulfide with kappa light chain (1'-214') [humanized V-KAPPA (*Homo sapiens* IGKV3-15*01 (87.40%) -IGKJ2*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimer (227-227":230-230")-bisdisulfide; conjugated, on an average of 2 cysteines, to the pyrrolobenzodiazepine (PBD) dimer SCX, via a cleavable (valine-alanine dipeptide as cathepsine B cleavage site) maleimide type linker containing a spacer PEG (n=8)
rovalpituzumab tésirine	immunoglobuline G1-kappa, anti-[*Homo sapiens* DLL3 (delta-like ligand 3)], anticorps monoclonal humanisé conjugué au dimère de pyrrolobenzodiazépine (PDB) SCX; chaîne lourde gamma1 (1-447) [VH humanisé (*Homo sapiens* IGHV1-18*01 (86.700%) -(IGHD)-IGHJ4*01) [8.8.11] (1-118) -*Homo sapiens* IGHG1*01 G1m17,1 (CH1 (119-216), charnière (217-231), CH2 (232-341), CH3 (342-446), CHS K2>del (447)) (119-447)], (221-214')-disulfure avec la chaîne légère kappa (1'-214') [V-KAPPA humanisé (*Homo sapiens* IGKV3-15*01 (87.40%) -IGKJ2*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimère (227-227":230-230")-bisdisulfure; conjugué, sur 2 cystéines en moyenne, au dimère de pyrrolobenzodiazépine (PBD) SCX, via un linker clivable (dipeptide valine-alanine clivable par la cathepsine B) de type maléimide et comprenant un espaceur PEG (n=8)
rovalpituzumab tesirina	inmunoglobulina G1-kappa, anti-[*Homo sapiens* DLL3 (delta-like ligando 3)], anticuerpo monoclonal humanizado conjugado con el dímero de pirrolobenzodiazepina (PDB) SCX; cadena pesada gamma1 (1-447) [VH humanizado (*Homo sapiens* IGHV1-18*01 (86.700%) -(IGHD)-IGHJ4*01) [8.8.11] (1-118) -*Homo sapiens* IGHG1*01 G1m17,1 (CH1 (119-216), bisagra(217-231), CH2 (232-341), CH3 (342-446), CHS K2>del (447)) (119-447)], (221-214')-disulfuro con la cadena ligera kappa (1'-214') [V-KAPPA humanizado (*Homo sapiens* IGKV3-15*01 (87.40%) -IGKJ2*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dímero (227-227":230-230")-bisdisulfuro; conjugado, en una media de 2 cisteinas, al dímero de pirrolobenzodiazepina (PBD) SCX, mediante un espaciador escindible (dipéptido valina-alanina escindible por la catepsina B) de tipo maleimida que comprende un espaciador PEG (n=8)

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGASVKV SCKASGYTFT NYGMNWVRQA PGQGLEWMGW  50
INTYTGEPTY ADDFKGRVTM TTDTSTSTAY MELRSLRSDD TAVYYCARIG 100
DSSPSDYWGQ GTLVTVSSAS TKGPSVFPLA PSSKSTSGGT AALGCLVKDY 150
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTQTYI 200
CNVNHKPSNT KVDKKVEPKS CDKTHTCPPC PAPELLGGPS VFLFPPKPKD 250
TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY 350
TLPPSRDELT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD 400
SDGSFFLYSK LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPG    447
```

Light chain / Chaîne légère / Cadena ligera

```
EIVMTQSPAT LSVSPGERAT LSCKASQSVS NDVVWYQQKP GQAPRLLIYY  50
ASNRYTGIPA RFSGSGSGTE FTLTISSLQS EDFAVYYCQQ DYTSPWTFGQ 100
GTKLEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

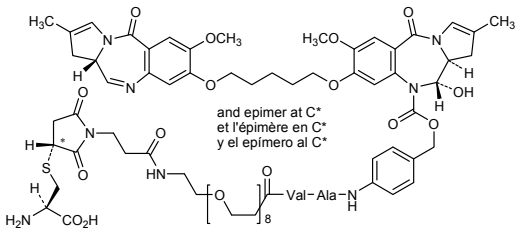
Intra-H (C23-C104)	22-96	145-201	262-322	368-426
	22"-96"	145"-201"	262"-322"	368"-426"
Intra-L (C23-C104)	23'-88'	134'-194'		
	23"'-88"'	134"'-194"'		
Inter-H-L (h 5-CL 126)*	221-214'	221"-214"'		
Inter-H-H (h 11, h 14)*	227-227"	230-230"		

*One or two of the inter-chain disulfide bridges are not present, an average of 2 cysteinyl being conjugated each via a thioether bond to a drug linker.
*Un ou deux des ponts disulfures inter-chaînes ne sont pas présents, 2 cystéinyl en moyenne étant chacun conjugué via une liaison thioéther à un linker-principe actif.
*Faltan uno o dos puentes disulfuro inter-catenarios, una media de 2 cisteinil está conjugada a conectores de principio activo.

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
298, 298"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

Potential modified residues / Résidus modifies potentiels / Restos modificados potenciales

C 214',214"' ; 221,221" ; 227,227" ; 230,230" "*S*-tesirine Cysteine"



sacituzumabum govitecanum #
sacituzumab govitecan

immunoglobulin G1-kappa, anti-[*Homo sapiens* TACSTD2 (tumor-associated calcium signal transducer 2, membrane component chromosome 1 surface marker 1, M1S1, gastrointestinal tumor-associated antigen GA7331, pancreatic carcinoma marker protein GA733-1, epithelial glycoprotein-1, EGP-1, trophoblast antigen-2, cell surface glycoprotein Trop-2, TROP2)], humanized monoclonal antibody conjugated to 7-ethyl-10-hydroxycamptothecin (SN-38), active metabolite of irinotecan;
gamma1 heavy chain (1-451) [humanized VH (*Homo sapiens* IGHV7-4-1*02 (85.70%) -(IGHD)-IGHJ2*01) [8.8.14] (1-121) -*Homo sapiens* IGHG1*03, Gm3 (CH1 (122-219), hinge (220-234), CH2 (235-344), CH3 (345-449), CHS (450-451)) (122-451)], (224-214')-disulfide with kappa light chain (1'-214') [humanized V-KAPPA (*Homo sapiens* IGKV1-9*01 (82.20%) -IGKJ4*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimer (230-230":233-233")-bisdisulfide; conjugated, on an average of 6 cysteinyl, to 7-ethyl-10-hydroxycamptothecin (SN-38), active metabolite of irinotecan (CPT-11, camptothecin-11),via a maleimide-type cleavable linker (carbonate group, self-immolative 4-aminobenzyl alcohol and cathepsine-B-cleavable dipeptide Phe-Lys) and containing a triazoline group and a spacer PEG (n=8).

sacituzumab govitecan	immunoglobuline G1-kappa, anti-[*Homo sapiens* TACSTD2 (transducteur 2 de signaux calciques associé aux tumeurs, composant membranaire du chromosome 1 marqueur de surface 1, M1S1, antigène GA7331 associé aux tumeurs gastrointestinales, protéine GA733-1 marqueur de carcinomes pancréatiques, glycoprotéine épithéliale 1, EGP-1, antigène 2 du trophoblaste, glycoprotéine Trop-2 à la surface des cellules, TROP2)], anticorps monoclonal humanisé conjugué à la 7-éthyl-10-hydroxycamptothécine (SN-38), métabolite actif de l'irinotécan; chaîne lourde gamma1 (1-451) [VH humanisé (*Homo sapiens* IGHV7-4-1*02 (85.70%) -(IGHD)-IGHJ2*01) [8.8.14] (1-121) -*Homo sapiens* IGHG1*03, Gm3 (CH1 (122-219), charnière (220-234), CH2 (235-344), CH3 (345-449), CHS (450-451)) (122-451)], (224-214')-disulfure avec la chaîne légère kappa (1'-214') [V-KAPPA humanisé (*Homo sapiens* IGKV1-9*01 (82.20%) -IGKJ4*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimère (230-230":233-233")-bisdisulfure; conjugué, sur 6 cystéinyl en moyenne, à la 7-éthyl-10-hydroxycamptothécine (SN-38), métabolite actif de l'irinotécan (CPT-11, camptothécine-11),via un linker de type maléimide, clivable (liaison carbonate et 4-aminobenzyl alcool et dipeptide Phe-Lys clivable par la cathepsine B) et comprenant un groupe triazoline et un espaceur PEG (n=8)
sacituzumab govitecán	inmunoglobulina G1-kappa, anti-[*Homo sapiens* TACSTD2 (transductor 2 de señales de calcio asociado a los tumores, componente de membrana del cromosoma 1 marcador de superficie 1, M1S1, antígeno GA7331 asociado a tumores gastrointestinales, proteína GA733-1 marcador de carcinomes pancreáticos glicoproteína epitelial 1, EGP-1, antígeno 2 de trofoblasto, glicoproteína Trop-2 de la superficie celular, TROP2)], anticuerpo monoclonal humanizado conjugado con la 7-etil-10-hidroxicamptotecina (SN-38), metabolito activo del irinotecán; cadena pesada gamma1 (1-451) [VH humanizado (*Homo sapiens* IGHV7-4-1*02 (85.70%) -(IGHD)-IGHJ2*01) [8.8.14] (1-121) -*Homo sapiens* IGHG1*03, Gm3 (CH1 (122-219), bisagra(220-234), CH2 (235-344), CH3 (345-449), CHS (450-451)) (122-451)], (224-214')-disulfuro con la cadena ligera kappa (1'-214') [V-KAPPA humanizado (*Homo sapiens* IGKV1-9*01 (82.20%) -IGKJ4*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dímero (230-230":233-233")-bisdisulfuro; conjugado, en una media de 6 restos cisteinil, con la 7-etil-10-hidroxicamptotecina (SN-38), metabolito activo del irinotecán (CPT-11, camptotecina-11), mediante un espaciadorde tipo maleimida, escindible (enlace carbonato y 4-aminobencil alcohol y dipéptido Phe-Lys escindible por catepsina B) y que comprende un grupo triazolina y un espaciador PEG (n=8).

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLQQSGSE LKKPGASVKV SCKASGYTFT NYGMNWVKQA PGQGLKWMGW  50
INTYTGEPTY TDDFKGRFAF SLDTSVSTAY LQISSLKADD TAVYFCARGG 100
FGSSYWYFDV WGQGSLVTVS SASTKGPSVF PLAPSSKSTS GGTAALGCLV 150
KDYFPEPVTV SWNSGALTSG VHTFPAVLQS SGLYSLSSVV TVPSSSLGTQ 200
TYICNVNHKP SNTKVDKRVE PKSCDKTHTC PPCPAPELLG GPSVFLFPPK 250
PKDTLMISRT PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY 300
NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP 350
QVYTLPPSRE EMTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP 400
VLDSDGSFFL YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG 450
K                                                       451
```

Light chain / Chaîne légère / Cadena ligera

```
DIQLTQSPSS LSASVGDRVS ITCKASQDVS IAVAWYQQKP GKAPKLLIYS  50
ASYRYTGVPD RFSGSGSGTD FTLTISSLQP EDFAVYYCQQ HYITPLTFGA 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104) 22-96 148-204 265-325 371-429
22''-96'' 148''-204'' 265''-325'' 371''-429''
Intra-L (C23-C104) 23'-88' 134'-194'
23'''-88''' 134'''-194'''
Inter-H-L (h 5-CL 126) * 224-214' 224''-214'''
Inter-H-H (h 11, h 14) * 230-230'' 233-233''

*Three of the inter-chain disulfide bridges are not present, an average of 6 cysteinyl being conjugated each via a thioether bond to a drug linker.
*Trois des ponts disulfures inter-chaînes ne sont pas présents, 6 cystéinyl en moyenne étant chacun conjugué via une liaison thioéther à un linker-principe actif.
*Faltan tres puentes disulfuro inter-catenarios, una media de 6 cisteinil está conjugada a conectores de principio activo.

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación

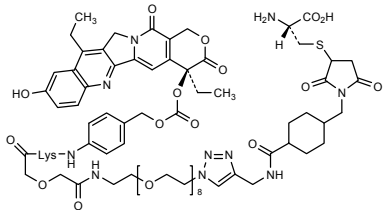
H CH2 N84.4:
301, 301''
Fucosylated complex bi-antennary Sp2/0-type glycans / glycanes de type Sp2/0 bi-antennaires complexes fucosylés / glicanos de tipo Sp2/0 biantenarios complejos fucosilados

Potential modified residues / Résidus modifiés potentiels / Restos modificados potenciales

C*

214'-214'''-224-224''-230-230''-233-233''

* an average of 6 are substituted
* en moyenne, 6 sont substitués
* una media de 6 está sustituída



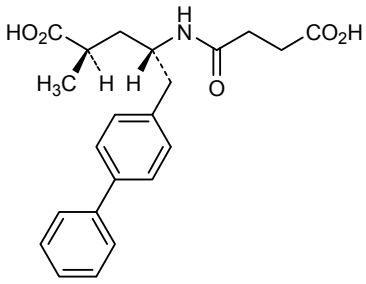
sacubitrilatum

sacubitrilat — (2*R*,4*S*)-5-([1,1'-biphenyl]-4-yl)-4-(3-carboxypropanamido)-2-methylpentanoic acid

sacubitrilate — acide (2*R*,4*S*)-5-([1,1'-biphényl]-4-yl)-4-(3-carboxypropanamido)-2-méthylpentanoïque

sacubitrilat — ácido (2*R*,4*S*)-5-([1,1'-bifenil]-4-il)-4-(3-carboxipropanamido)-2-metilpentanoico

$C_{22}H_{25}NO_5$



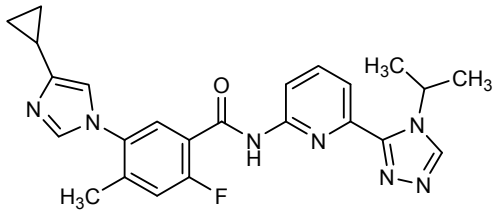
selonsertibum

selonsertib — 5-(4-cyclopropyl-1*H*-imidazol-1-yl)-2-fluoro-4-methyl-*N*-{6-[4-(propan-2-yl)-4*H*-1,2,4-triazol-3-yl]pyridin-2-yl}benzamide

sélonsertib — 5-(4-cyclopropyl-1*H*-imidazol-1-yl)-2-fluoro-4-méthyl-*N*-{6-[4-(propan-2-yl)-4*H*-1,2,4-triazol-3-yl]pyridin-2-yl}benzamide

selonsertib — 5-(4-ciclopropil-1*H*-imidazol-1-il)-2-fluoro-4-metil-*N*-{6-[4-(propan-2-il)-4*H*-1,2,4-triazol-3-il]piridin-2-yl}benzamida

$C_{24}H_{24}FN_7O$



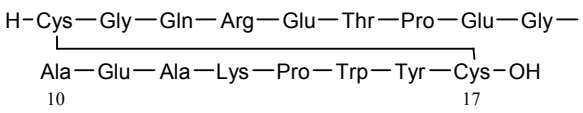
solnatidum

solnatide — L-cysteinylglycyl-[human tumor necrosis factor, membrane form-(178-191)-peptidyl]-L-cysteine, cyclic (1→17)-disulfide
or
L-cysteinylglycyl-[human tumor necrosis factor, soluble form-(102-115)-peptidyl]-L-cysteine, cyclic (1→17)-disulfide

solnatide — (1→17)-disulfure cyclique de L-cystéinylglycyl-[forme membranaire du facteur de nécrose tumorale humain-(178-191)-peptidyl]-L-cystéine
ou
(1→17)-disulfure cyclique de L-cystéinylglycyl-[forme soluble du facteur de nécrose tumorale humain-(102-115)-peptidyl]-L-cystéine

solnatida — (1→17)-disulfuro cíclico de L-cisteinilglicil-[forma de membrana del factor de necrosis tumoral humano-(178-191)-peptidil]-L-cisteina
o
(1→17)-disulfuro cíclico de L-cisteinilglicil-[forma soluble del factor de necrosis tumoral humano-(102-115)-peptidil]-L-cisteina

$C_{82}H_{119}N_{23}O_{27}S_2$



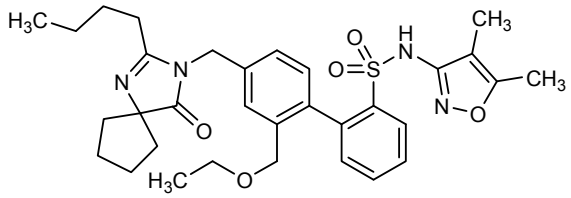
sparsentanum

sparsentan — 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-*N*-(4,5-dimethyl-1,2-oxazol-3-yl)-2'-(ethoxymethyl)[1,1'-biphenyl]-2-sulfonamide

sparsentan — 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-én-3-yl)méthyl]-*N*-(4,5-diméthyl-1,2-oxazol-3-yl)-2'-(éthoxyméthyl)[1,1'-biphényle]-2-sulfonamide

esparsentán — 4'-[(2-butil-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-il)metil]-*N*-(4,5-dimetil-1,2-oxazol-3-il)-2'-(etoximetil)[1,1'-bifenilo]-2-sulfonamida

$C_{32}H_{40}N_4O_5S$



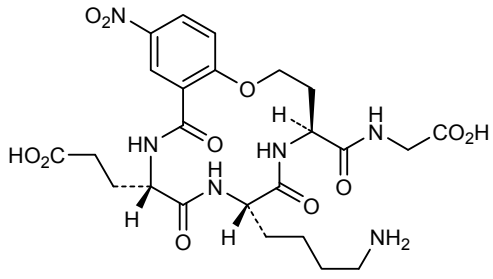
tavilermidum

tavilermide — 3-{(4*S*,7*S*,10*S*)-7-(4-aminobutyl)-4-[(carboxymethyl)carbamoyl]-14-nitro-6,9,12-trioxo-3,4,5,6,7,8,9,10,11,12-decahydro-2*H*-1,5,8,11-benzoxatriazacyclotetradecin-10-yl}propanoic acid

tavilermide — acide 3-{(4*S*,7*S*,10*S*)-7-(4-aminobutyl)-4-[(carboxyméthyl)carbamoyl]-14-nitro-6,9,12-trioxo-3,4,5,6,7,8,9,10,11,12-décahydro-2*H*-1,5,8,11-benzoxatriazacyclotétradécin-10-yl}propanoïque

tavilermida — ácido 3-{(4*S*,7*S*,10*S*)-7-(4-aminobutil)-4-[(carboximetil)carbamoil]-14-nitro-6,9,12-trioxo-3,4,5,6,7,8,9,10,11,12-decahidro-2*H*-1,5,8,11-benzoxatriazaciclotetradecin-10-il}propanoico

$C_{24}H_{32}N_6O_{11}$



tegoprazanum

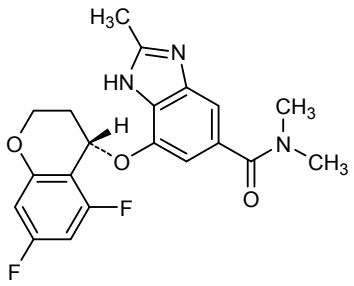
tegoprazan — 7-{[(4*S*)-5,7-difluoro-3,4-dihydro-2*H*-1-benzopyran-4-yl]oxy}-*N*,*N*,2-trimethyl-1*H*-benzimidazole-5-carboxamide

tégoprazan — 7-{[(4*S*)-5,7-difluoro-3,4-dihydro-2*H*-1-benzopyran-4-yl]oxy}-*N*,*N*,2-triméthyl-1*H*-benzimidazole-5-carboxamide

tegoprazán

7-{[(4*S*)-5,7-difluoro-3,4-dihidro-2*H*-1-benzopiran-4-il]oxi}-*N*,*N*,2-trimetil-1*H*-benzoimidazol-5-carboxamida

$C_{20}H_{19}F_2N_3O_3$



tesevatinibum

tesevatinib

N-(3,4-dichloro-2-fluorophenyl)-6-methoxy-7-{[(3a*R*,5*r*,6a*S*)-2-methyloctahydrocyclopenta[*c*]pyrrol-5-yl]methoxy}quinazolin-4-amine

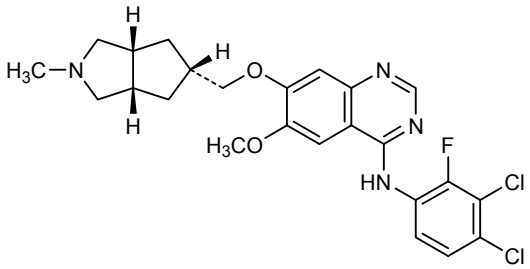
tésévatinib

N-(3,4-dichloro-2-fluorophényl)-6-méthoxy-7-{[(3a*R*,5*r*,6a*S*)-2-méthyloctahydrocyclopenta[*c*]pyrrol-5-yl]méthoxy}quinazolin-4-amine

tesevatinib

N-(3,4-dicloro-2-fluorofenil)- 7-{[(3a*R*,5*r*,6a*S*)-2-metiloctahidrociclopenta[*c*]pirrol-5-il]metoxi}-6-metoxi-quinazolin-4-amina

$C_{24}H_{25}Cl_2FN_4O_2$



tezepelumabum #

tezepelumab

immunoglobulin G2-lambda, anti-[*Homo sapiens* TSLP (thymic stromal lymphopoietin)], *Homo sapiens* monoclonal antibody;
gamma2 heavy chain (1-448) [*Homo sapiens* VH (IGHV3-33*01 (93.90%) -(IGHD)-IGHJ3*02) [8.8.15] (1-122) -IGHG2*01, G2m.. (CH1 (123-220), hinge (221-232), CH2 (233-341), CH3 (342-446), CHS (447-448)) (123-448)], (136-213')-disulfide with lambda light chain (1'-214') [*Homo sapiens* V-LAMBDA (IGLV3-21*02 (96.90%) -IGLJ2*01) [6.3.11] (1'-108') -IGLC2*01 (109'-214')]; dimer (224-224'':225-225'':228-228'':231-231'')-tetrakisdisulfide

tézépelumab

immunoglobuline G2-lambda, anti-[*Homo sapiens* TSLP (lymphopoïétine stromale thymique)], *Homo sapiens* anticorps monoclonal;
chaîne lourde gamma2 (1-448) [*Homo sapiens* VH (IGHV3-33*01 (93.90%) -(IGHD)-IGHJ3*02) [8.8.15] (1-122) -IGHG2*01, G2m.. (CH1 (123-220), charnière (221-232), CH2 (233-341), CH3 (342-446), CHS (447-448)) (123-448)], (136-213')-disulfure avec la chaîne légère lambda (1'-214') [*Homo sapiens* V-LAMBDA (IGLV3-21*02 (96.90%) -IGLJ2*01) [6.3.11] (1'-108') -IGLC2*01 (109'-214')]; dimère (224-224":225-225":228-228":231-231")-tétrakisdisulfure

tezepelumab

inmunoglobulina G2-lambda, anti-[*Homo sapiens* TSLP (linfopoyetina estromal tímica)], *Homo sapiens* anticuerpo monoclonal;
cadena pesada gamma2 (1-448) [*Homo sapiens* VH (IGHV3-33*01 (93.90%) -(IGHD)-IGHJ3*02) [8.8.15] (1-122) -IGHG2*01, G2m.. (CH1 (123-220),bisagra (221-232), CH2 (233-341), CH3 (342-446), CHS (447-448)) (123-448)], (136-213')-disulfuro con la cadena ligera lambda (1'-214') [*Homo sapiens* V-LAMBDA (IGLV3-21*02 (96.90%) -IGLJ2*01) [6.3.11] (1'-108') -IGLC2*01 (109'-214')]; dímero (224-224":225-225":228-228":231-231")-tetrakisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
QMQLVESGGG VVQPGRSLRL SCAASGFTFR TYGMHWVRQA PGKGLEWVAV  50
IWYDGSNKHY ADSVKGRFTI TRDNSKNTLN LQMNSLRAED TAVYYCARAP 100
QWELVHEAFD IWGQGTMVTV SSASTKGPSV FPLAPCSRST SESTAALGCL 150
VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ SSGLYSLSSV VTVPSSNFGT 200
QTYTCNVDHK PSNTKVDKTV ERKCCVECPP CPAPPVAGPS VFLFPPKPKD 250
TLMISRTPEV TCVVVDVSHE DPEVQFNWYV DGVEVHNAKT KPREEQFNST 300
FRVVSVLTVV HQDWLNGKEY KCKVSNKGLP APIEKTISKT KGQPREPQVY 350
TLPPSREEMT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPMLD 400
SDGSFFLYSK LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPGK   448
```

Light chain / Chaîne légère / Cadena ligera

```
SYVLTQPPSV SVAPGQTARI TCGGNNLGSK SVHWYQQKPG QAPVLVVYDD  50
SDRPSWIPER FSGSNSGNTA TLTISRGEAG DEADYYCQVW DSSSDHVVFG 100
GGTKLTVLGQ PKAAPSVTLF PPSSEELQAN KATLVCLISD FYPGAVTVAW 150
KADSSPVKAG VETTTPSKQS NNKYAASSYL SLTPEQWKSH RSYSCQVTHE 200
GSTVEKTVAP TECS                                        214
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-96	149-205	262-322	368-426
	22"-96"	149"-205"	262"-322"	368"-426"
Intra-L (C23-C104)	22'-87'	136'-195'		
	22'"-87'"	136'"-195'"		
Inter-H-L (CH1 10-CL 126)	136-213'	136"-213'"		
Inter-H-H (h 4, h 5, h 8, h 11)	224-224"	225-225"	228-228"	231-231"

*In addition to the isoform A, isoform A/B characterized by an inter-H-H (h 4 - CH1 10) 224-136" and an inter-H-L (h 4- CL 126) 224"-213'", instead of the inter-H-H (h 4 - h 4) 224-224" and of one of the two inter-H-L (CH1 10-CL 126) 136"-213'".
*En plus de l'isoforme A, isoforme A/B caractérisée par un inter-H-H (h 4 - CH1 10) 224-136" et un inter-H-L (h 4- CL 126) 224"-213'", au lieu de l'inter-H-H (h 4 - h 4) 224-224" et de l'un des deux inter-H-L (CH1 10-CL 126) 136"-213'".
* además de la isoforma A, isoforma A/B caracterizado por un inter-H-H (h 4 - CH1 10) 224-136" y un inter-H-L (h 4- CL 126) 224"-213'", en lugar del inter-H-H (h 4 - h 4) 224-224" y uno de los dos inter-H-L (CH1 10-CL 126) 136"-213'".

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
298, 298"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de typeCHO bi-antennaires complexes fucosylés / glicanosde tipo CHO biantenarios complejos fucosilados

tisotumabum #
tisotumab

immunoglobulin G1-kappa, anti-[*Homo sapiens* F3 (coagulation factor III (thromboplastin, tissue factor), CD142)], *Homo sapiens* monoclonal antibody;

	gamma1 heavy chain (1-448) [*Homo sapiens* VH (IGHV3-23*01 (93.90%) -(IGHD)-IGHJ5*01) [8.8.11] (1-118) -IGHG1*03, G1m3 (CH1 (119-216), hinge (217-231), CH2 (232-341), CH3 (342-446), CHS (447-448)) (119-448)], (221-214')-disulfide with kappa light chain (1'-214') [*Homo sapiens* V-KAPPA (IGKV1D-16*01 (96.80%) -IGKJ2*01) [6.3.9] (1'-107') -IGKC*01, Km3 (108'-214')]; dimer (227-227":230-230")-bisdisulfide
tisotumab	immunoglobuline G1-kappa, anti-[*Homo sapiens* F3 (facteur de coagulation III (thromboplastine, facteur tissulaire), CD142)], *Homo sapiens* anticorps monoclonal; chaîne lourde gamma1 (1-448) [*Homo sapiens* VH (IGHV3-23*01 (93.90%) -(IGHD)-IGHJ5*01) [8.8.11] (1-118) -IGHG1*03, G1m3 (CH1 (119-216), charnière (217-231), CH2 (232-341), CH3 (342-446), CHS (447-448)) (119-448)], (221-214')-disulfure avec la chaîne légère kappa (1'-214') [*Homo sapiens* V-KAPPA (IGKV1D-16*01 (96.80%) -IGKJ2*01) [6.3.9] (1'-107') -IGKC*01, Km3 (108'-214')]; dimère (227-227":230-230")-bisdisulfure
tisotumab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* F3 (factor de coagulación III (tromboplastina, factor tisular), CD142)], *Homo sapiens* anticuerpo monoclonal ; cadena pesada gamma1 (1-448) [*Homo sapiens* VH (IGHV3-23*01 (93.90%) -(IGHD)-IGHJ5*01) [8.8.11] (1-118) -IGHG1*03, G1m3 (CH1 (119-216), bisagra (217-231), CH2 (232-341), CH3 (342-446), CHS (447-448)) (119-448)], (221-214')-disulfuro con la cadena ligera kappa (1'-214') [*Homo sapiens* V-KAPPA (IGKV1D-16*01 (96.80%) -IGKJ2*01) [6.3.9] (1'-107') -IGKC*01, Km3 (108'-214')]; dímero (227-227":230-230")-bisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLLESGGG LVQPGGSLRL SCAASGFTFS NYAMSWVRQA PGKGLEWVSS  50
ISGSGDYTYY TDSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARSP 100
WGYYLDSWGQ GTLVTVSSAS TKGPSVFPLA PSSKSTSGGT AALGCLVKDY 150
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTQTYI 200
CNVNHKPSNT KVDKRVEPKS CDKTHTCPPC PAPELLGGPS VFLFPPKPKD 250
TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY 350
TLPPSREEMT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD 400
SDGSFFLYSK LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPGK   448
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPPS LSASAGDRVT ITCRASQGIS SRLAWYQQKP EKAPKSLIYA  50
ASSLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ YNSYPYTFGQ 100
GTKLEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-96	145-201	262-322	368-426
	22"-96"	145"-201"	262"-322"	368"-426"
Intra-L (C23-C104)	23'-88'	134'-194'		
	23'"-88'"	134'"-194'"		
Inter-H-L (h 5-CL 126)	221-214'	221"-214'"		
Inter-H-H (h 11, h 14)	227-227"	230-230"		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
298, 298"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

tisotumabum vedotinum #

tisotumab vedotin	immunoglobulin G1-kappa, anti-[*Homo sapiens* F3 (coagulation factor III (thromboplastin, tissue factor), CD142)], *Homo sapiens* monoclonal antibody conjugated to auristatin E; gamma1 heavy chain (1-448) [*Homo sapiens* VH (IGHV3-23*01 (93.90%) -(IGHD)-IGHJ5*01) [8.8.11] (1-118) -IGHG1*03, G1m3 (CH1 (119-216), hinge (217-231), CH2 (232-341), CH3 (342-446), CHS (447-448)) (119-448)], (221-214')-disulfide with kappa light chain (1'-214') [*Homo sapiens* V-KAPPA (IGKV1D-16*01 (96.80%) -IGKJ2*01) [6.3.9] (1'-107') -IGKC*01, Km3 (108'-214')]; dimer (227-227'':230-230'')-bisdisulfide; conjugated, on an average of 3 to 4 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker For the *vedotin* part, please refer to the document *"INN for pharmaceutical substances: Names for radicals, groups and others"*.*
tisotumab védotine	immunoglobuline G1-kappa, anti-[*Homo sapiens* F3 (facteur de coagulation III (thromboplastine, facteur tissulaire), CD142)], *Homo sapiens* anticorps monoclonal conjugué à l'auristatine E; chaîne lourde gamma1 (1-448) [*Homo sapiens* VH (IGHV3-23*01 (93.90%) -(IGHD)-IGHJ5*01) [8.8.11] (1-118) -IGHG1*03, G1m3 (CH1 (119-216), charnière (217-231), CH2 (232-341), CH3 (342-446), CHS (447-448)) (119-448)], (221-214')-disulfure avec la chaîne légère kappa (1'-214') [*Homo sapiens* V-KAPPA (IGKV1D-16*01 (96.80%) -IGKJ2*01) [6.3.9] (1'-107') -IGKC*01, Km3 (108'-214')]; dimère (227-227'':230-230'')-bisdisulfure; conjugué, sur 3 à 4 cystéinyl en moyenne, au monométhylauristatine E (MMAE), via un linker clivable de type maléimidocaproyl-valyl-citrullinyl-*p*-aminobenzyloxycarbonyl (mc-val-cit-PABC) Pour la partie *védotine*, veuillez-vous référer au document *"INN for pharmaceutical substances: Names for radicals, groups and others"*.*
tisotumab vedotina	inmunoglobulina G1-kappa, anti-[*Homo sapiens* F3 (factor de coagulación III (tromboplastina, factor tisular), CD142)], *Homo sapiens* anticuerpo monoclonal conjugado con la auristatina E; cadena pesada gamma1 (1-448) [*Homo sapiens* VH (IGHV3-23*01 (93.90%) -(IGHD)-IGHJ5*01) [8.8.11] (1-118) -IGHG1*03, G1m3 (CH1 (119-216), bisagra(217-231), CH2 (232-341), CH3 (342-446), CHS (447-448)) (119-448)], (221-214')-disulfuro con la cadena ligera kappa (1'-214') [*Homo sapiens* V-KAPPA (IGKV1D-16*01 (96.80%) -IGKJ2*01) [6.3.9] (1'-107') -IGKC*01, Km3 (108'-214')]; dímero (227-227'':230-230'')-bisdisulfuro; conjugado, en 3 - 4 restos cisteinil por termino medio, con monometilauristatina E (MMAE), mediante un espaciador escindible de tipo maleimidocaproil-valil-citrulinil-*p*-aminobenciloxicarbonil (mc-val-cit-PABC) La fracción *vedotina*, la pueden encontrar en el documento *"INN for pharmaceutical substances: Names for radicals, groups and others"*.*

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLLESGGG LVQPGGSLRL SCAASGFTFS NYAMSWVRQA PGKGLEWVSS  50
ISGSGDYTYY TDSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARSP 100
WGYYLDSWGQ GTLVTVSSAS TKGPSVFPLA PSSKSTSGGT AALGCLVKDY 150
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTQTYI 200
CNVNHKPSNT KVDKRVEPKS CDKTHTCPPC PAPELLGGPS VFLFPPKPKD 250
TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY 350
TLPPSREEMT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD 400
SDGSFFLYSK LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPGK   448
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPPS LSASAGDRVT ITCRASQGIS SRLAWYQQKP EKAPKSLIYA  50
ASSLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ YNSYPYTFGQ 100
GTKLEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104) 22-96 145-201 262-322 368-426
22"-96" 145"-201" 262"-322" 368"-426"
Intra-L (C23-C104) 23'-88' 134'-194'
23'"-88'" 134'"-194'"
Inter-H-L (h 5-CL 126)* 221-214' 221"-214'"
Inter-H-H (h 11, h 14)* 227-227" 230-230"

*Two or three of the inter-chain disulfide bridges are not present, an average of 3 to 4 cysteinyl being conjugated each via a thioether bond to a drug linker.
*Deux ou trois des ponts disulfures inter-chaînes ne sont pas présents, 3 à 4 cystéinyl en moyenne étant chacun conjugué via une liaison thioéther à un linker-principe actif.
*Faltan dos o tres puentes disulfuro inter-catenarios, una media de 3 a 4 cisteinil está conjugada a conectores de principio activo.

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
298, 298"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

trevogrumabum #

trevogrumab — immunoglobulin G4-kappa, anti-[*Homo sapiens* MSTN (myostatin, growth differentiation factor 8, GDF8, GDF-8)], human monoclonal antibody;
gamma4 heavy chain (1-447) [*Homo sapiens* VH (IGHV3-23*01 (93.90%) -(IGHD)-IGHJ6*01 T125>I (117) [8.8.13] (1-120) -IGHG4*01 (CH1 (121-218), hinge S10>P (228) (219-230), CH2 (231-340), CH3 (341-445), CHS (446-447)) (121-447)], (134-214')-disulfide with kappa light chain (1'-214') [*Homo sapiens* (V-KAPPA (IGKV1-27*01 (90.50%) -IGKJ4*01) [6.3.9] (1'-107') -IGKC*01, Km3 (108'-214')]; dimer (226-226":229-229")-bisdisulfide

trévogrumab — immunoglobuline G4-kappa, anti-[*Homo sapiens* MSTN (myostatine, facteur de croissance et de différenciation 8, GDF8, GDF-8)], anticorps monoclonal humain;
chaîne lourde gamma4 (1-447) [*Homo sapiens* VH (IGHV3-23*01 (93.90%) -(IGHD)-IGHJ6*01 T125>I (117) [8.8.13] (1-120) -IGHG4*01 (CH1 (121-218), charnière S10>P (228) (219-230), CH2 (231-340), CH3 (341-445), CHS (446-447)) (121-447)], (134-214')-disulfure avec la chaîne légère kappa (1'-214') [*Homo sapiens* (V-KAPPA (IGKV1-27*01 (90.50%) -IGKJ4*01) [6.3.9] (1'-107') -IGKC*01, Km3 (108'-214')]; dimère (226-226":229-229")-bisdisulfure

trevogrumab — inmunoglobulina G4-kappa, anti-[*Homo sapiens* MSTN (miostatina, factor de crecimiento y diferenciación 8, GDF8, GDF-8)], anticuerpo monoclonal humano;

cadena pesada gamma4 (1-447) [*Homo sapiens* VH (IGHV3-23*01 (93.90%) -(IGHD)-IGHJ6*01 T125>I (117) [8.8.13] (1-120) -IGHG4*01 (CH1 (121-218), bisagra S10>P (228) (219-230), CH2 (231-340), CH3 (341-445), CHS (446-447)) (121-447)], (134-214')-disulfuro con la cadena ligera kappa (1'-214') [*Homo sapiens* (V-KAPPA (IGKV1-27*01 (90.50%) -IGKJ4*01) [6.3.9] (1'-107') -IGKC*01, Km3 (108'-214')]; dímero (226-226":229-229")-bisdisulfuro

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQVLESGGD LVQPGGSLRL SCAASGFTFS AYAMTWVRQA PGKGLEWVSA  50
ISGSGGSAYY ADSVKGRFTI SRDNSKNTVY LQMNSLRAED TAVYYCAKDG 100
AWKMSGLDVW GQGTTVIVSS ASTKGPSVFP LAPCSRSTSE STAALGCLVK 150
DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGTKT 200
YTCNVDHKPS NTKVDKRVES KYGPPCPPCP APEFLGGPSV FLFPPKPKDT 250
LMISRTPEVT CVVVDVSQED PEVQFNWYVD GVEVHNAKTK PREEQFNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKGLPS SIEKTISKAK GQPREPQVYT 350
LPPSQEEMTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTPPVLDS 400
DGSFFLYSRL TVDKSRWQEG NVFSCSVMHE ALHNHYTQKS LSLSLGK    447
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPAS LSASVGDRVT ITCRASQDIS DYLAWYQQKP GKIPRLLIYT  50
TSTLQSGVPS RFRGSGSGTD FTLTISSLQP EDVATYYCQK YDSAPLTFGG 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-96	147-203	261-321	367-425
	22"-96"	147"-203"	261"-321"	367"-425"
Intra-L (C23-C104)	23'-88'	134'-194'		
	23'"-88'"	134'"-194'"		
Inter-H-L (CH1 10-CL 126)	134-214'	134"-214'"		
Inter-H-H (h 8, h 11)	226-226"	229-229"		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
297, 297"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

tucatinibum
tucatinib

N^6-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-*N*^{4}-[3-methyl-4-([1,2,4]triazolo[1,5-*a*]pyridin-7-yloxy)phenyl]quinazoline-4,6-diamine

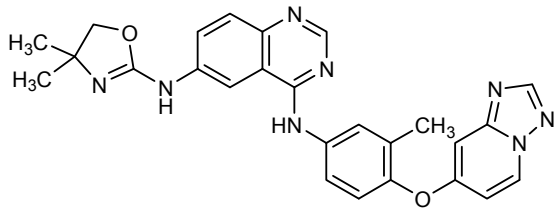
tucatinib

N^6-(4,4-diméthyl-4,5-dihydrooxazol-2-yl)-*N*^{4}-[3-méthyl-4-([1,2,4]triazolo[1,5-*a*]pyridin-7-yloxy)phényl]quinazoline-4,6-diamine

tucatinib

N^6-(4,4-dimetil-4,5-dihidrooxazol-2-il)-*N*^{4}-[3-metil-4-([1,2,4]triazolo[1,5-*a*]piridin-7-iloxi)fenil]quinazolina-4,6-diamina

$C_{26}H_{24}N_8O_2$

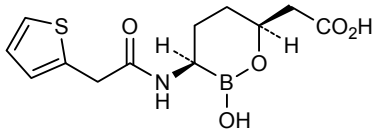


vaborbactamum
vaborbactam

{(3*R*,6*S*)-2-hydroxy-3-[2-(thiophen-2-yl)acetamido]-1,2-oxaborinan-6-yl}acetic acid

vaborbactam	acide {(3*R*,6*S*)-2-hydroxy-3-[2-(thiophén-2-yl)acétamido]-1,2-oxaborinan-6-yl}acétique
vaborbactam	ácido {(3*R*,6*S*)-2-hidroxi-3-[2-(tiofen-2-il)acetamido]-1,2-oxaborinan-6-il}acético

$C_{12}H_{16}BNO_5S$



vadastuximabum talirinum #

vadastuximab talirine	immunoglobulin G1-kappa, anti-[*Homo sapiens* CD33 (sialic acid binding Ig-like lectin 3, SIGLEC3, SIGLEC-3, gp67, p67)], chimeric monoclonal antibody conjugated to the pyrrolobenzodiazepine (PDB) dimer SGD-1882; gamma1 heavy chain (1-447) [*Mus musculus* VH (IGHV1-85*01 -(IGHD)-IGHJ4*01) [8.8.10] (1-117) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (118-215), hinge (216-230), CH2 S3>C (239) (231-340), CH3 (341-445), CHS (446-447)) (118-447)], (220-214')-disulfide with kappa light chain (1'-214') [*Mus musculus* V-KAPPA (IGKV14-111*01 -*Homo sapiens* IGKJ4*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimer (226-226":229-229")-bisdisulfide; conjugated, on two site-specific drug attachment engineered cysteines (C239, C239"), to a maximum of 2 pyrrolobenzodiazepine (PDB) dimers SGD-1882, each via a cleavable (valine-alanine dipeptide as cathepsine B cleavage site) maleimidocaproyl type linker
vadastuximab talirine	immunoglobuline G1-kappa, anti-[*Homo sapiens* CD33 (lectine 3 de type Ig-like liant l'acide sialique, SIGLEC3, SIGLEC-3, gp67, p67)], anticorps monoclonal chimérique conjugué au dimère de pyrrolobenzodiazépine (PDB) SGD-1882; chaîne lourde gamma1 (1-447) [*Mus musculus* VH (IGHV1-85*01 -(IGHD)-IGHJ4*01) [8.8.10] (1-117) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (118-215), charnière (216-230), CH2 S3>C (239) (231-340), CH3 (341-445), CHS (446-447)) (118-447)], (220-214')-disulfure avec la chaîne légère kappa (1'-214') [*Mus musculus* V-KAPPA (IGKV14-111*01 -*Homo sapiens* IGKJ4*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimère (226-226":229-229")-bisdisulfure; conjugué, sur deux cystéines sites de fixation spécifique du linker-produit actif (C239, C239"), à un maximum de 2 dimères de pyrrolobenzodiazépine (PDB) SGD-1882, chacun via un linker clivable (dipeptide valine-alanine clivable par la cathepsine B) de type maléimidocaproyle

vadastuximab talirina

inmunoglobulina G1-kappa, anti-[*Homo sapiens* CD33 (lectina 3 de tipo Ig-like que liga el ácido siálico, SIGLEC3, SIGLEC-3, gp67, p67)], anticuerpo monoclonal quimérico conjugado con el dimero de pyirolobenzodiazepina (PDB) SGD-1882;
cadena pesada gamma1 (1-447) [*Mus musculus* VH (IGHV1-85*01 -(IGHD)-IGHJ4*01) [8.8.10] (1-117) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (118-215), bisagra (216-230), CH2 S3>C (239) (231-340), CH3 (341-445), CHS (446-447)) (118-447)], (220-214')-disulfuro con la cadena ligera kappa (1'-214') [*Mus musculus* V-KAPPA (IGKV14-111*01 -*Homo sapiens* IGKJ4*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dímero (226-226":229-229")-bisdisulfuro; conjugado, en dos císteinas sitios de fijación específicos del linker-producto activo (C239, C239"), con un máximo de 2 dímeros de pirrolobenzodiazepina (PDB) SGD-1882, cada uno mediante un espaciador escindible (dipéptido valina-alanina escindible por la catepsina B) de tipo maleimidocaproil

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGASVKV SCKASGYTFT NYDINWVRQA PGQGLEWIGW  50
IYPGDGSTKY NEKFKAKATL TADTSTSTAY MELRSLRSDD TAVYYCASGY 100
EDAMDYWGQG TTVTVSSAST KGPSVFPLAP SSKSTSGGTA ALGCLVKDYF 150
PEPVTVSWNS GALTSGVHTF PAVLQSSGLY SLSSVVTVPS SSLGTQTYIC 200
NVNHKPSNTK VDKKVEPKSC DKTHTCPPCP APELLGGPCV FLFPPKPKDT 250
LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT 350
LPPSRDELTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTPPVLDS 400
DGSFFLYSKL TVDKSRWQQG NVFSCSVMHE ALHNHYTQKS LSLSPGK    447
```

Light chain / Chaîne légère / Cadena ligera

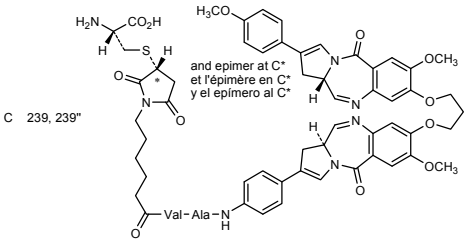
```
DIQMTQSPSS LSASVGDRVT INCKASQDIN SYLSWFQQKP GKAPKTLIYR  50
ANRLVDGVPS RFSGSGSGQD YTLTISSLQP EDFATYYCLQ YDEFPLTFGG 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-96	144-200	261-321	367-425
	22"-96"	144"-200"	261"-321"	367"-425"
Intra-L (C23-C104)	23'-88'	134'-194'		
	23'"-88'"	134'"-194'"		
Inter-H-L (h 5-CL 126)	220-214'	220"-214'"		
Inter-H-H (h 11, h 14)	226-226"	229-229"		

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
297, 297"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

Modified residues / Résidus modifiés / Restos modificados



velmanasum alfa #
velmanase alfa

human lysosomal alpha-mannosidase (Laman, EC3.2.1.24, mannosidase alpha class 2B member 1), produced in CHO (Chinese Hamster Ovary) cells, alfa glycoform

velmanase alfa

alpha mannosidase lysosomiale humaine (Laman, EC3.2.1.24, membre 1 de classe 2B de la mannosidase alpha), produite par la cellule ovarienne de hamster chinois (CHO), forme glycosylée alfa

velmanasa alfa

alfa manosidasa lisosómica humana (Laman, EC3.2.1.24, miembro 1 de la clase 2B de la manosidasa alfa), producida por células ováricas de hamster chino (CHO), forma glicosilada alfa

```
GGYETCPTVQ  PNMLNVHLLP  HTHDDVGWLK  TVDQYFYGIK  NDIQHAGVQY 50
ILDSVISALL  ADPTRRFIYV  EIAFFSRWWH  QQTNATQEVV  RDLVRQGRLE 100
FANGGWVMND  EAATHYGAIV  DQMTLGLRFL  EDTFGNDGRP  RVAWHIDPFG 150
HSREQASLFA  QMGFDGFFFG  RLDYQDKWVR  MQKLEMEQVW  RASTSLKPPT 200
ADLFTGVLPN  GYNPPRNLCW  DVLCVDQPLV  EDPRSPEYNA  KELVDYFLNV 250
ATAQGRYYRT  NHTVMTMGSD  FQYENANMWF  KNLDKLIRLV  NAQQAKGSSV 300
HVLYSTPACY  LWELNKANLT  WSVKHDDFFP  YADGPHQFWT  GYFSSRPALK 350
RYERLSYNFL  QVCNQLEALV  GLAANVGPYG  SGDSAPLNEA  MAVLQHHDAV 400
SGTSRQHVAN  DYARQLAAGW  GPCEVLLSNA  LARLRGFKDH  FTFCQQLNIS 450
ICPLSQTAAR  FQVIVYNPLG  RKVNWMVRLP  VSEGVFVVKD  PNGRTVPSDV 500
VIFPSSDSQA  HPPELLFSAS  LPALGFSTYS  VAQVPRWKPQ  ARAPQPIPRR 550
SWSPALTIEN  EHIRATFDPD  TGLLMEIMNM  NQQLLLPVRQ  TFFWYNASIG 600
DNESDQASGA  YIFRPNQQKP  LPVSRWAQIH  LVKTPLVQEV  HQNFSAWCSQ 650
VVRLYPGQRH  LELEWSVGPI  PVGDTWGKEV  ISRFDTPLET  KGRFYTDSNG 700
REILERRRDY  RPTWKLNQTE  PVAGNYYPVN  TRIYITDGNM  QLTVLTDRSQ 750
GGSSLRDGSL  ELMVHRRLLK  DDGRGVSEPL  MENGSGAWVR  GRHLVLLDTA 800
QAAAAGHRLL  AEQEVLAPQV  VLAPGGGAAY  NLGAPPRTQF  SGLRRDLPPS 850
VHLLTLASWG  PEMVLLRLEH  QFAVGEDSGR  NLSAPVTLNL  RDLFSTFTIT 900
RLQETTLVAN  QLREAASRLK  WTTNTGPTPH  QTPYQLDPAN  ITLEPMEIRT 950
FLASVQWKEV  DG                                          962
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
6-309 219-224 363-423 444-452

Glycosylation sites (potential) / Sites de glycosylation (potentiels) / Posiciones de glicosilación (potenciales)
Asn-84 Asn-261 Asn-318 Asn-448 Asn-596 Asn-602
Asn-643 Asn-717 Asn-783 Asn-881 Asn-940

vesatolimodum
vesatolimod

4-amino-2-butoxy-8-({3-[(pyrrolidin-1-yl)methyl]phenyl}methyl)-7,8-dihydropteridin-6(5*H*)-one

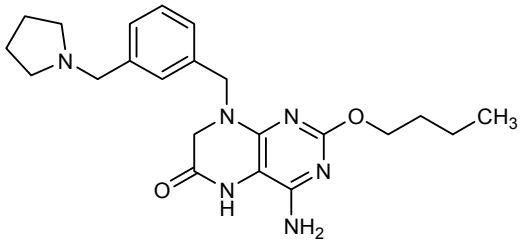
vésatolimod

4-amino-2-butoxy-8-({3-[(pyrrolidin-1-yl)méthyl]phényl}méthyl)-7,8-dihydroptéridin-6(5*H*)-one

vesatolimod

4-amino-2-butoxi-8-({3-[(pirrolidin-1-il)metil]fenil}metil)-7,8-dihidropteridin-6(5*H*)-ona

$C_{22}H_{30}N_6O_2$



vistusertibum
vistusertib

3-{2,4-bis[(3*S*)-3-methylmorpholin-4-yl]pyrido[2,3-*d*]pyrimidin-7-yl}-*N*-methylbenzamide

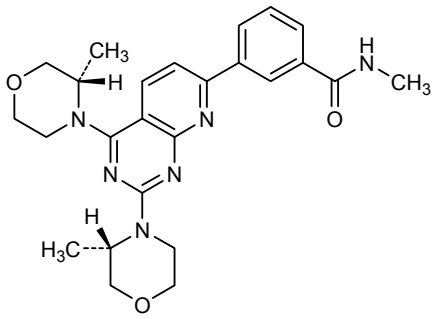
vistusertib

3-{2,4-bis[(3*S*)-3-méthylmorpholin-4-yl]pyrido[2,3-*d*]pyrimidin-7-yl}-*N*-méthylbenzamide

vistusertib

3-{2,4-bis[(3*S*)-3-metilmorfolin-4-il]pirido[2,3-*d*]pirimidin-7-il}-*N*-metilbenzamida

$C_{25}H_{30}N_6O_3$



volanesorsenum

volanesorsen

all-P-ambo-2'-*O*-(2-methoxyethyl)-*P*-thioadenylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-*P*-thioguanylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiouridylyl-(3'→5')-2'-deoxy-5-methyl-*P*-thiocytidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-deoxy-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-deoxy-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-deoxy-*P*-thioadenylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-deoxy-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-*P*-thioadenylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyluridine

volanésorsen

tout-P-ambo-2'-*O*-(2-méthoxyéthyl)-*P*-thioadénylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-*P*-thioguanylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiouridylyl-(3'→5')-2'-déoxy-5-méthyl-*P*-thiocytidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-déoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-déoxy-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-déoxy-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-déoxy-*P*-thioadénylyl-(3'→5')-2'-déoxy-*P*-thioguanylyl-(3'→5')-2'-déoxy-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-*P*-thioadénylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyluridine

volanesorsén

todo-P-ambo-2'-*O*-(2-metoxietil)-*P*-tioadenilil-(3'→5')-2'-*O*-(2-metoxietil)-*P*-tioguanilil-(3'→5')-2'-*O*-(2-metoxietil)-5-metil-*P*-tiocitidilil-(3'→5')-2'-*O*-(2-metoxietil)-5-metil-*P*-tiouridilil-(3'→5')-2'-*O*-(2-metoxietil)-5-metil-*P*-tiouridilil-(3'→5')-2'-desoxi-5-metil-*P*-tiocitidilil-(3'→5')-*P*-tiotimidilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-5-metil-*P*-tiocitidilil-(3'→5')-2'-desoxi-5-metil-*P*-tiocitidilil-(3'→5')-2'-desoxi-*P*-tioadenilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-2'-desoxi-5-metil-*P*-tiocitidilil-(3'→5')-2'-*O*-(2-metoxietil)-5-metil-*P*-tiouridilil-(3'→5')-2'-*O*-(2-metoxietil)-5-metil-*P*-tiouridilil-(3'→5')-2'-*O*-(2-metoxietil)-*P*-tioadenilil-(3'→5')-2'-*O*-(2-metoxietil)-5-metiluridina

$C_{230}H_{320}N_{63}O_{125}P_{19}S_{19}$

(3'-5')(P-thio)(Amoe-Gmoe-mCmoe-Tmoe-Tmoe-dmC-dT-dT-dG-dT-dmC-dmC-dA-dG-dmC-Tmoe-Tmoe-Tmoe-Amoe-Tmoe)
d (as prefix) = 2'-deoxy
m (as prefix) = 5-methyl
moe (as suffix) = 2'-O-[2-methoxy(ethyl)]

volixibatum

volixibat

N-(3-*O*-benzyl-6-*O*-sulfo-β-D-glucopyranosyl)-*N'*-{3-[(3*S*,4*R*,5*R*)-3-butyl-7-(dimethylamino)-3-ethyl-4-hydroxy-1,1-dioxo-2,3,4,5-tetrahydro-1*H*-1λ^6-benzothiepin-5-yl]phenyl}urea

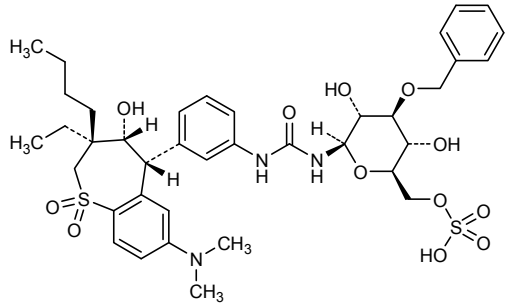
volixibat

N-(3-*O*-benzyl-6-*O*-sulfo-β-D-glucopyranosyl)-*N'*-{3-[(3*S*,4*R*,5*R*)-3-butyl-7-(diméthylamino)-3-éthyl-4-hydroxy-1,1-dioxo-2,3,4,5-tétrahydro-1*H*-1λ^6-benzothiépin-5-yl]phényl}urée

volixibat

N-(3-*O*-bencil-6-*O*-sulfo-β-D-glucopiranosil)-*N'*-{3-[(3*S*,4*R*,5*R*)-3-butil-7-(dimetilamino)-3-etil-4-hidroxi-1,1-dioxo-2,3,4,5-tetrahidro-1*H*-1λ^6-benzotiepin-5-il]fenil}urea

$C_{38}H_{51}N_3O_{12}S_2$



voxilaprevirum

voxilaprevir

(1a*R*,5*S*,8*S*,9*S*,10*R*,22a*R*)-5-*tert*-butyl-*N*-{(1*R*,2*R*)-2-(difluoromethyl)-1-[(1-methylcyclopropanesulfonyl)carbamoyl]cyclopropyl}-9-ethyl-18,18-difluoro-14-methoxy-3,6-dioxo-1,1a,3,4,5,6,9,10,18,19,20,21,22,22a-tetradecahydro-8*H*-7,10-methanocyclopropa[18,19][1,10,3,6]dioxadiazacyclononadecino[11,12-*b*]quinoxaline-8-carboxamide

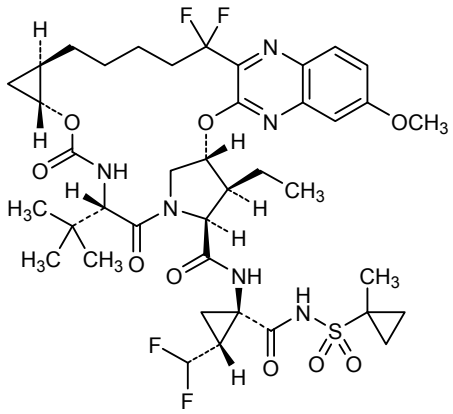
voxilaprévir

(1a*R*,5*S*,8*S*,9*S*,10*R*,22a*R*)-5-*tert*-butyl-*N*-{(1*R*,2*R*)-2-(difluorométhyl)-1-[(1-méthylcyclopropanesulfonyl) carbamoyl]cyclopropyl}-9-éthyl-18,18-difluoro-14-méthoxy-3,6-dioxo-1,1a,3,4,5,6,9,10,18,19,20,21,22,22a-tétradécahydro-8*H*-7,10-méthanocyclopropa[18,19] [1,10,3,6]dioxadiazacyclononadécino[11,12-*b*]quinoxaline-8-carboxamide

voxilaprevir

(1a*R*,5*S*,8*S*,9*S*,10*R*,22a*R*)-5-*terc*-butil-*N*-{(1*R*,2*R*)-2-(difluorometil)-1-[(1-metilciclopropanosulfonil) carbamoil]ciclopropil}-9-etil-18,18-difluoro-14-metoxi-3,6-dioxo-1,1a,3,4,5,6,9,10,18,19,20,21,22,22a-tetradecahidro-8*H*-7,10-metanociclopropa[18,19][1,10,3,6] dioxadiazaciclononadecino[11,12-*b*]quinoxalina-8-carboxamida

$C_{40}H_{52}F_4N_6O_9S$



zidebactamum

zidebactam

(1*R*,2*S*,5*R*)-7-oxo-2-{2-[(3*R*)-piperidine-3-carbonyl]hydrazinecarbonyl}-1,6-diazabicyclo[3.2.1]octan-6-yl hydrogen sulfate

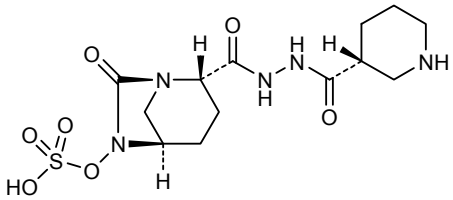
zidébactam

hydrogénosulfate de (1*R*,2*S*,5*R*)-7-oxo-2-{2-[(3*R*)-pipéridine-3-carbonyl]hydrazinecarbonyl}-1,6-diazabicyclo[3.2.1]octan-6-yle

zidebactam

hidrógenosulfato de (1*R*,2*S*,5*R*)-7-oxo-2-{2-[(3*R*)-piperidina-3-carbonil]hidrazinacarbonil}-1,6-diazabiciclo[3.2.1]octan-6-ilo

$C_{13}H_{21}N_5O_7S$



AMENDMENTS TO PREVIOUS LISTS
MODIFICATIONS APPORTÉES AUX LISTES ANTÉRIEURES
MODIFICACIONES A LAS LISTAS ANTERIORES

Recommended International Nonproprietary Names (Rec. INN): List 73
Dénominations communes internationales recommandées (DCI Rec.): Liste 73
Denominaciones Comunes Internacionales Recomendadas (DCI Rec.): Lista 73
(WHO Drug Information, Vol. 29, No. 1, 2015)

p. 64 **albenatidum#**
albenatide
albénatide
albenatida

replace the description and the structure by the following ones
remplacer la description et la structure par les suivantes
sustitúyase la descripción y la estructura por las siguientes

S$^{3.34}$-[1-(3-{[2-(2-{2-[exendin-4 *Heloderma suspectum* precursor-(48-86)-peptidyl (exenatidyl)-L-lysinamide-*N*^{6}-yl]-2-oxo-ethoxy}ethoxy)ethyl]amino}-3-oxopropyl)-2,5-dioxopyrrolidin-3-yl]human serum albumin.
Peptide is synthetic, and human serum albumin is produced in *Saccharomyces cerevisiae*.

S$^{3.34}$-[1-(3-{[2-(2-{2-[précurseur de l'exendin-4 de *Heloderma suspectum*-(48-86)-peptidyl (exénatidyle)-L-lysinamide-*N*^{6}-yl]-2-oxo-éthoxy}éthoxy)éthyl]amino}-3-oxopropyl)-2,5-dioxopyrrolidin-3-yl]albumine sérique humaine.
Le peptide est synthétique et l'albumine sérique humaine est produite par *Saccharomyces cerevisiae*.

S$^{3.34}$-[1-(3-{[2-(2-{2-[precursor de la exendina-4 de *Heloderma suspectum*-(48-86)-peptidil (exenatidilo)-L-lisinamida-*N*^{6}-il]-2-oxo-etoxi}etoxi)etil]amino}-3-oxopropil)-2,5-dioxopirrolidin-3-il]albúmina sérica humana.
El péptido es sintético y la albúmina sérica humana la produce el *Saccharomyces cerevisiae*.

Human albumin / Albumine humaine / Albumina humana

```
DAHKSEVAHR FKDLGEENFK ALVLIAFAQY LQQCPFEDHV KLVNEVTEFA 50
KTCVADESAE NCDKSLHTLF GDKLCTVATL RETYGEMADC CAKQEPERNE 100
CFLQHKDDNP NLPRLVRPEV DVMCTAFHDN EETFLKKYLY EIARRHPYFY 150
APELLFFAKR YKAAFTECCQ AADKAACLLP KLDELRDEGK ASSAKQRLKC 200
ASLQKFGERA FKAWAVARLS QRFPKAEFAE VSKLVTDLTK VHTECCHGDL 250
LECADDRADL AKYICENQDS ISSKLKECCE KPLLEKSHCI AEVENDEMPA 300
DLPSLAADFV ESKDVCKNYA EAKDVFLGMF LYEYARRHPD YSVVLLLRLA 350
KTYETTLEKC CAAADPHECY AKVFDEFKPL VEEPQNLIKQ NCELFEQLGE 400
YKFQNALLVR YTKKVPQVST PTLVEVSRNL GKVGSKCCKH PEAKRMPCAE 450
DYLSVVLNQL CVLHEKTPVS DRVTKCCTES LVNRRPCFSA LEVDETYVPK 500
EFNAETFTFH ADICTLSEKE RQIKKQTALV ELVKHKPKAT KEQLKAVMDD 550
FAAFVEKCCK ADDKETCFAE EGKKLVAASQ AALGL                 585
```

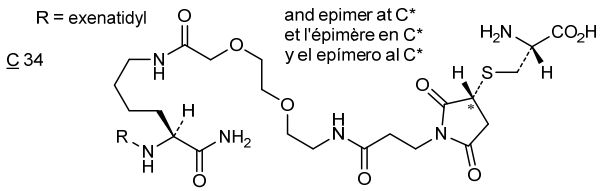
Exenatidyl / Exénatidyle / Exenatidilo

```
HGEGTFTSDL SKQMEEEAVR LFIEWLKNGG PSSGAPPPS-            39
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

53-62 75-91 90-101 124-169 168-177 200-246 245-253 265-279 278-289
316-361 360-369 392-438 437-448 461-477 476-487 514-559 558-567

Modified residue / Résidu modifié / Resto modificado



p. 103 - 104

pegvaliasum #

pegvaliase
pegvaliase
pegvaliasa

replace the description by the following one
remplacer la description par la suivante
sustitúyase la descripción por la siguiente

pegylated, recombinant DNA derived *Anabaena variabilis* phenylalanine ammonia lyase mutein (S 503, S 565), produced in *Escherichia coli*:
[503-serine (C>S),565-serine (C>S)]phenylalanine ammonia-lyase (EC 4.3.1.24) *Anabaena variabilis* in which at least 6 lysyl residues are N^6-{6-[ω-methoxypoly(oxyethylene)]hexanoyl} substituted

mutéine (S 503, S 565) de phénylalanine ammoniac-lyase de *Anabaena variabilis*, pégylée, produite par *Escherichia coli* à partir d'ADN recombinant:
[503-sérine (C>S),565-sérine (C>S)]phénylalanine ammoniac-lyase (EC 4.3.1.24) de *Anabaena variabilis* dont au moins 6 résidus lysyl sont N^6-{6-[ω-méthoxypoly(oxyéthylène)]hexanoyl} substitués

muteína (S 503, S 565) de la fenilalanina amoniaco-liasa de *Anabaena variabilis*, pegilada, producida en *Escherichia coli* a partir de ADN recombinante:
[503-serina (C>S),565-serina (C>S)]fenilalanina amoniaco-liasa (EC 4.3.1.24) de *Anabaena variabilis* de cuyos restos lisil 5, por término medio, están N^6-{6-[ω-metoxipoli(oxietileno)]hexanoil} substituidos

Recommended International Nonproprietary Names (Rec. INN): List 74
Dénominations communes internationales recommandées (DCI Rec.): Liste 74
Denominaciones Comunes Internacionales Recomendadas (DCI Rec.): Lista 74
(WHO Drug Information, Vol. 29, No. 3, 2015)

p. 421

somapacitanum #

somapacitan
somapacitan
somapacitán

replace the description and the structure by the following ones
remplacer la description et la structure par les suivantes
sustitúyase la descripción y la estructura por las siguientes

[101-{*S*-[(8*S*,22*S*,27*S*)-8,22,27-tricarboxy-2,10,19,24,29,38,42,42,44-nonaoxo-59-(1*H*-tetrazol-5-yl)-12,15,31,34-tetraoxa-42λ^6-thia-3,9,18,23,28,37,43-heptaazanonapentacontan-1-yl]-L-cysteine}]human somatropin

[101-{*S*-[(8*S*,22*S*,27*S*)-8,22,27-tricarboxy-2,10,19,24,29,38,42,42,44-nonaoxo-59-(1*H*-tétrazol-5-yl)-12,15,31,34-tétraoxa-42λ^6-thia-3,9,18,23,28,37,43-heptaazanonapentacontan-1-yl]-L-cystéine}]somatropine humaine

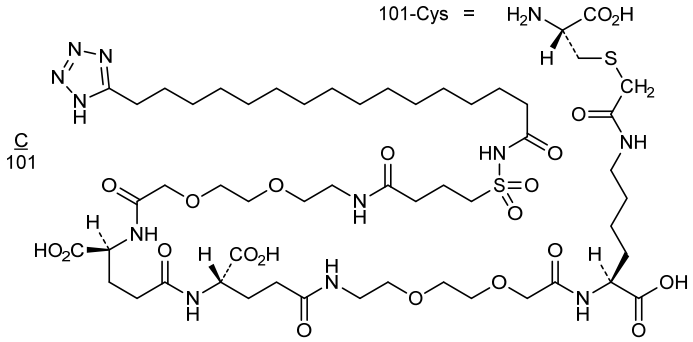
[101-{*S*-[(8*S*,22*S*,27*S*)-8,22,27-tricarboxi-2,10,19,24,29,38,42,42,44-nonaoxo-59-(1*H*-tetrazol-5-il)-12,15,31,34-tetraoxa-42λ^6-tia-3,9,18,23,28,37,43-heptaazanonapentacontan-1-il]-L-cisteina}]somatropina humana

Sequence / Séquence / Secuencia

```
FPTIPLSRLF DNAMLRAHRL HQLAFDTYQE FEEAYIPKEQ KYSFLQNPQT 50
SLCFSESIPT PSNREETQQK SNLELLRISL LLIQSWLEPV QFLRSVFANS 100
CVYGASDSNV YDLLKDLEEG IQTLMGRLED GSPRTGQIFK QTYSKFDTNS 150
HNDDALLKNY GLLYCFRKDM DKVETFLRIV QCRSVEGSCG F          191
```

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
53-165 182-189

Modified residue / Résidu modifié / Resto modificado



Electronic structure available on Mednet: http://mednet.who.int/
Structure électronique disponible sur Mednet: http://mednet.who.int/
Estructura electrónica disponible en Mednet: http://mednet.who.int/
* http://www.who.int/medicines/services/inn/publication/en/

Procedure and Guiding Principles / Procédure et Directives / Procedimientos y principios generales

The text of the *Procedures for the Selection of Recommended International Nonproprietary Names for Pharmaceutical Substances* and *General Principles for Guidance in Devising International Nonproprietary Names for Pharmaceutical Substances* will be reproduced in proposed INN lists only.

Les textes de la *Procédure à suivre en vue du choix de dénominations communes internationales recommandées pour les substances pharmaceutiques* et des *Directives générales pour la formation de dénominations communes internationales applicables aux substances pharmaceutiques* seront publiés seulement dans les listes des DCI proposées.

El texto de los *Procedimientos de selección de denominaciones comunes internacionales recomendadas para las sustancias farmacéuticas* y de los *Principios generales de orientación para formar denominaciones comunes internacionales para sustancias farmacéuticas* aparece solamente en las listas de DCI propuestas.

目次

1.　毒薬・劇薬等の指定審査資料のまとめ 2

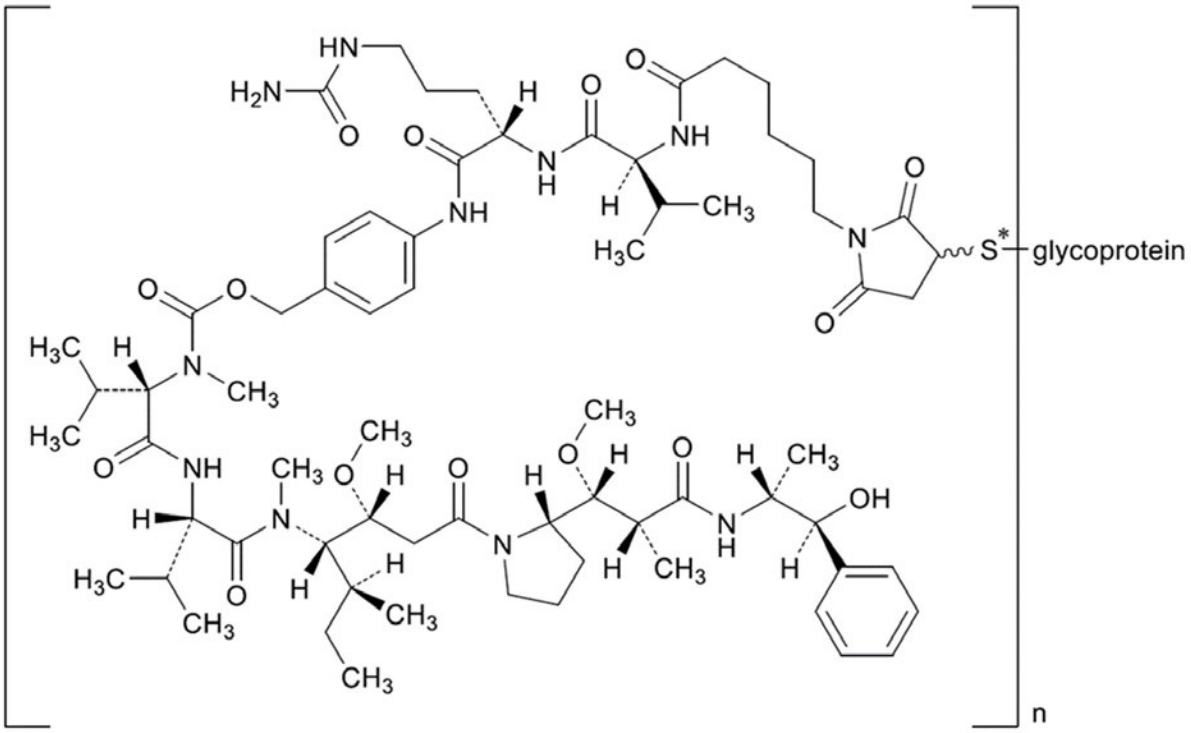
1. 毒薬・劇薬等の指定審査資料のまとめ

<table>
<tr><td>化学名・別名</td><td>チソツマブ　ベドチンは，抗体薬物複合体（分子量：約 153,000）であり，遺伝子組換えモノクローナル抗体の平均 4 個の Cys 残基に，モノメチルアウリスタチン E とリンカーからなるベドチン（(3RS)-1-(6-{[(2S)-1-{[(2S)-5-(カルバモイルアミノ)-1-{4-[({[(2S)-1-{[(2S)-1-{[(3R,4S,5S)-1-{(2S)-2-[(1R,2R)-3-{[(1S,2R)-1-ヒドロキシ-1-フェニルプロパン-2-イル]アミノ}-1-メトキシ-2-メチル-3-オキソプロピル]ピロリジン-1-イル}-3-メトキシ-5-メチル-1-オキソヘプタン-4-イル](メチル)アミノ}-3-メチル-1-オキソブタン-2-イル]アミノ}-3-メチル-1-オキソブタン-2-イル](メチル)カルバモイル}オキシ)メチル]アニリノ}-1-オキソペンタン-2-イル]アミノ}-3-メチル-1-オキソブタン-2-イル]アミノ}-6-オキソヘキシル)-2,5-ジオキソピロリジン-3-イル基（C₆₈H₁₀₆N₁₁O₁₅；分子量：1,317.63））が結合している．抗体部分は，ヒト組織因子に対する遺伝子組換えヒト IgG1 モノクローナル抗体であり，チャイニーズハムスター卵巣細胞により産生される．タンパク質部分は，448 個のアミノ酸残基からなる H 鎖（γ1 鎖）2 本及び 214 個のアミノ酸残基からなる L 鎖（κ 鎖）2 本で構成される糖タンパク質（分子量：約 147,500）である．
別名　チソツマブ　ベドチン（遺伝子組換え）</td></tr>
<tr><td>構造式</td><td>別紙のとおり</td></tr>
<tr><td>効能・効果</td><td>がん化学療法後に増悪した進行又は再発の子宮頸癌</td></tr>
<tr><td>用法・用量</td><td>通常、成人にはチソツマブ　ベドチン（遺伝子組換え）として 1 回 2 mg/kg（体重）を 30 分以上かけて、3 週間間隔で点滴静注する。ただし、1 回量として 200 mg を超えないこと。</td></tr>
<tr><td>劇薬等の指定</td><td></td></tr>
<tr><td>市販名及び有効成分・分量</td><td>原体：チソツマブ　ベドチン（遺伝子組換え）
製剤：テブダック点滴静注用 40mg
（1 バイアル中、チソツマブ　ベドチン（遺伝子組換え）40 mg 含有）</td></tr>
<tr><td>毒性</td><td>反復投与毒性
<table>
<tr><th>動物種</th><th>投与期間</th><th>投与経路</th><th>投与量</th><th>無毒性量</th><th>主な所見</th></tr>
<tr><td>カニクイザル</td><td>13 週間（3 週間間隔で 5 回）</td><td>静脈内</td><td>1、3、5 mg/kg</td><td>1 mg/kg（雌）
<1 mg/kg（雄）</td><td>- 死亡
- 末梢血白血球数（主として好中球）及び赤血球パラメーター低下、並びに顆粒球低形成及び胸骨骨髄の細胞密度低下
- アルブミン濃度低値及びグロブリン濃度高値に伴うアルブミン／グロブリン比低下、並びにハプトグロビン濃度高値
- 皮膚反応（潰瘍性皮膚炎、皮下混合型炎症性細胞浸潤、上皮水腫性変性／過形成、及び出血）
- 精巣の小型化、精子数減少／完全消失、精子運動低下及び関連する病理組織学的検査所見（精巣の精細管萎縮、並びに精巣</td></tr>
</table></td></tr>
</table>

<table>
<tr><td></td><td>
<table>
<tr><td></td><td></td><td></td><td></td><td></td><td>上体の無精子、精子減少及び上皮空胞化）</td></tr>
</table>
</td></tr>
<tr><td>副作用</td><td>国際共同第 III 相 SGNTV-003 試験において、本剤投与を受けた 250 例中 219 例（87.6%）に副作用が認められた。主な副作用は以下のとおりであった。
<table>
<tr><td>副作用の種類（基本語）</td><td>発現例数（%）n=250</td></tr>
<tr><td>結膜炎</td><td>76 (30.4%)</td></tr>
<tr><td>悪心</td><td>73 (29.2%)</td></tr>
<tr><td>末梢性感覚ニューロパチー</td><td>67 (26.8%)</td></tr>
<tr><td>脱毛症</td><td>61 (24.4%)</td></tr>
<tr><td>鼻出血</td><td>57 (22.8%)</td></tr>
</table>
</td></tr>
<tr><td>会社</td><td>ジェンマブ株式会社　製剤：輸入</td></tr>
</table>

【別紙】

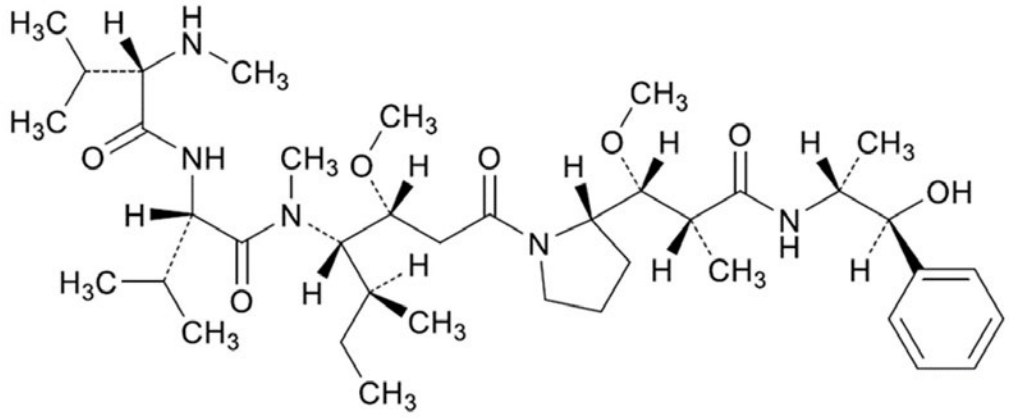
ベドチン部位の構造式



n は平均 4 である

*抗体部分の Cys 残基の硫黄原子

モノメチルアウリスタチン E の構造式



$C_{6418}H_{9906}N_{1710}O_{2022}S_{44}$（タンパク質部分，4 本鎖）

H 鎖　$C_{2183}H_{3367}N_{579}O_{674}S_{16}$

L 鎖　$C_{1026}H_{1590}N_{276}O_{337}S_{6}$

アミノ酸配列及びジスルフィド結合

L 鎖

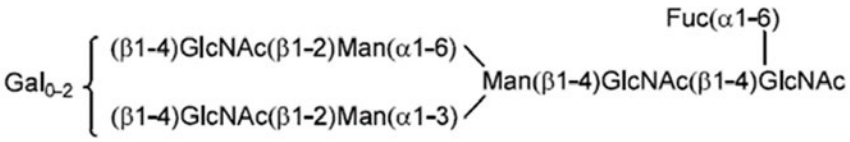
DIQMTQSPPS LSASAGDRVT ITCRASQGIS SRLAWYQQKP EKAPKSLIYA
ASSLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ YNSYPYTFGQ
GTKLEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG
LSSPVTKSFN RGEC

H 鎖

EVQLLESGGG LVQPGGSLRL SCAASGFTFS NYAMSWVRQA PGKGLEWVSS
ISGSGDYTYY TDSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARSP
WGYYLDSWGQ GTLVTVSSAS TKGPSVFPLA PSSKSTSGGT AALGCLVKDY
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTQTYI
CNVNHKPSNT KVDKRVEPKS CDKTHTCPPC PAPELLGGPS VFLFPPKPKD
TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYNST
YRVVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY
TLPPSREEMT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD
SDGSFFLYSK LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPGK

H 鎖 E1：部分的ピログルタミン酸；H 鎖 N298：糖鎖結合；H 鎖 K448：部分的プロセシング
L 鎖 C214，H 鎖 C221，H 鎖 C227，H 鎖 C230：薬物結合可能部位
L 鎖 C214－H 鎖 C221，H 鎖 C227－H 鎖 C227，H 鎖 C230－H 鎖 C230：ジスルフィド結合

主な糖鎖の推定構造



別紙様式１

生物由来製品又は特定生物由来製品の指定資料のまとめ

一般名：	チソツマブ　ベドチン（遺伝子組換え）
販売名：	テブダック点滴静注用 40mg
申請者：	ジェンマブ株式会社
効能・効果：	がん化学療法後に増悪した進行又は再発の子宮頸癌
用法・用量：	通常、成人にはチソツマブ　ベドチン（遺伝子組換え）として 1 回 2 mg/kg（体重）を 30 分以上かけて、3 週間間隔で点滴静注する。ただし、1 回量として 200 mg を超えないこと。
生物由来原料等の使用の有無	■使用→使用している場合は以下の欄を記入 □不使用
使用した生物由来原料等	□ヒト由来細胞・組織、□ヒト由来成分（血液、尿、その他）、 ■動物由来細胞・組織、□動物由来成分（血液、その他） 原材料名：チャイニーズハムスター卵巣（CHO）細胞株
生物由来原料等の使用目的	■宿主細胞、□培地添加物、□その他の製造原材料、 □製剤添加物、□その他（　　）
原料等の由来となるヒト・動物のスクリーニング・管理の内容：	セル・バンクの純度試験を実施した。その結果を別添 1 に示す。以下の基準に基づき管理している。 「ヒト又は動物細胞株を用いて製造されるバイオテクノロジー応用医薬品のウイルス安全性評価」について（ICH Q5A）（医薬審第 329 号、平成 12 年 2 月 22 日） 「生物薬品（バイオテクノロジー応用医薬品／生物起源由来医薬品）製造用細胞基剤の由来、調製及び特性解析」について（ICH Q5D）（医薬審第 873 号、平成 12 年 7 月 14 日）
生物由来原料等に対する不活化処理等の内容：	生物由来原料の製造工程における不活化処理等は実施していない。 なお、宿主細胞である CHO 細胞株は、tisotumab の産生細胞株の樹立過程において使用されている。
ウイルスクリアランス試験結果の概要：	別添 3 を参照
製造工程の概要（フローチャート）： （不活化処理には下線を付し、処理条件を具体的に記載）	別添 2 を参照

別紙様式２

使用した生物由来原料等の名称	チャイニーズハムスター卵巣（CHO）細胞株 （動物種：チャイニーズハムスター、使用部位：卵巣）
使用した生物由来原料等の分類	□ヒト血液由来成分、□ヒト細胞組織、□ヒト尿由来成分、□ヒト由来成分（血液、細胞組織又は尿を除くもの）、□反芻動物由来成分、■動物細胞組織、□動物由来成分、□その他（　　）
生物由来原料等の使用目的	□有効成分、■宿主細胞、□培地添加物、□その他の製造原料等（　　）、□製剤添加物、□その他（　　）
生物由来原料等の由来となるヒト・動物のスクリーニング・管理の内容	セル・バンクの純度試験を実施した。その結果を別添 1 に示す。以下の基準に基づき管理している。 「ヒト又は動物細胞株を用いて製造されるバイオテクノロジー応用医薬品のウイルス安全性評価」について（ICH Q5A）（医薬審第 329 号、平成 12 年 2 月 22 日） 「生物薬品（バイオテクノロジー応用医薬品／生物起源由来医薬品）製造用細胞基剤の由来、調製及び特性解析」について（ICH Q5D）（医薬審第 873 号、平成 12 年 7 月 14 日）
生物由来原料等のウイルス等の不活化及び除去処理等の内容	生物由来原料の製造工程における不活化処理等は実施していない。 なお、宿主細胞である CHO 細胞株は、tisotumab の産生細胞株の樹立過程において使用されている。
製造工程の概要（フローチャート） （不活化及び除去処理には下線を付し、条件を具体的に記載）	別添 2 を参照
ウイルスクリアランス試験結果の概要	別添 3 を参照

別添 1　チャイニーズハムスター卵巣（Chinese hamster ovary、CHO）細胞のスクリーニング・管理の内容

tisotumab のセル・バンク［マスター・セル・バンク（master cell bank、MCB）、ワーキング・セル・バンク（working cell bank、WCB）］及び in vitro 細胞齢の上限における生産終了時セル・バンク（end of production cell bank、EOPC）の純度試験結果を Table 1 に示す。

Table 1　tisotumab の MCB、WCB 及び EOPC の外来性感染性物質試験結果

試験項目	判定基準	試験結果		
		MCB	WCB	EOPC
無菌性				
無菌（日局）	増殖を認めない	適合	適合	適合
マイコプラズマ［ヘキスト染色（Ph. Eur., PTC 93）］	マイコプラズマを認めない	適合	適合	適合
レトロウイルス試験				
ウイルス、[redacted]（定量的透過型電子顕微鏡観察）	報告	細胞[redacted]個中[redacted]%に[redacted]粒子を、[redacted]%に[redacted]粒子をそれぞれ認めた。	−	細胞[redacted]個中[redacted]%に[redacted]粒子を、[redacted]%に[redacted]粒子をそれぞれ認めた。
[redacted]レトロウイルス（[redacted]）	MCB：報告 EOPC：検出せず	[redacted]レトロウイルス検出せず	−	適合
[redacted]レトロウイルス（[redacted]）	MCB：報告 EOPC：検出せず	[redacted]ウイルス検出せず	−	適合
[redacted]レトロウイルス（[redacted]、[redacted]）	検出せず	−		適合
外来性ウイルス				
In vitro ウイルス試験	検出せず	適合	適合	適合
In vivo ウイルス試験	検出せず	適合	−	適合
[redacted]抗体産生試験	検出せず	適合	−	−
[redacted]抗体産生試験	検出せず	適合	−	−
In vitro [redacted]ウイルス試験	検出せず	適合	−	−
In vitro [redacted]ウイルス試験	検出せず	適合	−	−
[redacted]ウイルス試験（[redacted]）	報告	陰性	−	−
[redacted]ウイル試験（[redacted]）	報告	陰性	−	−
[redacted]（[redacted]）	検出せず	適合	−	適合
[redacted]ウイルス[redacted]（[redacted]）	検出せず	適合	−	適合

−：試験実施せず

別添２　製造工程の概要（流れ図）

tisotumab の細胞培養・ハーベスト工程及び精製工程の流れ図をそれぞれ、Figure 1 及び Figure 2 に示す。ウイルス不活化及び除去処理に下線を付した。

Figure 1　tisotumab の細胞培養・ハーベスト工程の流れ図

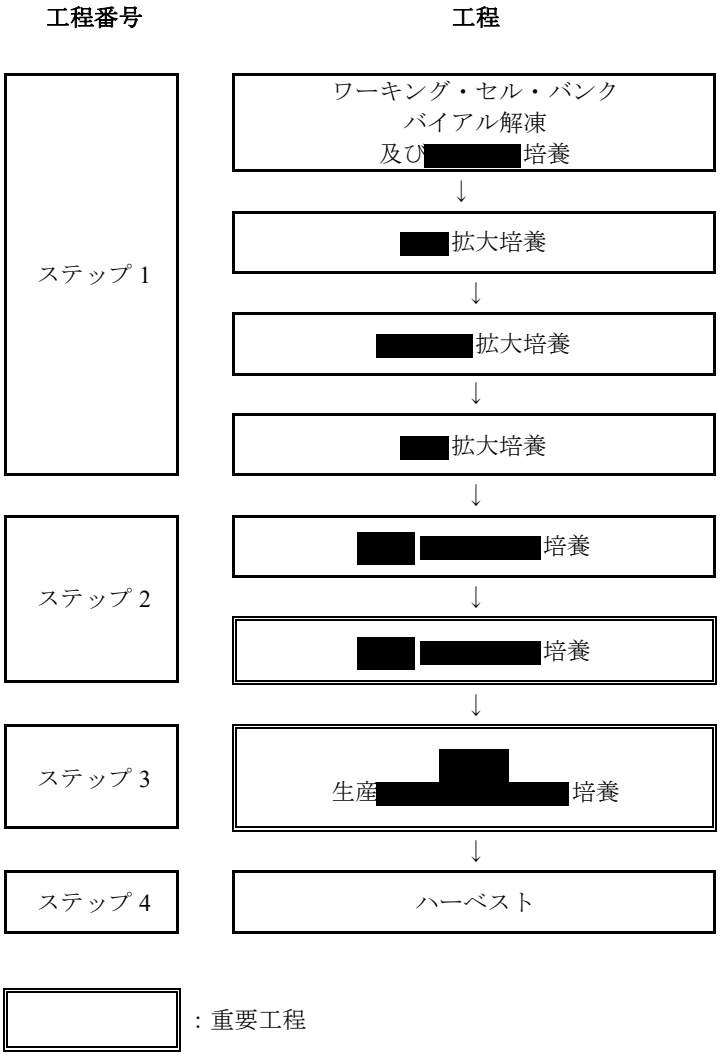
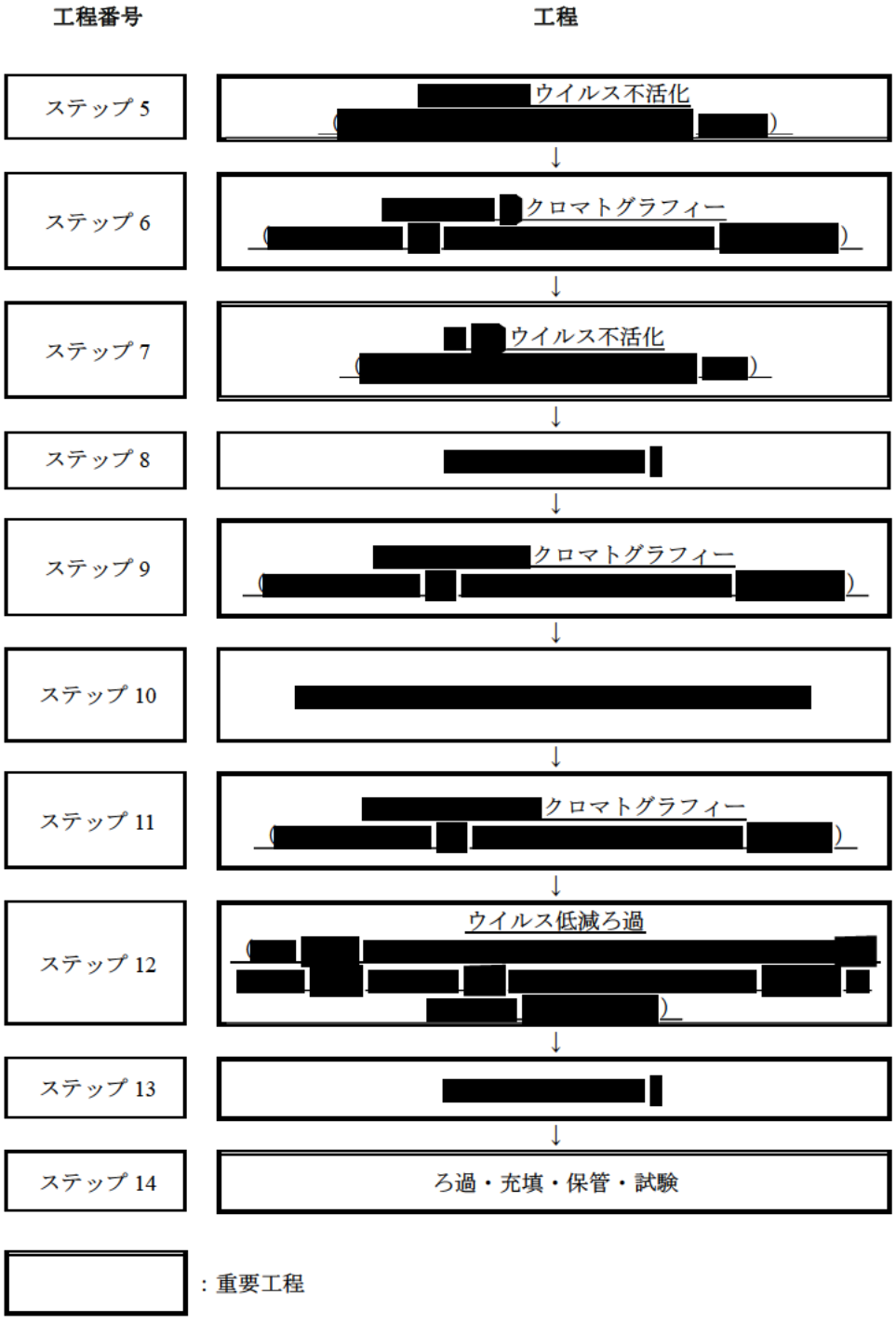


Figure 2　tisotumab の精製工程の流れ図



別添 3　ウイルスクリアランス試験結果の概要

1.　モデルウイルスの選択

tisotumab のウイルスクリアランス試験では、異種指向性マウス白血病ウイルス（MLV）、仮性狂犬病ウイルス（PRV）、レオウイルス 3 型（REO）、マウスマイニュートウイルス(MMV）の 4 種類のモデルウイルスが使用された。エンベロープ RNA レトロウイルスである MLV は、マウス細胞株に存在する内在性レトロウイルス様粒子の特異的モデルである。PRV、REO 及び MMV は、異なる特性を有するウイルスを除去又は不活化する精製工程の頑健性を示すために用いられる、非特異的モデルウイルスである。[redacted]処理及び[redacted]処理による不活化を試験するために、追加のエンベロープウイルスとして PRV を選択した。[redacted] 処理及び[redacted]処理に対する耐性を有する、エンベロープを持たない中型ウイルスのモデルウイルスとして REO を選択した。MMV は、物理化学的処理に対する耐性が高い、エンベロープを持たない小型の一本鎖 DNA ウイルスであり、ウイルスフィルターのサイズ排除能の評価に使用する。選択したモデルウイルス及びそれらの特徴を Table 2 に示す。

Table 2　モデルウイルスとその特徴

Virus	Family	Genome	Size (nm)	Enveloped	Physicochemical resistance
MLV	Retro	RNA	80 to 110	Yes	Low
PRV	Herpes	DNA	120 to 200	Yes	Low to Medium
REO	Reo	RNA	60 to 80	No	Medium to High
MMV	Parvo	DNA	18 to 24	No	Very high

2.　tisotumab のウイルスクリアランス試験結果の概要

各工程で得られたウイルスクリアランス値の最小値を合計して、tisotumab の精製工程による全対数減少係数（log reduction factor、LRF）を求め、Table 3 に結果を示す。

全 LRF は MLV で 21.94[redacted] 以上、PRV で 19.76[redacted] 以上、REO で 12.17[redacted] 以上、MMV で 7.55[redacted] 以上であった。

Table 3　tisotumab の精製工程におけるウイルスクリアランス

Step	MLV	PRV	REO	MMV
	Log reduction factor (LRF)			
[redacted] chromatography	[redacted]	[redacted]	[redacted]	[redacted]
treatment				
chromatography				
chromatography				
Virus reduction filtration	[redacted]	[redacted]	[redacted]	[redacted]
Cumulative Log_{10} reduction factor	≥21.94[redacted]	≥19.76[redacted]	≥12.17[redacted]	≥7.55[redacted]

MLV=murine leukemia virus; MMV=murine minute virus; NT=not tested; PRV=pseudorabies virus; REO=reovirus type 3
NR= Not reportable, reduction factors of [redacted] log10 are not statistically significant, not included in the cumulative log10 reduction factor.

第3部（モジュール3）：品質に関する文書　添付資料一覧
3.2　データ又は報告書
3.2.S tisotumab

添付資料番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別
3.2.S.1 一般情報				
3.2.S.1.1	Nomenclature	海外	社内資料	評価資料
3.2.S.1.2	Structure	海外	社内資料	評価資料
3.2.S.1.3	General Properties	海外	社内資料	評価資料
3.2.S.2 製造				
3.2.S.2.1	Manufacturer(s)	海外	社内資料	評価資料
3.2.S.2.2	Description of Manufacturing Process and Process Controls	海外	社内資料	評価資料
3.2.S.2.3	Control of Materials	海外	社内資料	評価資料
3.2.S.2.4	Controls of Critical Steps and Intermediates	海外	社内資料	評価資料
3.2.S.2.5	Process Validation and/or Evaluation	海外	社内資料	評価資料
3.2.S.2.6	Manufacturing Process Development	海外	社内資料	評価資料
3.2.S.3 特性				
3.2.S.3.1	Elucidation of Structure and other Characteristics	海外	社内資料	評価資料
3.2.S.3.2	Impurities	海外	社内資料	評価資料

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3.2 データ又は報告書
3.2.S tisotumab

添付資料番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別
3.2.S.4 tisotumabの管理				
3.2.S.4.1	Specification	海外	社内資料	評価資料
3.2.S.4.2	Analytical Procedures	海外	社内資料	評価資料
3.2.S.4.3	Validation of Analytical Procedures	海外	社内資料	評価資料
3.2.S.4.4	Batch Analyses	海外	社内資料	評価資料
3.2.S.4.5	Justification of Specification	海外	社内資料	評価資料
3.2.S.5 標準品又は標準物質				
3.2.S.5	Reference Standards or Materials	海外	社内資料	評価資料
3.2.S.6 容器及び施栓系				
3.2.S.6	Container Closure System	海外	社内資料	評価資料
3.2.S.7 安定性				
3.2.S.7.1	Stability Summary and Conclusions	海外	社内資料	評価資料
3.2.S.7.2	Post-approval Stability Protocol and Stability Commitment	海外	社内資料	評価資料
3.2.S.7.3	Stability Data	海外	社内資料	評価資料

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3.2 データ又は報告書
3.2.S vcMMAE

添付資料番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別
3.2.S.1 一般情報				
3.2.S.1.1	Nomenclature	海外	社内資料	評価資料
3.2.S.1.2	Structure	海外	社内資料	評価資料
3.2.S.1.3	General Properties	海外	社内資料	評価資料
3.2.S.2 製造				
3.2.S.2.1	Manufacturer(s)	海外	社内資料	評価資料
3.2.S.2.2	Description of Manufacturing Process and Process Controls	海外	社内資料	評価資料
3.2.S.2.3	Control of Materials	海外	社内資料	評価資料
3.2.S.2.4	Controls of Critical Steps and Intermediates	海外	社内資料	評価資料
3.2.S.2.5	Process Validation and/or Evaluation	海外	社内資料	評価資料
3.2.S.2.6	Manufacturing Process Development	海外	社内資料	評価資料
3.2.S.3 特性				
3.2.S.3.1	Elucidation of Structure and other Characteristics	海外	社内資料	評価資料
3.2.S.3.2	Impurities	海外	社内資料	評価資料

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3.2 データ又は報告書
3.2.S vcMMAE

添付資料番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別
3.2.S.4 vcMMAEの管理				
3.2.S.4.1	Specification	海外	社内資料	評価資料
3.2.S.4.2	Analytical Procedures	海外	社内資料	評価資料
3.2.S.4.3	Validation of Analytical Procedures	海外	社内資料	評価資料
3.2.S.4.4	Batch Analyses	海外	社内資料	評価資料
3.2.S.4.5	Justification of Specification	海外	社内資料	評価資料
3.2.S.5 標準品又は標準物質				
3.2.S.5	Reference Standards or Materials	海外	社内資料	評価資料
3.2.S.6 容器及び施栓系				
3.2.S.6	Container Closure System	海外	社内資料	評価資料
3.2.S.7 安定性				
3.2.S.7.1	Stability Summary and Conclusions	海外	社内資料	評価資料
3.2.S.7.2	Post-approval Stability Protocol and Stability Commitment	海外	社内資料	評価資料
3.2.S.7.3	Stability Data	海外	社内資料	評価資料

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3.2　データ又は報告書
3.2.S 原薬

添付資料番号	タイトル	報種類 （国内／海外）	掲載誌	評価資料・ 参考資料の別
3.2.S.1 一般情報				
3.2.S.1.1	Nomenclature	海外	社内資料	評価資料
3.2.S.1.2	Structure	海外	社内資料	評価資料
3.2.S.1.3	General Properties	海外	社内資料	評価資料
3.2.S.2 製造				
3.2.S.2.1	Manufacturer(s)	海外	社内資料	評価資料
3.2.S.2.2	Description of Manufacturing Process and Process Controls	海外	社内資料	評価資料
3.2.S.2.3	Control of Materials	海外	社内資料	評価資料
3.2.S.2.4	Controls of Critical Steps and Intermediates	海外	社内資料	評価資料
3.2.S.2.5	Process Validation and/or Evaluation	海外	社内資料	評価資料
3.2.S.2.6	Manufacturing Process Development	海外	社内資料	評価資料
3.2.S.3 特性				
3.2.S.3.1	Elucidation of Structure and other Characteristics	海外	社内資料	評価資料
3.2.S.3.2	Impurities	海外	社内資料	評価資料

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3.2　データ又は報告書
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添付資料番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別
3.2.S.4 原薬の管理				
3.2.S.4.1	Specification	海外	社内資料	評価資料
3.2.S.4.2	Analytical Procedures	海外	社内資料	評価資料
3.2.S.4.3	Validation of Analytical Procedures	海外	社内資料	評価資料
3.2.S.4.4	Batch Analyses	海外	社内資料	評価資料
3.2.S.4.5	Justification of Specification	海外	社内資料	評価資料
3.2.S.5 標準品又は標準物質				
3.2.S.5	Reference Standards or Materials	海外	社内資料	評価資料
3.2.S.6 容器及び施栓系				
3.2.S.6	Container Closure System	海外	社内資料	評価資料
3.2.S.7 安定性				
3.2.S.7.1	Stability Summary and Conclusions	海外	社内資料	評価資料
3.2.S.7.2	Post-approval Stability Protocol and Stability Commitment	海外	社内資料	評価資料
3.2.S.7.3	Stability Data	海外	社内資料	評価資料

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3.2　データ又は報告書
3.2.P　製剤

添付資料番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別
3.2.P.1 製剤及び処方				
3.2.P.1	Description and Composition of the Drug Product	海外	社内資料	評価資料
3.2.P.2 製剤開発の経緯				
3.2.P.2.1	Components of the Drug Product	海外	社内資料	評価資料
3.2.P.2.2	Drug Product	海外	社内資料	評価資料
3.2.P.2.3	Manufacturing Process Development	海外	社内資料	評価資料
3.2.P.2.4	Container Closure System	海外	社内資料	評価資料
3.2.P.2.5	Microbiological Attributes	海外	社内資料	評価資料
3.2.P.2.6	Compatibility	海外	社内資料	評価資料
3.2.P.3 製造				
3.2.P.3.1	Manufacturer(s)	海外	社内資料	評価資料
3.2.P.3.2	Batch Formula	海外	社内資料	評価資料
3.2.P.3.3	Description of Manufacturing Process and Process Controls	海外	社内資料	評価資料
3.2.P.3.4	Controls of Critical Steps and Intermediates	海外	社内資料	評価資料

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3.2.P 製剤

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3.2.P.3.5	Process Validation and/or Evaluation	海外	社内資料	評価資料
3.2.P.4 添加剤の管理				
3.2.P.4.1	Specifications	海外	社内資料	評価資料
3.2.P.4.2	Analytical Procedures	海外	社内資料	評価資料
3.2.P.4.3	Validation of Analytical Procedures	海外	社内資料	評価資料
3.2.P.4.4	Justification of Specifications	海外	社内資料	評価資料
3.2.P.4.5	Excipients of Human or Animal Origin	海外	社内資料	評価資料
3.2.P.4.6	Novel Excipients	海外	社内資料	評価資料
3.2.P.5 製剤の管理				
3.2.P.5.1	Specification(s)	海外	社内資料	評価資料
3.2.P.5.2	Analytical Procedures	海外	社内資料	評価資料
3.2.P.5.3	Validation of Analytical Procedures	海外	社内資料	評価資料
3.2.P.5.4	Batch Analyses	海外	社内資料	評価資料
3.2.P.5.5	Characterisation of Impurities	海外	社内資料	評価資料

第3部（モジュール3）：品質に関する文書 添付資料一覧
3.2 データ又は報告書
3.2.P 製剤

添付資料番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別
3.2.P.5.6	Justification of Specification(s)	海外	社内資料	評価資料
3.2.P.6 標準品又は標準物質				
3.2.P.6	Reference Standards or Materials	海外	社内資料	評価資料
3.2.P.7 容器及び施栓系				
3.2.P.7	Container Closure System	海外	社内資料	評価資料
3.2.P.8 安定性				
3.2.P.8.1	Stability Summary and Conclusion	海外	社内資料	評価資料
3.2.P.8.2	Post-approval Stability Protocol and Stability Commitment	海外	社内資料	評価資料
3.2.P.8.3	Stability Data	海外	社内資料	評価資料

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3.2　データ又は報告書
3.2.A　その他

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3.2.A.1	Facilities and Equipment	海外	社内資料	評価資料
3.2.A.2	Adventitious Agents Safety Evaluation	海外	社内資料	評価資料
3.2.A.3	Novel Excipients	海外	社内資料	評価資料

3.2.R　各極の要求資料

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3.2.R	Regional Information：該当なし			

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3.3　参考文献:

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3.3	Literature references：該当なし

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4.2　試験報告書
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添付資料番号	報告書番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別
4.2.1.1　効力を裏付ける試験					
4.2.1.1-1	■1015-091	TF expression and incidence in multiple tumor indications	海外	社内資料	参考資料
4.2.1.1-2	■1015-178	The Development and Analytical Validation of an Immunohistochemistry Assay to Detect Tissue Factor	海外	社内資料	評価資料
4.2.1.1-3	GMB1015-254	Tissue factor expression in colon cancer	海外	社内資料	評価資料
4.2.1.1-4	GMB1015-257	Tissue factor expression in human tumor biopsies	海外	社内資料	参考資料
4.2.1.1-5	GMB1015-055	Hybridoma and transfectoma generation	海外	社内資料	評価資料

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4.2.1.1-6	GMB1015-083	Binding characteristics of TF-specific HuMabs and antibody-drug conjugates	海外	社内資料	評価資料
4.2.1.1-7	■1015-191	X-ray structure analysis of human Fab antibody fragment in complex with Tissue Factor	海外	社内資料	評価資料
4.2.1.1-8	GMB1015-085	Effect of TF-specific HuMabs on binding of factor VIIa (FVIIa) to tissue factor (TF) and on TF:FVIIa-dependent intracellular signaling *in vitro*	海外	社内資料	評価資料
4.2.1.1-9	GMB1015-087	Evaluation of lysosomal trafficking of TF-specific HuMabs and induction of cell kill *in vitro* by TF-specific antibody-drug conjugates	海外	社内資料	評価資料
4.2.1.1-10	GMB1015-229	Effect of P-glycoprotein expression on tisotumab vedotin-induced cytotoxicity *in vitro*	海外	社内資料	評価資料

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添付資料番号	報告書番号	タイトル	報種類 （国内／海外）	掲載誌	評価資料・ 参考資料の別
4.2.1.1-11	GMB1015-179	Induction of bystander cytotoxicity by tisotumab vedotin *in vitro*	海外	社内資料	評価資料
4.2.1.1-12	[redacted]-5666	Induction of Immunogenic Cell Death by Tisotumab Vedotin	海外	社内資料	評価資料
4.2.1.1-13	[redacted]-[redacted]-000451	Tisotumab vedotin has immunomodulatory activity in vivo in a xenograft tumor model	海外	社内資料	評価資料
4.2.1.1-14	GMB1015-084	Evaluation of the induction of ADCC, CDC and apoptosis and inhibition of proliferation by TF-specific HuMabs and antibody-drug conjugates	海外	社内資料	評価資料
4.2.1.1-15	[redacted]-5631	Antibody-dependent cellular phagocytosis of tisotumab and tisotumab vedotin	海外	社内資料	評価資料

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4.2.1.1-16	GMB1015-082	Evaluation of the efficacy of auristatin-conjugated TF specific antibodies *in vivo*	海外	社内資料	評価資料
4.2.1.1-17	GMB1015-213	Anti-tumor activity of the combination of tisotumab vedotin and pembrolizumab in a breast cancer xenograft model *in vivo*	海外	社内資料	評価資料
4.2.1.1-18	GMB1015-081	Evaluation of the efficacy of TF-specific HuMabs *in vivo*	海外	社内資料	評価資料
4.2.1.1-19	GMB1015-102	Incidental observation of intra-tumoral hemorrhages in mouse xenograft studies performed to evaluate the anti-tumor activity of HuMax-TF and HuMax-TF-ADC *in vivo*	海外	社内資料	参考資料
4.2.1.1-20	GMB1015-149	Therapeutic evaluation of HuMax-TF-ADC in four patient derived tumor xenograft models of different indications	海外	社内資料	評価資料

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4.2.1.1-21	GMB1015-223	Anti-tumor activity of tisotumab vedotin monotherapy in two patient-derived cervical cancer xenograft models *in vivo*	海外	社内資料	評価資料
4.2.1.1-22	GMB1015-211	Anti-tumor activity of tisotumab vedotin in combination with chemotherapy in patient-derived cervical cancer xenograft models *in vivo*	海外	社内資料	評価資料
4.2.1.1-23	GMB1015-210	Anti-tumor activity of tisotumab vedotin in combination with bevacizumab in cervical cancer xenograft models *in vivo*	海外	社内資料	評価資料
4.2.1.1-24	GMB1015-148	Therapeutic evaluation of HuMax-TF-ADC in three patient derived tumor xenograft models of different indications	海外	社内資料	参考資料
4.2.1.1-25	GMB1015-212	Anti-tumor activity of tisotumab vedotin in combination with chemotherapy in a bladder cancer xenograft model *in vivo*	海外	社内資料	参考資料

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4.2 試験報告書

4.2.1 薬理試験

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4.2.1.1-26	GMB1015-224	Anti-tumor activity of tisotumab vedotin in an esophageal cancer xenograft model *in vivo*	海外	社内資料	参考資料
4.2.1.1-27	GMB1015-225	Anti-tumor activity of tisotumab vedotin in non-small cell lung cancer xenograft models *in vivo*	海外	社内資料	参考資料
4.2.1.1-28	GMB1015-226	Anti-tumor activity of tisotumab vedotin in two ovarian cancer xenograft models *in vivo*	海外	社内資料	参考資料
4.2.1.1-29	GMB1015-227	Anti-tumor activity of tisotumab vedotin alone or in combination with gemcitabine and Abraxane in a pancreatic cancer xenograft model *in vivo*	海外	社内資料	参考資料
4.2.1.1-30	GMB1015-228	Analysis of tissue factor expression levels in cancer xenograft models *in situ* in relation to the anti-tumor activity of tisotumab vedotin *in vivo*	海外	社内資料	評価資料
4.2.1.2 副次的薬理試験					

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4.2.1.2-1	GMB1015-086	Effect of TF-specific HuMabs on TF-induced FXa generation and clotting *in vitro*	海外	社内資料	評価資料
4.2.1.2-2	[redacted]264005	Effects of HuMax-TF-ADC, HuMax-TF, IgG1-1015-098, IgG1-1015-111 and HuMax-HepC on Prothrombin Time (PT)	海外	社内資料	評価資料
4.2.1.2-3	[redacted]-[redacted]-Study-Report-0364	Evaluation of the effect of Genmab's anti-tissue factor antibodies on endogenous tissue factor (TF) activity in blood	海外	社内資料	参考資料
4.2.1.2-4	[redacted]-[redacted]-Study-Report-0361	Functional tissue factor inhibition as estimated by dynamic haemostasis models of fibrin formation and thrombin generation	海外	社内資料	参考資料
4.2.1.3　安全性薬理試験					
4.2.1.3-1	[redacted]129-09-001	Determine the dose-response relation of SGD-1010 block of hERG K^+ channels heterologously expressed in Human Embryonic Kidney (HEK293) cells using the conventional whole-cell voltage clamp	海外	社内資料	参考資料

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4.2.1　薬理試験

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4.2.1.4　薬力学的薬物相互作用試験：該当なし					

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添付資料番号	報告書番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別
4.2.2.1 分析法及びバリデーション報告書					
4.2.2.1-1	[redacted]315274	Validation of MMAE and IgG ELISA Methodology to Detect HuMax-TF-ADC in Cynomolgus Monkey Plasma	海外	社内資料	評価資料
4.2.2.1-2	[redacted]316168	Validation of IgG ELISA Methodology to Detect IgG1-1015-011 in Cynomolgus Monkey Plasma	海外	社内資料	評価資料
4.2.2.1-3	[redacted]8263943	Validation of an Analytical Procedure for the Determination of MMAE in Monkey Plasma (K_2EDTA) using Solid Phase Extraction with Liquid Chromatography with Tandem Mass Spectrometric Detection (LC-MS/MS)	海外	社内資料	評価資料
4.2.2.1-4	[redacted]7646-115	Validation of a Method for the Determination of Free MMAE in Monkey Serum by HPLC with MS/MS Detection	海外	社内資料	評価資料

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添付資料番号	報告書番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別
4.2.2.1-5	[redacted]7646-119	Abbreviated Validation of a Method for the Determination of Free MMAE in Rat Serum by HPLC with MS/MS Detection	海外	社内資料	評価資料
4.2.2.1-6	[redacted]8212326	Validation of a Method for the Determination of Free MMAE in Rat Amniotic Fluid by HPLC with MS/MS Detection	海外	社内資料	評価資料
4.2.2.1-7	[redacted]315253	Validation of ECL Methodology to Determine the Presence and Titre Level of Antibodies to HuMax-TF-ADC in Cynomolgus Monkey Serum	海外	社内資料	評価資料
4.2.2.1-8	[redacted]1015-002	Detection of PAHA against IgG1-1015-011 in serum from cynomolgous monkeys pilot toxicology study ([redacted] Study No. 514850) using a bridging ELISA	海外	社内資料	参考資料
4.2.2.2 吸収					

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4.2.2.2-1	MR1015-143-33	3-Week single dose pharmacokinetic study of HuMax-TF and HuMax-TF-ADC in SCID mice	海外	社内資料	評価資料
4.2.2.3 分布					
4.2.2.3-1	[redacted]0001	Determination of Whole Body Distribution of i.v. Bolus [Zr-89]-Df-IAb456_FL by Positron Emission Tomography (PET)	海外	社内資料	参考資料
4.2.2.3-2	[redacted]001	Biodistribution of ^{89}Zr-Df-IAb37_FLA and ^{89}Zr-Df-IAb37_FL in a high TF-expressing pancreas cancer xenograft model	海外	社内資料	参考資料
4.2.2.3-3	[redacted]-1201	Tissue Distribution via Quantitative Whole-Body Autoradiography in Male Long-Evans Rats Following a Single Intravenous Bolus Administration of [^{3}H]MMAE	海外	社内資料	参考資料

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4.2.2.3-4	[redacted]-0025	Plasma Protein Binding Assay of MMAE by Ultracentrifugation	国内	社内資料	参考資料
4.2.2.3-5	[redacted]-0271	Evaluation of In Vitro MMAE Red Blood Cell Partitioning Potential in Mouse, Rat, Cynomolgus Monkey, and Human	海外	社内資料	参考資料
4.2.2.4 代謝					
4.2.2.4-1	[redacted]084006	Reaction Phenotyping: Identification of human CYP enzymes involved in the *in vitro* metabolism of [^{3}H]-MMAE	海外	社内資料	参考資料
4.2.2.4-2	[redacted]084007	Metabolite characterization of [^{3}H]-MMAE in rat, monkey and human hepatocytes	海外	社内資料	参考資料

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4.2.2.4-3	[redacted]-[redacted]35-001	Cross-species comparison of MMAE metabolism and excretion	海外	社内資料	参考資料
4.2.2.5 排泄					
4.2.2.5-1	[redacted]420501	Excretion, Mass Balance and Pharmacokinetics of Radioactivity in Sprague-Dawley Rats Following a Single Intravenous Bolus Dose of cAC10-vc-^{3}H-MMAE or ^{3}H-MMAE	海外	社内資料	参考資料
4.2.2.6 薬物動態学的薬物相互作用（非臨床）					
4.2.2.6-1	[redacted]133043	*In Vitro* Evaluation of MMAE as an Inducer of Cytochrome P450 Expression in Cultured Human Hepatocytes	海外	社内資料	参考資料
4.2.2.6-2	[redacted]085021	*In Vitro* Evaluation of MMAE as an Inhibitor of Human Cytochrome P450 Enzymes	海外	社内資料	参考資料

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4.2.2.6-3	[redacted]108004	*In vitro* Interaction Studies of MMAE with Human MDR1 (ABCB1/P-gp) ABC (efflux) Transporter	海外	社内資料	参考資料
4.2.2.6-4	[redacted]-01709	Caco-2 Permeability and Efflux Transporter Interactions of MMAE (ML00733334 or SGD-1010)	海外	社内資料	参考資料
4.2.2.6-5	[redacted]-3234	*In vitro* Interaction Studies of MMAE with human BCRP, BSEP and MRP2 Efflux (ABC) Transporters, and with human OAT1, OAT3, OATP1B1, OATP1B3, OCT1 and OCT2 Uptake Transporters	海外	社内資料	参考資料
4.2.2.6-6	[redacted]-0008	*In vitro* interaction of MMAE with human OATP1B1	海外	社内資料	参考資料

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4.2.2.6-7	[redacted]-0009	*In vitro* interaction of MMAE with human OATP1B3	海外	社内資料	参考資料
4.2.2.6-8	[redacted]-0010	*In vitro* interaction of MMAE with human OCT2	海外	社内資料	参考資料
4.2.2.6-9	[redacted]-0011	*In vitro* interaction of MMAE with human OAT1	海外	社内資料	参考資料
4.2.2.6-10	[redacted]-0012	*In vitro* interaction of MMAE with human OAT3	海外	社内資料	参考資料
4.2.2.7 その他の薬物動態試験					

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4.2.2.7-1	[redacted]1015-109-01	In vitro stability assessement of HuMax-TF-ADC	海外	社内資料	参考資料

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4.2　試験報告書
4.2.3　毒性試験

添付資料番号	報告書番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別
4.2.3.1 単回投与毒性試験					
4.2.3.1-1	[redacted]1019-001	A Comparison Study of the Acute Effects of Monomethyl Auristatin E (MMAE) and MMAE-based Antibody-drug Conjugates Administered Intravenously in the Rat	海外	社内資料	参考資料
4.2.3.1-2	[redacted]-15	Single Dose Intravenous Toxicity Study of SGN-35 and SGD-1010 in Male and Female Rats	海外	社内資料	参考資料
4.2.3.1-3	[redacted]-33	Single Dose, Bone Marrow and Hematology Toxicity Kinetic Study of SGD-1010 in the Rat	海外	社内資料	参考資料
4.2.3.2 反復投与毒性試験					
4.2.3.2-1	[redacted]514850	HuMab-TF (IgG1-1015-011): Pilot Repeat Dose Toxicology Study in Cynomolgus Monkeys	海外	社内資料	参考資料

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4.2.3.2-2	[redacted]520010	Tissue Factor Antibody Drug Conjugates (IgG1-1015-098-1006, IgG1-1015-098-1269, IgG1-1015-011-1006, IgG1-1015-011-1269, IgG1-B12-1006, IgG1-B12-1269, IgG1-1015-111-1006, IgG1-1015-111-1269): Pilot Repeat Dose Toxicology Study in Cynomolgus Monkeys	海外	社内資料	参考資料
4.2.3.2-3	[redacted]521988	Tissue Factor Antibody Drug Conjugates (IgG1-1015-098-vcMMAE and IgG1-1015-011-vcMMAE): 10 Week Dose Range Finding Study in Cynomolgus Monkeys with a 6 Week Recovery Period	海外	社内資料	参考資料
4.2.3.2-4	[redacted]522531	HuMax-TF-ADC: 13 Week Repeat Dose Toxicity Study in Cynomolgus Monkeys with a 6 Week Recovery Period	海外	社内資料	評価資料
4.2.3.2-5	[redacted]-13	Multiple Dose Intravenous Toxicity Study of SGN-35 and SGD-1010 in Male and Female Rats	海外	社内資料	参考資料

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4.2.3　毒性試験

添付資料番号	報告書番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別
4.2.3.2-6	[redacted]7646-118	A 4-Week Intravenous Injection Toxicity and Toxicokinetic Study of SGN-35, SGD-1010, and SGN-30 in Rats with a 4-Week Recovery	海外	社内資料	評価資料
4.2.3.2-7	[redacted].163.19	A Pilot Intravenous Dose Range Finding and Toxicity Study of SGD-1010 in Cynomolgus Monkeys	海外	社内資料	参考資料
4.2.3.2-8	[redacted].163.16	An 11-Week Repeat-Dose Intravenous Infusion Toxicity Study of SGN-35 and SGD-1010 in Cynomolgus Monkeys with a Five-Week Recovery Period	海外	社内資料	評価資料
4.2.3.2-9	[redacted]163.66	A 4-Week Repeat Intravenous Dose Study of h00-1006(4) in Cynomolgus Monkeys with a 4-Week Recovery Period (GLP)	海外	社内資料	評価資料
4.2.3.3 遺伝毒性試験					
4.2.3.3.1 In Vitro試験					

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4.2.3.3.1-1	[redacted]AA66EH.503.BTL	Bacterial Reverse Mutation Assay	海外	社内資料	評価資料
4.2.3.3.1-2	[redacted]8204155	L5178Y $TK^{+/-}$ Mouse Lymphoma Forward Mutation Assay with a Confirmatory Assay	海外	社内資料	評価資料
4.2.3.3.2　In Vivo試験					
4.2.3.3.2-1	[redacted]8204151	*In Vivo* Rat Bone Marrow Micronucleus Assay	海外	社内資料	評価資料
4.2.3.4　がん原性試験：該当なし					
4.2.3.4.1　長期がん原性試験：該当なし					
4.2.3.4.2　短期又は中期がん原性試験：該当なし					
4.2.3.4.3　その他の試験：該当なし					

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4.2.3.5 生殖発生毒性試験					
4.2.3.5.1 受胎能及び着床までの初期胚発生に関する試験：該当なし					
4.2.3.5.2 胚・胎児発生に関する試験					
4.2.3.5.2-1	[redacted]8204397	Intravenous Injection Study for Effects on Embryofetal Developmental and Toxicokinetics with SGN-35 and SGD-1010 in Rats	海外	社内資料	評価資料
4.2.3.5.3 出生前及び出生後の発生並びに母体の機能に関する試験：該当なし					
4.2.3.5.4 新生児を用いた試験：該当なし					
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4.2.3.7.1 抗原性試験：該当なし					
4.2.3.7.2 免疫毒性試験：該当なし					
4.2.3.7.3 毒性発現の機序に関する試験：該当なし					
4.2.3.7.4 依存性試験：該当なし					

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4.2.3.7.5 代謝物の毒性試験：該当なし					
4.2.3.7.6 不純物の毒性試験：該当なし					
4.2.3.7.7 その他の試験					
4.2.3.7.7-1	GMB1015-088	Cross-reactivity of HuMax-TF with TF from various animal species	海外	社内資料	参考資料
4.2.3.7.7-2	[redacted]20023264	A Tissue Cross-Reactivity Study of IgG1-1015-011-FITC and IgG1-1015-011-vcMMAE-FITC in Normal Human and Cynomolgus Monkey Tissues	海外	社内資料	評価資料
4.2.3.7.7-3	[redacted]-2926-A	SGD-1006, SGD-1427 and SGD-1010 photosafety evaluation	海外	社内資料	参考資料

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添付資料番号	著者・タイトル・掲載誌
4.3-1	Abdulkadir SA, Carvalhal GF, Kaleem Z, Kisiel W, Humphrey PA, Catalona WJ, et al. Tissue factor expression and angiogenesis in human prostate carcinoma. Hum Pathol. 2000;31(4):443-7.
4.3-2	Abu Saadeh F, Norris L, O'Toole S, Mohamed BM, Langhe R, O'Leary J, et al. Tumour expresion of tissue factor and tissue factor pathway inhibitor in ovarian cancer- relationship with venous thrombosis risk. Thromb Res. 2013;132(5):627-34.
4.3-3	Acharya SS, Coughlin A, Dimichele DM, North American Rare Bleeding Disorder Study Group. Rare Bleeding Disorder Registry: deficiencies of factors II, V, VII, X, XIII, fibrinogen and dysfibrinogenemias. J Thromb Haemost. 2004;2(2):248-56.
4.3-4	ADCETRIS European Public Assessment Report. Takeda Global Research and Development Centre, 2012.
4.3-5	Akashi T, Furuya Y, Ohta S, Fuse H. Tissue factor expression and prognosis in patients with metastatic prostate cancer. Urology. 2003;62(6):1078-82.
4.3-6	Albrektsen T, Sørensen BB, Hjortø GM, Fleckner J, Rao LVM, Petersen LC. Transcriptional program induced by factor VIIa-tissue factor, PAR1 and PAR2 in MDA-MB-231 cells. J Thromb Haemost. 2007;5(8):1588-97.
4.3-7	Amirkhosravi A, Alexander M, May K, Francis DA, Warnes G, Biggerstaff J, et al. The importance of platelets in the expression of monocyte tissue factor antigen measured by a new whole blood flow cytometric assay. Thromb Haemost. 1996;75(1):87-95.
4.3-8	Ando R, Kase S, Ohashi T, Dong Z, Fukuhara J, Kanda A, et al. Tissue factor expression in human pterygium. Mol Vis. 2011;17:63-9.
4.3-9	Antoniak S, Mackman N. Multiple roles of the coagulation protease cascade during virus infection. Blood. 2014;123(17):2605-13.
4.3-10	Bach RR. Tissue factor encryption. Arterioscler Thromb Vasc Biol. 2006;26:456-61.
4.3-11	Banner DW, D'Arcy A, Chene C, Winkler FK, Guha A, Konigsberg WH, et al. The crystal structure of the complex of blood coagulation factor VIIa with soluble tissue factor. Nature. 1996;380(6569):41-6.
4.3-12	Barbas 3rd, CF, Collet TA, Amberg W, Roben P, Binley JM, Hoekstra D, et al. Molecular profile of an antibody response to HIV-1 as probed by combinatorial libraries. J Mol Biol. 1993;230:812-23.
4.3-13	Belting M, Dorrell MI, Sandgren S, Aguilar E, Ahamed J, Dorfleutner A, et al. Regulation of angiogenesis by tissue factor cytoplasmic domain signaling. Nat Med. 2004;10(5):502-9.
4.3-14	Bluff JE, Brown NJ, Reed MW, Staton CA. Tissue factor, angiogenesis and tumour progression. Breast Cancer Res. 2008;10(2):204.
4.3-15	Bogdanov VY, Balasubramanian V, Hathcock J, Vele O, Lieb M, Nemerson Y. Alternatively spliced human tissue factor: a circulating, soluble, thrombogenic protein. Nat Med. 2003;9(4):458-62.
4.3-16	Breij EC, de Goeij BE, Verploegen S, Schuurhuis DH, Amirkhosravi A, Francis J. An antibody-drug conjugate that targets tissue factor exhibits potent therapeutic activity against a broad range of solid tumors. Cancer Res. 2014;74(4):1214-26.
4.3-17	Brown JS, Sundar R, Lopez J. Combining DNA damaging therapeutics with immunotherapy: more haste, less speed. Br J Cancer. 2018;118(3):312-24.
4.3-18	Broze GJ, Jr., Girard TJ. Factor V, tissue factor pathway inhibitor, and east Texas bleeding disorder. J Clin Invest. 2013;123(9):3710-2.
4.3-19	Bugge TH, Xiao Q, Kombrinck KW, Flick MJ, Holmbäck K, Danton MJ, et al. Fatal embryonic bleeding events in mice lacking tissue factor, the cell-associated initiator of blood coagulation. Proc Natl Acad Sci USA. 1996;93(13):6258-63.
4.3-20	Busso N, Morard C, Salvi R, Péclat V, So A. Role of the tissue factor pathway in synovial inflammation. Arthritis Rheum. 2003;48(3):651-9.

第4部（モジュール4）：非臨床試験報告書 添付資料一覧
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添付資料番号	著者・タイトル・掲載誌
4.3-21	Butenas S, Bouchard BA, Brummel-Ziedins KE, Parhami-Seren B, Mann KG. Tissue factor activity in whole blood. Blood. 2005;105(7):2764-70.
4.3-22	Carmeliet P, Mackman N, Moons L, Luther T, Gressens P, Van Vlaenderen I, et al. Role of tissue factor in embryonic blood vessel development. Nature. 1996;383(6595):73-5.
4.3-23	Censarek P, Bobbe A, Grandoch M, Schrör K, Weber AA. Alternatively spliced human tissue factor (asHTF) is not pro-coagulant. Thromb Haemost. 2007;97(1):11-4.
4.3-24	Chanakira A, Westmark PR, Ong IM, Sheehan JP. Tissue factor-factor VIIa complex triggers protease activated receptor 2-dependent growth factor release and migration in ovarian cancer. Gynecol Oncol. 2017;145(1):167-75.
4.3-25	Chen L, Lu Y, Chu Y, Xie J, Ding W, Wang F. Tissue factor expression in rheumatoid synovium: a potential role in pannus invasion of rheumatoid arthritis. Acta Histochem. 2013;115(7):692-7.
4.3-26	Chen K, Li Z, Jiang P, Zhang X, Zhang Y, Jiang Y, et al. Co-expression of CD133, CD44v6 and human tissue factor is associated with metastasis and poor prognosis in pancreatic carcinoma. Oncol Rep. 2014;32(2):755-63.
4.3-27	Chen L, Luo G, Tan Y, Wei J, Wu C, Zheng L, et al. Immunolocalisation of tissue factor in esophageal cancer is correlated with intratumoral angiogenesis and prognosis of the patient. Acta Histochem. 2010;112(3):233-9.
4.3-28	Chen R, Hou J, Newman E, Kim Y, Donohue C, Liu X, et al. CD30 Downregulation, MMAE Resistance, and MDR1 Upregulation Are All Associated with Resistance to Brentuximab Vedotin. Mol Cancer Ther. 2015;14(6):1376-84.
4.3-29	Cho Y, Cao X, Shen D, Tuo J, Parver LM, Rickles FR, et al. Evidence for enhanced tissue factor expression in age-related macular degeneration. Lab Invest. 2011;91(4):519-26.
4.3-30	Chu AJ. Tissue factor, blood coagulation, and beyond: an overview. Int J Inflam. 2011;367284.
4.3-31	Cirillo P, Calì G, Golino P, Calabrò P, Forte L, De Rosa S, et al. Tissue factor binding of activated factor VII triggers smooth muscle cell proliferation via extracellular signal-regulated kinase activation. Circulation. 2004;109(23):2911-6.
4.3-32	Cocco E, Hu Z, Richter CE, Bellone S, Casagrande F, Bellone M, et al. hI-con1, a factor VII-IgGFc chimeric protein targeting tissue factor for immunotherapy of uterine serous papillary carcinoma. Br J Cancer. 2010;103(6):812-819.
4.3-33	Cocco E, Varughese J, Buza N, Bellone S, Glasgow M, Bellone M, et al. Expression of tissue factor in adenocarcinoma and squamous cell carcinoma of the uterine cervix: implications for immunotherapy with hI-con1, a factor VII-IgGFc chimeric protein targeting tissue factor. BMC Cancer. 2011a;11:263.
4.3-34	Cocco E, Varughese J, Buza N, Bellone S, Lin KY, Bellone M, et al. Tissue factor expression in ovarian cancer: implications for immunotherapy with hI-con1, a factor VII-IgGF(c) chimeric protein targeting tissue factor. Clin Exp Metastasis. 2011b;28(7):689-700.
4.3-35	Coughlin SR. Protease-activated receptors in hemostasis, thrombosis and vascular biology. J Thromb Haemost. 2005;3(8):1800-14.
4.3-36	Davila M, Amirkhosravi A, Coll E, Desai H, Robles L, Colon J, et al. Tissue factor-bearing microparticles derived from tumor cells: impact on coagulation activation. J Thromb Haemost. 2008;6(9):1517-24.
4.3-37	de Bono JS, Concin N, Hong DS, Thistlethwaite FC, Machiels JP, Arkenau HT, et al. Tisotumab vedotin in patients with advanced or metastatic solid tumours (InnovaTV 201): a first-in-human, multicentre, phase 1–2 trial. Lancet Oncol. 2019;20(3):383-93.

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添付資料番号	著者・タイトル・掲載誌
4.3-38	de Bono JS, Harris JR, Burm SM, Vanderstichele A, Houtkamp MA, Aarass S, et al. Systematic study of tissue factor expression in solid tumors. Cancer Rep (Hoboken). 2023;6(2):e1699.
4.3-39	de Goeij BE, Satijn D, Freitag CM, Wubbolts R, Bleeker WK, Khasanov A, et al. High turnover of tissue factor enables efficient intracellular delivery of antibody-drug conjugates. Mol Cancer Ther. 2015;14(5):1130-40.
4.3-40	de Taeye SW, Rispens T, Vidarsson G. The ligands for human IgG and their effector functions. Antibodies (Basel). 2019;8(2):30.
4.3-41	Del Conde I, Shrimpton CN, Thiagarajan P, Lopez JA. Tissue-factor-bearing microvesicles arise from lipid rafts and fuse with activated platelets to initiate coagulation. Blood. 2005;106(5):1604-11.
4.3-42	Disse J, Petersen HH, Larsen KS, Persson E, Esmon N, Esmon CT, et al. The endothelial protein C receptor supports tissue factor ternary coagulation initiation complex signaling through protease-activated receptors. J Biol Chem. 2011;286(7):5756-67.
4.3-43	Donaghy H. Effects of antibody, drug and linker on the preclinical and clinical toxicities of antibody-drug conjugates. MAbs. 2016;8(4):659-71.
4.3-44	Dorfleutner A, Hintermann E, Tarui T, Takada Y, Ruf W. Cross-talk of integrin alpha3beta1 and tissue factor in cell migration. Mol Biol Cell. 2004;15(10):4416-25.
4.3-45	Doronina SO, Mendelsohn BA, Bovee TD, Cerveny CG, Alley SC, Meyer DL, et al. Enhanced activity of monomethylauristatin F through monoclonal antibody delivery: effects of linker technology on efficacy and toxicity. Bioconjug Chem. 2006;17(1):114-24.
4.3-46	Doronina SO, Toki BE, Torgov MY, Mendelsohn BA, Cerveny CG, Chace DF, et al. Development of potent monoclonal antibody auristatin conjugates for cancer therapy. Nat Biotechnol. 2003;21(7):778-84.
4.3-47	Drake TA, Morrissey JH, Edgington TS. Selective cellular expression of tissue factor in human tissues. Implications for disorders of hemostasis and thrombosis. Am J Pathol. 1989;134(5):1087-97.
4.3-48	Edén D, Panagiotou G, Mokhtari D, Eriksson JW, Åberg M, Siegbahn A, et al. Adipocytes express tissue factor and FVII and are procoagulant in a TF/FVIIa-dependent manner. Ups J Med Sci. 2019;124(3):158-67.
4.3-49	Eglen RM, Reisine T, Roby P, Rouleau N, Illy C, Bosse R, et al. The use of AlphaScreen technology in HTS: current status. Curr Chem Genomics. 2008;1:2-10.
4.3-50	Egorina EM, Sovershaev MA, Olsen JO, Østerud B. Granulocytes do not express but acquire monocyte-derived tissue factor in whole blood: evidence for a direct transfer. Blood. 2008;111(3):1208-16.
4.3-51	Erlich J, Parry GC, Fearns C, Muller M, Carmeliet P, Luther T, et al. Tissue factor is required for uterine hemostasis and maintenance of the placental labyrinth during gestation. Proc Natl Acad Sci USA. 1999;96(14):8138-43.
4.3-52	Fadare O, Renshaw IL, Liang SX. Expression of tissue factor and heparanase in endometrial clear cell carcinoma: possible role for tissue factor in thromboembolic events. Int J Gynecol Pathol. 2011;30(3):252-61.
4.3-53	Fleck RA, Rao LV, Rapaport SI, Varki N. Localization of human tissue factor antigen by immunostaining with monospecific, polyclonal anti-human tissue factor antibody. Thromb Res. 1990;59(2):421-37.
4.3-54	Francisco JA, Cerveny CG, Meyer DL, Mixan BJ, Klussman K, Chace DF, et al. cAC10-vcMMAE, an anti-CD30-monomethyl auristatin E conjugate with potent and selective antitumor activity. Blood. 2003;102(4):1458-65.

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添付資料番号	著者・タイトル・掲載誌
4.3-55	Galluzzi L, Buque A, Kepp O, Zitvogel L, Kroemer G. Immunogenic cell death in cancer and infectious disease. Nat Rev Immunol. 2017;17(2):97-111.
4.3-56	Gerber HP, Sapra P, Loganzo F, May C. Combining antibody-drug conjugates and immune-mediated cancer therapy: what to expect? Biochem Pharmacol. 2016;102:1-6.
4.3-57	Gessler F, Voss V, Dutzmann S, Seifert V, Gerlach R, Kögel D, et al. Inhibition of tissue factor/protease-activated receptor-2 signaling limits proliferation, migration and invasion of malignant glioma cells. Neuroscience. 2010;165(4):1312-22.
4.3-58	Glennie MJ, French RR, Cragg MS, Taylor RP. Mechanisms of killing by anti-CD20 monoclonal antibodies. Mol Immunol. 2007;44(16):3823-37.
4.3-59	Goldin-Lang P, Tran QV, Fichtner I, Eisenreich A, Antoniak S, Schulze K, et al. Tissue factor expression pattern in human non-small cell lung cancer tissues indicate increased blood thrombogenicity and tumor metastasis. Oncol Rep. 2008;20(1):123-8.
4.3-60	Griffin CT, Srinivasan Y, Zheng YW, Huang W, Coughlin SR. A role for thrombin receptor signaling in endothelial cells during embryonic development. Science. 2001;293(5535):1666-70.
4.3-61	Grossniklaus HE, Ling JX, Wallace TM, Dithmar S, Lawson DH, Cohen C, et al. Macrophage and retinal pigment epithelium expression of angiogenic cytokines in choroidal neovascularization. Mol Vis. 2002;8:119-26.
4.3-62	Guan M, Jin J, Su B, Liu WW, Lu Y. Tissue factor expression and angiogenesis in human glioma. Clin Biochem. 2002;35(4):321-5.
4.3-63	Haas SL, Jesnowski R, Steiner M, Hummel F, Ringel J, Burstein C, et al. Expression of tissue factor in pancreatic adenocarcinoma is associated with activation of coagulation. World J Gastroenterol. 2006;12(30):4843-9.
4.3-64	Hamada K, Kuratsu J, Saitoh Y, Takeshima H, Nishi T, Ushio Y. Expression of tissue factor correlates with grade of malignancy in human glioma. Cancer. 1996;77(9):1877-83.
4.3-65	Han TH, Gopal AK, Ramchandren R, Goy A, Chen R, Matous JV, et al. CYP3A-mediated drug-drug interaction potential and excretion of brentuximab vedotin, an antibody-drug conjugate, in patients with CD30-positive hematologic malignancies. J Clin Pharmacol. 2013;53(8):866-77.
4.3-66	Hansen CB, Pyke C, Petersen LC, Rao LV. Tissue factor-mediated endocytosis, recycling, and degradation of factor VIIa by a clathrin-independent mechanism not requiring the cytoplasmic domain of tissue factor. Blood. 2001;97(6):1712-20.
4.3-67	Hausott B, Vallant N, Hochfilzer M, Mangger S, Irschick R, Haugsten EM, et al. Leupeptin enhances cell surface localization of fibroblast growth factor receptor 1 in adult sensory neurons by increased recycling. Eur J Cell Biol. 2012;91(2):129-38.
4.3-68	Hemker HC, Giesen PL, Ramjee M, Wagenvoord R, Béguin S. The thrombogram: monitoring thrombin generation in platelet-rich plasma. Thromb Haemost. 2000;83(4):589-91.
4.3-69	Hjortoe GM, Petersen LC, Albrektsen T, Sorensen BB, Norby PL, Mandal SK, et al. Tissue factor-factor VIIa-specific up-regulation of IL-8 expression in MDA-MB-231 cells is mediated by PAR-2 and results in increased cell migration. Blood. 2004;103(8):3029-37.
4.3-70	Hu L, Xia L, Zhou H, Wu B, Mu Y, Wu Y, et al. TF/FVIIa/PAR2 promotes cell proliferation and migration via PKCα and ERK-dependent c-Jun/AP-1 pathway in colon cancer cell line SW620. Tumour Biol. 2013;34(5):2573-81.
4.3-71	Iba T, Levy JH, Levi M, Connors JM, Thachil J. Coagulopathy of coronavirus disease 2019. Crit Care Med. 2020;48(9):1358-64.

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添付資料番号	著者・タイトル・掲載誌
4.3-72	Jiao JA, Kelly AB, Marzec UM, Nieves E, Acevedo J, Burkhardt M, et al. Inhibition of acute vascular thrombosis in chimpanzees by an anti-human tissue factor antibody targeting the factor X binding site. Thromb Haemost. 2010;103(1):224-33.
4.3-73	Kagedal M, Samineni D, Gillespie WR, Lu D, Fine BM, Girish S, et al. Time-to-event modeling of peripheral neuropathy: platform analysis of eight valine-citrulline-monomethylauristatin E antibody-drug conjugates. CPT Pharmacometrics Syst Pharmacol. 2019;8(8):606-15.
4.3-74	Kaido T, Oe H, Yoshikawa A, Mori A, Arii S, Imamura M. Tissue factor is a useful prognostic factor of recurrence in hepatocellular carcinoma in 5-year survivors. Hepatogastroenterology. 2005;52(65):1383-7.
4.3-75	Kakkar AK, Lemoine NR, Scully MF, Tebbutt S, Williamson RC. Tissue factor expression correlates with histological grade in human pancreatic cancer. Br J Surg. 1995;82(8):1101-4.
4.3-76	Kasthuri RS, Taubman MB, Mackman N. Role of tissue factor in cancer. J Clin Oncol. 2009;27(29):4834-8.
4.3-77	Kaushal V, Mukunyadzi P, Siegel ER, Dennis RA, Johnson DE, Kohli M. Expression of tissue factor in prostate cancer correlates with malignant phenotype. Appl Immunohistochem Mol Morphol. 2008;16(1):1-6.
4.3-78	Keizer RJ, Huitema AD, Schellens JH, Beijnen JH. Clinical pharmacokinetics of therapeutic monoclonal antibodies. Clin Pharmacokinet. 2010;49(8):493-507.
4.3-79	Khorana AA, Ahrendt SA, Ryan CK, Francis CW, Hruban RH, Hu YC, et al. Tissue factor expression, angiogenesis, and thrombosis in pancreatic cancer. Clin Cancer Res. 2007;13(10):2870-5.
4.3-80	Kocaturk B, Tieken C, Vreeken D, Unlu B, Engels CC, de Kruijf EM, et al. Alternatively spliced tissue factor synergizes with the estrogen receptor pathway in promoting breast cancer progression. J Thromb Haemost. 2015;13(9):1683-93.
4.3-81	Kocaturk B, Van den Berg YW, Tieken C, Mieog JS, de Kruijf EM, Engels CC, et al. Alternatively spliced tissue factor promotes breast cancer growth in a beta1 integrin-dependent manner. Proc Natl Acad Sci USA. 2013;110(28):11517-22.
4.3-82	Koomagi R, Volm M. Tissue-factor expression in human non-small-cell lung carcinoma measured by immunohistochemistry: correlation between tissue factor and angiogenesis. Int J Cancer. 1998;79(1):19-22.
4.3-83	Kroemer G, Galluzzi L, Kepp O, Zitvogel L. Immunogenic cell death in cancer therapy. Annu Rev Immunol. 2013;31:51-72.
4.3-84	Lechner D, Weltermann A. Circulating tissue factor-exposing microparticles. Thromb Res. 2008;122(Suppl 1):S47-54.
4.3-85	Leppert U, Eisenreich A. The role of tissue factor isoforms in cancer biology. Int J Cancer. 2015;137(3):497-503.
4.3-86	Levi M, Thachil J, Iba T, Levy JH. Coagulation abnormalities and thrombosis in patients with COVID-19. Lancet Haematol. 2020;7(6):e438-40.
4.3-87	Levkowitz G, Waterman H, Zamir E, Kam Z, Oved S, Langdon WY, et al. c-Cbl/Sli-1 regulates endocytic sorting and ubiquitination of the epidermal growth factor receptor. Genes Dev. 1998;12(23):3663-74.
4.3-88	Li F, Emmerton KK, Jonas M, Zhang X, Miyamoto JB, Setter JR, et al. Intracellular Released Payload Influences Potency and Bystander-Killing Effects of Antibody-Drug Conjugates in Preclinical Models. Cancer Res. 2016;76(9):2710-9.
4.3-89	Li F, Ulrich M, Jonas M, Stone I, Linares G, Zhang X, et al. Tumor-associated macrophages can contribute to antitumor activity through FcgammaR-mediated processing of antibody-drug conjugates. Mol Cancer Ther. 2017;16(7):1347-54.

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4.3 参考文献

添付資料番号	著者・タイトル・掲載誌
4.3-90	Li T, Ling YH, Goldman ID, Perez-Soler R. Schedule-dependent cytotoxic synergism of pemetrexed and erlotinib in human non-small cell lung cancer cells. Clin Cancer Res. 2007;13(11):3413-22.
4.3-91	Li W, Zheng X, Gu J, Hunter J, Ferrell GL, Lupu F, et al. Overexpressing endothelial cell protein C receptor alters the hemostatic balance and protects mice from endotoxin. J Thromb Haemost. 2005;3(7):1351-9.
4.3-92	Liang HP, Kerschen EJ, Hernandez I, Basu S, Zogg M, Botros F, et al. EPCR-dependent PAR2 activation by the blood coagulation initiation complex regulates LPS-triggered interferon responses in mice. Blood. 2015;125(18):2845-54.
4.3-93	Lin K, Rubinfeld B, Zhang C, Firestein R, Harstad E, Roth L, et al. Preclinical development of an anti-NaPi2b (SLC34A2) antibody-drug conjugate as a therapeutic for non-small cell lung and ovarian cancers. Clin Cancer Res. 2015;21(22):5139-50.
4.3-94	Lin YS, Nguyen C, Mendoza JL, Escandon E, Fei D, Meng YG, et al. Preclinical pharmacokinetics, interspecies scaling, and tissue distribution of a humanized monoclonal antibody against vascular endothelial growth factor. J Pharmacol Exp Ther. 1999;288(1):371-8.
4.3-95	Liu Y, Mueller BM. Protease-activated receptor-2 regulates vascular endothelial growth factor expression in MDA-MB-231 cells via MAPK pathways. Biochem Biophys Res Commun. 2006;344(4):1263-70.
4.3-96	Liu-Kreyche P, Shen H, Marino AM, Iyer RA, Humphreys WG, Lai Y. Lysosomal P-gp-MDR1 Confers Drug Resistance of Brentuximab Vedotin and Its Cytotoxic Payload Monomethyl Auristatin E in Tumor Cells. Front Pharmacol. 2019;10:749.
4.3-97	Lonberg N, Huszar D. Human antibodies from transgenic mice. Int Rev Immunol. 1995;13(1):65-93.
4.3-98	Mackman N. Role of tissue factor in hemostasis, thrombosis, and vascular development. Arterioscler Thromb Vasc Biol. 2004;24(6):1015-22.
4.3-99	Madhusudhan T, Kerlin BA, Isermann B. The emerging role of coagulation proteases in kidney disease. Nat Rev Nephrol. 2016;12(2):94-109.
4.3-100	Madkhali Y, Featherby S, Collier ME, Maraveyas A, Greenman J, Ettelaie C. The ratio of factor VIIa: tissue factor content within microvesicles determines the differential influence on endothelial cells. TH Open. 2019;3(2):e132-45.
4.3-101	McLean K, Schirm S, Johns A, Morser J, Light DR. FXa-induced responses in vascular wall cells are PAR-mediated and inhibited by ZK-807834. Thromb Res. 2001;103(4):281-97.
4.3-102	McVey JH. The role of the tissue factor pathway in haemostasis and beyond. Curr Opin Hematol. 2016;23(5):453-61.
4.3-103	Merle NS, Church SE, Fremeaux-Bacchi V, Roumenina LT. Complement System Part I - Molecular Mechanisms of Activation and Regulation. Front Immunol. 2015;6:262.
4.3-104	Moberg L, Johansson H, Lukinius A, Berne C, Foss A, Källen R, et al. Production of tissue factor by pancreatic islet cells as a trigger of detrimental thrombotic reactions in clinical islet transplantation. Lancet. 2002;360(9350):2039-45.
4.3-105	Monroe DM, Key NS. The tissue factor-factor VIIa complex: procoagulant activity, regulation, and multitasking. J Thromb Haemost. 2007;5(6):1097-105.
4.3-106	Moro M, Bertolini G, Tortoreto M, Pastorino U, Sozzi G, Roz L. Patient-derived xenografts of non small cell lung cancer: resurgence of an old model for investigation of modern concepts of tailored therapy and cancer stem cells. J Biomed Biotechnol. 2012;568567.
4.3-107	Morris PE, Steingrub JS, Huang BY, Tang S, Liu PM, Rhode PR, et al. A phase I study evaluating the pharmacokinetics, safety and tolerability of an antibody-based tissue factor antagonist in subjects with acute lung injury or acute respiratory distress syndrome. BMC Pulm Med. 2012;12:5.

第4部（モジュール4）：非臨床試験報告書　添付資料一覧
4.3 参考文献

添付資料番号	著者・タイトル・掲載誌
4.3-108	Motoori M, Yano M, Tomita Y, Takahashi H, Tanaka K, Sugimura K, et al. Tissue factor predicts response to chemotherapy in esophageal cancer. J Surg Res. 2014;191(1):99-105.
4.3-109	Mueller BM, Reisfeld RA, Edgington TS, Ruf W. Expression of tissue factor by melanoma cells promotes efficient hematogenous metastasis. Proc Natl Acad Sci USA. 1992;89(24):11832-6.
4.3-110	Muller I, Klocke A, Alex M, Kotzsch M, Luther T, Morgenstern E, et al. Intravascular tissue factor initiates coagulation via circulating microvesicles and platelets. FASEB J. 2003;17(3):476-8.
4.3-111	Muller P, Kreuzaler M, Khan T, Thommen DS, Martin K, Glatz K, et al. Trastuzumab emtansine (T-DM1) renders HER2+ breast cancer highly susceptible to CTLA-4/PD-1 blockade. Sci Transl Med. 2015;7(315):315ra188.
4.3-112	Muller P, Martin K, Theurich S, Schreiner J, Savic S, Terszowski G, et al. Microtubule-depolymerizing agents used in antibody-drug conjugates induce antitumor immunity by stimulation of dendritic cells. Cancer Immunol Res. 2014;2(8):741-55.
4.3-113	Muller YA, Ultsch MH, de Vos AM. The crystal structure of the extracellular domain of human tissue factor refined to 1.7 A resolution. J Mol Biol. 1996;256(1):144-59.
4.3-114	Nakasaki T, Wada H, Shigemori C, Miki C, Gabazza EC, Nobori T, et al. Expression of tissue factor and vascular endothelial growth factor is associated with angiogenesis in colorectal cancer. Am J Hematol. 2002;69(4):247-54.
4.3-115	Naldini A, Sower L, Bocci V, Meyers B, Carney DH. Thrombin receptor expression and responsiveness of human monocytic cells to thrombin is linked to interferon-induced cellular differentiation. J Cell Physiol. 1998;177(1):76-84.
4.3-116	Ngo C, Scallon B, Tawadros R, McCabe F, Millar H, Nakada MT, et al. Enhanced Tumor Inhibition of MDA-MB-231 Breast Carcinoma by the Anti-Tissue Factor Antibody, CNTO 860, Is Mediated by Antibody Dependent Cellular Cytotoxicity. J Immunother. 2004;27(6):S10.
4.3-117	Nieuwland R, Berckmans RJ, McGregor S, Boing AN, Romijn FP, Westendorp RG, et al. Cellular origin and procoagulant properties of microparticles in meningococcal sepsis. Blood. 2000;95(3):930-5.
4.3-118	Nitori N, Ino Y, Nakanishi Y, Yamada T, Honda K, Yanagihara K, et al. Prognostic significance of tissue factor in pancreatic ductal adenocarcinoma. Clin Cancer Res. 2005;11(7):2531-9.
4.3-119	Ohta S, Wada H, Nakazaki T, Maeda Y, Nobori T, Shiku H, et al. Expression of tissue factor is associated with clinical features and angiogenesis in prostate cancer. Anticancer Res. 2002;22(5):2991-6.
4.3-120	Okeley NM, Miyamoto JB, Zhang X, Sanderson RJ, Benjamin DR, Sievers EL, et al. Intracellular activation of SGN-35, a potent anti-CD30 antibody-drug conjugate. Clin Cancer Res. 2010;16(3):888-97.
4.3-121	Ollivier V, Wang J, Manly D, Machlus KR, Wolberg AS, Jandrot-Perrus M, et al. Detection of endogenous tissue factor levels in plasma using the calibrated automated thrombogram assay. Thromb Res. 2010;125(1):90-6.
4.3-122	Orfeo T, Butenas S, Brummel-Ziedins KE, Mann KG. The tissue factor requirement in blood coagulation. J Biol Chem. 2005;280(52):42887-96.
4.3-123	Ossovskaya VS, Bunnett NW. Protease-activated receptors: contribution to physiology and disease. Physiol Rev. 2004;84(2):579-621.
4.3-124	Østerud B. Tissue factor expression in blood cells. Thromb Res. 2010;125(Suppl 1):S31-4.
4.3-125	Østerud B, Bjorklid E. Sources of tissue factor. Semin Thromb Hemost. 2006;32(1):11-23.

第4部（モジュール4）：非臨床試験報告書　添付資料一覧
4.3 参考文献

添付資料番号	著者・タイトル・掲載誌
4.3-126	Overdijk MB, Verploegen S, van den Brakel JH, Lammerts van Bueren JJ, Vink T, van de Winkel JG, et al. Epidermal growth factor receptor (EGFR) antibody-induced antibody-dependent cellular cytotoxicity plays a prominent role in inhibiting tumorigenesis, even of tumor cells insensitive to EGFR signaling inhibition. J Immunol. 2011;187(6):3383-90.
4.3-127	PADCEV European Public Assessment Report. Astellas Pharma Europe B.V. 2022.
4.3-128	Palumbo JS, Talmage KE, Massari JV, La Jeunesse CM, Flick MJ, Kombrinck KW, et al. Tumor cell-associated tissue factor and circulating hemostatic factors cooperate to increase metastatic potential through natural killer cell-dependent and-independent mechanisms. Blood. 2007;110(1):133-41.
4.3-129	Palumbo JS, Kombrinck KW, Drew AF, Grimes TS, Kiser JH, Degen JL, et al. Fibrinogen is an important determinant of the metastatic potential of circulating tumor cells. Blood. 2000;96(10):3302-9.
4.3-130	Parry GC, Erlich JH, Carmeliet P, Luther T, Mackman N. Low levels of tissue factor are compatible with development and hemostasis in mice. J Clin Invest. 1998;101(3):560-9.
4.3-131	Patry G, Hovington H, Larue H, Harel F, Fradet Y, Lacombe L. Tissue factor expression correlates with disease-specific survival in patients with node-negative muscle-invasive bladder cancer. Int J Cancer. 2008;122(7):1592-7.
4.3-132	Pawlinski R, Fernandes A, Kehrle B, Pedersen B, Parry G, Erlich J, et al. Tissue factor deficiency causes cardiac fibrosis and left ventricular dysfunction. Proc Natl Acad Sci USA. 2002;99(24):15333-8.
4.3-133	Pedersen B, Holscher T, Sato Y, Pawlinski R, Mackman N. A balance between tissue factor and tissue factor pathway inhibitor is required for embryonic development and hemostasis in adult mice. Blood. 2005;105(7):2777-82.
4.3-134	Peyvandi F, Palla R, Menegatti M, Siboni SM, Halimeh S, Faeser B, et al. Coagulation factor activity and clinical bleeding severity in rare bleeding disorders: results from the European Network of Rare Bleeding Disorders. J Thromb Haemost. 2012;10(4):615-21.
4.3-135	Pfirschke C, Engblom C, Rickelt S, Cortez-Retamozo V, Garris C, Pucci F, et al. Immunogenic Chemotherapy Sensitizes Tumors to Checkpoint Blockade Therapy. Immunity. 2016;44(2):343-54.
4.3-136	Poon RT, Lau CP, Ho JW, Yu WC, Fan ST, Wong J. Tissue factor expression correlates with tumor angiogenesis and invasiveness in human hepatocellular carcinoma. Clin Cancer Res. 2003;9(14):5339-45.
4.3-137	Rallabhandi P, Nhu QM, Toshchakov VY, Piao W, Medvedev AE, Hollenberg MD, et al. Analysis of proteinase-activated receptor 2 and TLR4 signal transduction: a novel paradigm for receptor cooperativity. J Biol Chem. 2008;283(36):24314-25.
4.3-138	Ramchandren R, Advani RH, Ansell SM, Bartlett NL, Chen R, Connors JM, et al. Brentuximab vedotin plus chemotherapy in North American patients with newly diagnosed stage III or IV Hodgkin lymphoma. Clin Cancer Res. 2019;25(6):1718-26.
4.3-139	Regina S, Valentin JB, Lachot S, Lemarié E, Rollin J, Gruel Y. Increased tissue factor expression is associated with reduced survival in non-small cell lung cancer and with mutations of TP53 and PTEN. Clin Chem. 2009;55(10):1834-42.
4.3-140	Regina S, Rollin J, Bléchet C, Iochmann S, Reverdiau P, Gruel Y. Tissue factor expression in non-small cell lung cancer: relationship with vascular endothelial growth factor expression, microvascular density, and K-ras mutation. J Thorac Oncol. 2008;3(7):689-97.
4.3-141	Rickles FR, Hair GA, Zeff RA, Lee E, Bona RD. Tissue factor expression in human leukocytes and tumor cells. Thromb Haemost. 1995;74(1):391-5.

第4部（モジュール4）：非臨床試験報告書　添付資料一覧
4.3 参考文献

添付資料番号	著者・タイトル・掲載誌
4.3-142	Rondon AMR, Kroone C, Kapteijn MY, Versteeg HH, Buijs JT. Role of tissue factor in tumor progression and cancer-associated thrombosis. Semin Thromb Hemost. 2019;45(4):396-412.
4.3-143	Rosen ED, Chan JC, Idusogie E, Clotman F, Vlasuk G, Luther T, et al. Mice lacking factor VII develop normally but suffer fatal perinatal bleeding. Nature. 1997;390(6657):290-4.
4.3-144	Roskoski R, Jr. ERK1/2 MAP kinases: structure, function, and regulation. Pharmacol Res. 2012;66(2):105-43.
4.3-145	Ruf W. Tissue factor and PAR signaling in tumor progression [published correction appears in Thromb Res. 2008;123(1):187-90]. Thromb Res. 2007;120 Suppl 2:S7-12.
4.3-146	Ruf W, Mueller BM. Tissue factor in cancer angiogenesis and metastasis. Curr Opin Hematol. 1996;3(5):379-84.
4.3-147	Ryden L, Grabau D, Schaffner F, Jönsson PE, Ruf W, Belting M. Evidence for tissue factor phosphorylation and its correlation with protease-activated receptor expression and the prognosis of primary breast cancer. Int J Cancer. 2010;126(10):2330-40.
4.3-148	Saber H, Leighton JK. An FDA oncology analysis of antibody-drug conjugates. Regul Toxicol Pharmacol. 2015;71(3):444-52.
4.3-149	Sawada M, Miyake S, Ohdama S, Matsubara O, Masuda S, Yakumaru K, et al. Expression of tissue factor in non-small-cell lung cancers and its relationship to metastasis. Br J Cancer. 1999;79(3-4):472-7.
4.3-150	Schaffner F, Versteeg HH, Schillert A, Yokota N, Petersen LC, Mueller BM, et al. Cooperation of tissue factor cytoplasmic domain and PAR2 signaling in breast cancer development. Blood. 2010;116(26):6106-13.
4.3-151	Sen P, Neuenschwander PF, Pendurthi UR, Rao LV. Analysis of factor VIIa binding to relipidated tissue factor by surface plasmon resonance. Blood Coagul Fibrinolysis. 2010;21(4):376-9.
4.3-152	Seto S, Onodera H, Kaido T, Yoshikawa A, Ishigami S, Arii S, et al. Tissue factor expression in human colorectal carcinoma: correlation with hepatic metastasis and impact on prognosis. Cancer. 2000;88(2):295-301.
4.3-153	Shigemori C, Wada H, Matsumoto K, Shiku H, Nakamura S, Suzuki H. Tissue factor expression and metastatic potential of colorectal cancer. Thromb Haemost. 1998;80(6):894-8.
4.3-154	Shimizu S, Ogawa T, Takezawa K, Tojima I, Kouzaki H, Shimizu T. Tissue factor and tissue factor pathway inhibitor in nasal mucosa and nasal secretions of chronic rhinosinusitis with nasal polyp. Am J Rhinol Allergy. 2015;29(4):235-42.
4.3-155	Song HB, Park KD, Kim JH, Kim DH, Yu YS, Kim JH. Tissue factor regulates tumor angiogenesis of retinoblastoma via the extracellular signal-regulated kinase pathway. Oncol Rep. 2012;28(6):2057-62.
4.3-156	Sorensen BB, Rao LV, Tornehave D, Gammeltoft S, Petersen LC. Antiapoptotic effect of coagulation factor VIIa. Blood. 2003;102(5):1708-15.
4.3-157	Sorkin A, Goh LK. Endocytosis and intracellular trafficking of ErbBs. Exp Cell Res. 2009;315(4):683-96.
4.3-158	Srinivasan R, Ozhegov E, van den Berg YW, Aronow BJ, Franco RS, Palascak MB, et al. Splice variants of tissue factor promote monocyte-endothelial interactions by triggering the expression of cell adhesion molecules via integrin-mediated signaling. J Thromb Haemost. 2011;9(10):2087-96.

第4部（モジュール4）：非臨床試験報告書　添付資料一覧
4.3 参考文献

添付資料番号	著者・タイトル・掲載誌
4.3-159	Stagg NJ, Shen BQ, Brunstein F, Li C, Kamath AV, Zhong F, et al. Peripheral neuropathy with microtubule inhibitor containing antibody drug conjugates: challenges and perspectives in translatability from nonclinical toxicology studies to the clinic. Regul Toxicol Pharmacol. 2016;82:1-13.
4.3-160	Stampfli SF, Akhmedov A, Hausladen S, Varga Z, Dedes KJ, Hellermann J, et al. Tissue Factor Expression Does Not Predict Mortality in Breast Cancer Patients. Anticancer Res. 2017;37(6):3259-64.
4.3-161	Sturm U, Luther T, Albrecht S, Flössel C, Grossmann H, Müller M. Immunohistological detection of tissue factor in normal and abnormal human mammary glands using monoclonal antibodies. Virchows Arch A Pathol Anat Histopathol. 1992;421(2):79-86.
4.3-162	Suh TT, Holmback K, Jensen NJ, Daugherty CC, Small K, Simon DI, et al. Resolution of spontaneous bleeding events but failure of pregnancy in fibrinogen-deficient mice. Genes Dev. 1995;9(16):2020-33.
4.3-163	Sun WY, Witte DP, Degen JL, Colbert MC, Burkart MC, Holmbäck K, et al. Prothrombin deficiency results in embryonic and neonatal lethality in mice. Proc Natl Acad Sci USA. 1998;95(13):7597-602.
4.3-164	Takano S, Tsuboi K, Tomono Y, Mitsui Y, Nose T. Tissue factor, osteopontin, αvβ3 integrin expression in microvasculature of gliomas associated with vascular endothelial growth factor expression. Br J Cancer. 2000;82(12):1967-73.
4.3-165	Takeshima H, Nishi T, Kuratsu J, Kamikubo Y, Kochi M, Ushio Y. Suppression of the tissue factor-dependent coagulation cascade: a contributing factor for the development of intratumoral hemorrhage in glioblastoma. Int J Mol Med. 2000;6(3):271-6.
4.3-166	Tentler JJ, Tan AC, Weekes CD, Jimeno A, Leong S, Pitts TM, et al. Patient-derived tumour xenografts as models for oncology drug development. Nat Rev Clin Oncol. 2012;9(6):338-50.
4.3-167	Thachil J, Tang N, Gando S, Falanga A, Cattaneo M, Levi M, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. J Thromb Haemost. 2020;18(5):1023-6.
4.3-168	Tomayko MM, Reynolds CP. Determination of subcutaneous tumor size in athymic (nude) mice. Cancer Chemother Pharmacol. 1989;24(3):148-54.
4.3-169	Toomey JR, Kratzer KE, Lasky NM, Broze GJ, Jr. Effect of tissue factor deficiency on mouse and tumor development. Proc Natl Acad Sci USA. 1997;94(13):6922-6.
4.3-170	Toomey JR, Kratzer KE, Lasky NM, Stanton JJ, Broze GJ, Jr. Targeted disruption of the murine tissue factor gene results in embryonic lethality. Blood. 1996;88(5):1583-7.
4.3-171	Tripodi A. Thrombin generation assay and its application in the clinical laboratory. Clin Chem. 2016;62(5):699-707.
4.3-172	Tuddenham EG, Pemberton S, Cooper DN. Inherited factor VII deficiency: genetics and molecular pathology. Thromb Haemost. 1995;74(1):313-21.
4.3-173	Ueno T, Toi M, Koike M, Nakamura S, Tominaga T. Tissue factor expression in breast cancer tissues: its correlation with prognosis and plasma concentration. Br J Cancer. 2000;83(2):164-70.
4.3-174	Uno K, Homma S, Satoh T, Nakanishi K, Abe D, Matsumoto K, et al. Tissue factor expression as a possible determinant of thromboembolism in ovarian cancer. Br J Cancer. 2007;96(2):290-5.

第4部（モジュール4）：非臨床試験報告書　添付資料一覧
4.3 参考文献

添付資料番号	著者・タイトル・掲載誌
4.3-175	van den Berg YW, van den Hengel LG, Myers HR, Ayachi O, Jordanova E, Ruf W, et al. Alternatively spliced tissue factor induces angiogenesis through integrin ligation. Proc Natl Acad Sci USA. 2009;106(46):19497-502.
4.3-176	van den Hengel LG, Versteeg HH. Tissue factor signaling: a multi-faceted function in biological processes. Front Biosci (Schol Ed). 2011;3(4):1500-10.
4.3-177	van der Logt CP, Dirven RJ, Reitsma PH, Bertina RM. Expression of tissue factor and tissue factor pathway inhibitor in monocytes in response to bacterial lipopolysaccharide and phorbolester. Blood Coagul Fibrinolysis. 1994;5(2):211-20.
4.3-178	Versteeg HH. Tissue factor: old and new links with cancer biology. Semin Thromb Hemost. 2015;41(7):747-55.
4.3-179	Versteeg HH, Heemskerk JW, Levi M, Reitsma PH. New fundamentals in hemostasis. Physiol Rev. 2013;93(1):327-58.
4.3-180	Versteeg HH, Schaffner F, Kerver M, Petersen HH, Ahamed J, Felding-Habermann B, et al. Inhibition of tissue factor signaling suppresses tumor growth. Blood. 2008a;111(1):190-9.
4.3-181	Versteeg HH, Schaffner F, Kerver M, Ellies LG, Andrade-Gordon P, Mueller BM, et al. Protease-activated receptor (PAR) 2, but not PAR1, signaling promotes the development of mammary adenocarcinoma in polyoma middle T mice. Cancer Res. 2008b;68(17):7219-27.
4.3-182	Versteeg HH, Spek CA, Slofstra SH, Diks SH, Richel DJ, Peppelenbosch MP. FVIIa:TF induces cell survival via G12/G13-dependent Jak/STAT activation and BclXL production. Circ Res. 2004a;94(8):1032-40.
4.3-183	Versteeg HH, Spek CA, Richel DJ, Peppelenbosch MP. Coagulation factors VIIa and Xa inhibit apoptosis and anoikis. Oncogene. 2004b;23(2):410-7.
4.3-184	Vincent MJ, Bergeron E, Benjannet S, Erickson BR, Rollin PE, Ksiazek TG, et al. Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. Virol J. 2005;2:69.
4.3-185	Vrana JA, Stang MT, Grande JP, Getz MJ. Expression of tissue factor in tumor stroma correlates with progression to invasive human breast cancer: paracrine regulation by carcinoma cell-derived members of the transforming growth factor beta family. Cancer Res. 1996;56(21):5063-70.
4.3-186	Wan Y, Wu N, Wang Z, Ju X, Zhu J, Liu Y, et al. Relationship between tissue factor expression and hepatic metastasis and prognosis in rectal cancer. Zhonghua Zhong Liu Za Zhi. 2002;24(4):378-80.
4.3-187	Wang B, Xiong S, Hua Q, Chen C, Liao H, Chen L, et al. Tissue factor is strongly expressed in pericarcinomatous tissue in patients with laryngeal carcinoma. Int J Clin Exp Pathol. 2015;8(10):13719-24.
4.3-188	Wang B, Berger M, Masters G, Albone E, Yang Q, Sheedy J, et al. Radiotherapy of human xenograft NSCLC tumors in nude mice with a 90Y-labeled anti-tissue factor antibody. Cancer Biother Radiopharm. 2005;20(3):300-9.
4.3-189	Wang JG, Manly D, Kirchhofer D, Pawlinski R, Mackman N. Levels of microparticle tissue factor activity correlate with coagulation activation in endotoxemic mice. J Thromb Haemost. 2009;7(7):1092-8.
4.3-190	Wikkelsoe AJ, Afshari A, Wetterslev J, Brok J, Moeller AM. Monitoring patients at risk of massive transfusion with Thrombelastography or Thromboelastometry: a systematic review. Acta Anaesthesiol Scand. 2011;55(10):1174-89.
4.3-191	Witkowski M, Landmesser U, Rauch U. Tissue factor as a link between inflammation and coagulation. Trends Cardiovasc Med. 2016;26(4):297-303.

第4部（モジュール4）：非臨床試験報告書　添付資料一覧
4.3 参考文献

添付資料番号	著者・タイトル・掲載誌
4.3-192	Wojtukiewicz MZ, Rucinska M, Zacharski LR, Kozlowski L, Zimnoch L, Piotrowski Z, et al. Localization of blood coagulation factors in situ in pancreatic carcinoma. Thromb Haemost. 2001;86(6):1416-20.
4.3-193	Wojtukiewicz MZ, Sierko E, Skalij P, Kaminska M, Zimnoch L, Brekken RA, et al. Granulocyte-Colony Stimulating Factor Receptor, Tissue Factor, and VEGF-R Bound VEGF in Human Breast Cancer In Loco. Adv Clin Exp Med. 2016;25(3):505-11.
4.3-194	Wojtukiewicz MZ, Zacharski LR, Rucinska M, Zimnoch L, Jaromin J, Rozanska-Kudelska M, et al. Expression of tissue factor and tissue factor pathway inhibitor in situ in laryngeal carcinoma. Thromb Haemost. 1999;82(6):1659-62.
4.3-195	Wu B, Zhou H, Hu L, Mu Y, Wu Y. Involvement of PKCα activation in TF/VIIa/PAR2-induced proliferation, migration, and survival of colon cancer cell SW620. Tumour Biol. 2013;34(2):837-46.
4.3-196	Xue J, Wu Q, Westfield LA, Tuley EA, Lu D, Zhang Q, et al. Incomplete embryonic lethality and fatal neonatal hemorrhage caused by prothrombin deficiency in mice. Proc Natl Acad Sci USA. 1998;95(13):7603-7.
4.3-197	Yao JL, Ryan CK, Francis CW, Kohli M, Taubman MB, Khorana AA. Tissue factor and VEGF expression in prostate carcinoma: a tissue microarray study. Cancer Invest. 2009;27(4):430-4.
4.3-198	Yokota N, Koizume S, Miyagi E, Hirahara F, Nakamura Y, Kikuchi K, et al. Self-production of tissue factor-coagulation factor VII complex by ovarian cancer cells. Br J Cancer. 2009;101(12):2023-9.
4.3-199	Zhao X, Cheng C, Gou J, Yi T, Qian Y, Du X, et al. Expression of tissue factor in human cervical carcinoma tissue. Exp Ther Med. 2018;16(5):4075-81.
4.3-200	Zhou JN, Ljungdahl S, Shoshan MC, Swedenborg J, Linder S. Activation of tissue-factor gene expression in breast carcinoma cells by stimulation of the RAF-ERK signaling pathway. Mol Carcinog. 1998;21(4):234-43.

第5部（モジュール5）：臨床試験報告書　添付資料一覧

5.2 臨床試験一覧表

添付資料番号	タイトル	報種類 （国内／海外）	掲載誌	評価資料・ 参考資料の別	申請電子データの提出有無
5.2	Tabular Listing of All Clinical Studies	－	社内資料	－	－

第5部（モジュール5）：臨床試験報告書　添付資料一覧
5.3　試験報告書及び関連情報

添付資料番号	報告書番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別	申請電子データの提出有無
5.3.1 生物薬剤学試験報告書						
5.3.1.1 バイオアベイラビリティ（BA）試験報告書：該当なし						
5.3.1.2 比較 BA 試験及び生物学的同等性（BE）試験報告書：該当なし						
5.3.1.3 In Vitro-In Vivo の関連を検討した試験報告書：該当なし						
5.3.1.4 生物学的及び理化学的分析法検討報告書						
5.3.1.4-1	[redacted]200EL-132003-D	VALIDATION OF A METHOD FOR THE DETERMINATION OF HUMAX®-TF-ADC (MMAE specific) IN HUMAN PLASMA SAMPLES BY ELISA	海外	社内資料	評価資料	無
5.3.1.4-2	[redacted]200EL-132003-F	VALIDATION OF A METHOD FOR THE DETECTION, CONFIRMATION AND QUANTIFICATION OF ANTI-HUMAX-TF-ADC ANTIBODIES IN HUMAN SERUM SAMPLES BY MSD	海外	社内資料	評価資料	無
5.3.1.4-3	[redacted]200EL-132003-I	VALIDATION OF A METHOD FOR THE DETERMINATION OF HUMAX®-TF-ADC (IgG1 SPECIFIC) IN HUMAN PLASMA SAMPLES BY ELISA	海外	社内資料	評価資料	無

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5.3.1.4-4	8291518	Validation of an Analytical Procedure for the Determination of Free MMAE in Human Plasma following dosing with HuMax-TF-ADC using Solid Phase extraction followed by Liquid Chromatography with Tandem Mass Spectrometric Detection (LC-MS/MS)	海外	社内資料	評価資料	無
5.3.1.4-5	[redacted]695EL-156953-B	REVALIDATION OF A METHOD FOR THE DETERMINATION OF HUMAX®-TF-ADC (MMAE SPECIFIC) IN HUMAN PLASMA SAMPLES BY ELISA	海外	社内資料	評価資料	無
5.3.1.4-6	[redacted]1015-221	Qualification of an assay to characterize neutralizing antibody response against Tisotumab Vedotin in human serum samples by ECLIA	海外	社内資料	評価資料	無
5.3.1.4-7	[redacted]105EL-181053-C	VALIDATION OF A METHOD FOR THE DETECTION, CONFIRMATION AND QUANTIFICATION OF ANTI-HUMAX-TF-ADC ANTIBODIES IN HUMAN SERUM SAMPLES BY BRIDGING ECLIA	海外	社内資料	評価資料	無
5.3.1.4-8	[redacted]012UL-170127-D	VALIDATION OF A METHOD FOR THE DETERMINATION OF HUMAX®-TF-ANTIBODY DRUG CONJUGATE (ADC) IN HUMAN K2-EDTA PLASMA SAMPLES BY ELISA	海外	社内資料	評価資料	無

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5.3.1.4-9	[redacted]012UL-170127-F	VALIDATION OF A METHOD FOR THE DETERMINATION OF HUMAX-TF-ADC ANTIBODY IN HUMAN K2-EDTA PLASMA SAMPLES BY ELISA	海外	社内資料	評価資料	無
5.3.1.4-10	[redacted]012UL-170127-B	VALIDATION OF A METHOD FOR THE DETERMINATION OF MMAE IN HUMAN SODIUM CITRATE PLASMA SAMPLES BY LC-MS/MS (TRIPLE QUAD 5500)	海外	社内資料	評価資料	無
5.3.1.4-11	[redacted]012UL-170127-H	VALIDATION OF A METHOD FOR THE DETECTION, CONFIRMATION AND TITRATION OF ANTI-HUMAX-TF-ADC ANTIBODIES IN HUMAN SERUM SAMPLES BY ECLIA	海外	社内資料	評価資料	無
5.3.1.4-12	976-R12090	Validation Report for Method [redacted]-3584: Quantitation of HuMax-TF-ADC Total Antibody (TAb) in Human Plasma by Enzyme-Linked Immunosorbent Assay (ELISA)	海外	社内資料	評価資料	無

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5.3.1.4-13	976-R11942	Validation Report for Method [redacted]-3522: Electrochemiluminescence Immunoassay for the Screening, Confirmation, and Titration of Anti-HuMax-TF-ADC Antibodies in Human Serum	海外	社内資料	評価資料	無
5.3.1.4-14	976-R10960	Report for the Validation of Method [redacted]-3105-R0: Determination of Free MMAE in K_2EDTA Human Plasma by LC-MS/MS	海外	社内資料	評価資料	無
5.3.1.4-15	976-R12959	Validation Report for Method [redacted]-3889: A Cell-Based Assay for the Detection of Neutralizing Antibodies Against Humax-TF-ADC in Human Serum.	海外	社内資料	参考資料	無
5.3.1.4-16	[redacted]124EL-131243-A	DETERMINATION OF HUMAX®-TF-ADC (IgG1 SPECIFIC) IN HUMAN PLASMA SAMPLES BY ELISA	海外	社内資料	参考資料	無
5.3.1.4-17	[redacted]124EL-131243-B	DETERMINATION OF HUMAX®-TF-ADC (MMAE SPECIFIC) IN HUMAN PLASMA SAMPLES BY ELISA	海外	社内資料	参考資料	無

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5.3.1.4-18	[redacted]124EL-131243-C	DETECTION, CONFIRMATION AND SEMI-QUANTIFICATION OF ANTI-HUMAX®-TF-ADC ANTIBODIES IN HUMAN SERUM SAMPLES BY ECLIA	海外	社内資料	参考資料	無
5.3.1.4-19	8291591	Determination of Free MMAE in Human Plasma Following Dosing with HuMax®-TF-ADC from a Phase I Clinical Study using Solid Phase Extraction Followed by Liquid Chromatography with Tandem Mass Spectrometric Detection (LC-MS/MS)	海外	社内資料	参考資料	無
5.3.1.4-20	[redacted]361EL-153613-A	DETERMINATION OF HUMAX®-TF-ADC (MMAE-SPECIFIC) IN HUMAN PLASMA SAMPLES BY ELISA	海外	社内資料	参考資料	無
5.3.1.4-21	[redacted]361EL-153613-B	DETERMINATION OF HUMAX®-TF-ADC (IgG1 SPECIFIC) IN HUMAN PLASMA SAMPLES BY ELISA	海外	社内資料	参考資料	無
5.3.1.4-22	[redacted]361EL-153613-C	DETECTION, CONFIRMATION AND SEMI-QUANTIFICATION OF ANTI- HUMAX®-TF-ADC ANTIBODIES IN HUMAN SERUM SAMPLES BY ECLIA	海外	社内資料	参考資料	無

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5.3.1.4-23	8336662	Determination of Free MMAE in Human Plasma Following Dosing with HuMax®-TF-ADC from a Phase I Clinical Study using Solid Phase Extraction Followed by Liquid Chromatography with Tandem Mass Spectrometric Detection (LC-MS/MS)	海外	社内資料	参考資料	無
5.3.1.4-24	[redacted]469EL-184693-A	DETERMINATION OF HUMAX®-TF-ADC (IgG1 SPECIFIC) IN HUMAN PLASMA SAMPLES BY ELISA	海外	社内資料	評価資料	無
5.3.1.4-25	[redacted]469EL-184693_B	DETERMINATION OF HUMAX®-TF-ADC (MMAE SPECIFIC) IN HUMAN PLASMA SAMPLES BY ELISA	海外	社内資料	評価資料	無
5.3.1.4-26	[redacted]469EL-184693-C	DETECTION OF ANTI-HUMAX®-TF-ADC ANTIBODIES IN HUMAN SERUM SAMPLES BY ECLIA	海外	社内資料	評価資料	無
5.3.1.4-27	8406185	Determination of MMAE in Human Plasma using Liquid Chromatography with Tandem Mass Spectrometric Detection (LC-MS/MS) for Sponsor Reference Number GCT1015-06	海外	社内資料	評価資料	無

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5.3.1.4-28	[redacted]1015-H003	Bioanalytical Phase Report: Determination of neutralizing antibody responses to Tisotumab Vedotin in human serum samples of clinical trial study GCT1015-06 by ECLIA	海外	社内資料	参考資料	無
5.3.1.4-29	[redacted]036EL-170363-B	INTERIM BIOANALYTICAL REPORT DETERMINATION OF HUMAX®-TF-ADC (MMAE SPECIFIC) IN HUMAN PLASMA SAMPLES BY ELISA	海外	社内資料	参考資料	無
5.3.1.4-30	[redacted]036EL-170363-A	INTERIM BIOANALYTICAL REPORT DETERMINATION OF HUMAX®-TF-ADC (IgG1 SPECIFIC) IN HUMAN PLASMA SAMPLES BY ELISA	海外	社内資料	参考資料	無
5.3.1.4-31	[redacted]036EL-170363-C	INTERIM BIOANALYTICAL REPORT DETECTION, CONFIRMATION AND SEMI-QUANTIFICATION OF ANTI-HUMAX®-TF-ADC ANTIBODIES IN HUMAN SERUM SAMPLES BY ECLIA	海外	社内資料	参考資料	無
5.3.1.4-32	8385307	Determination of MMAE in Human Plasma using Liquid Chromatography with Tandem Mass Spectrometric Detection (LC-MS/MS) for Sponsor Reference Number GCT1015-04	海外	社内資料	参考資料	無

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5.3.1.4-33	[redacted]1015-222	Bioanalytical Phase Report: Determination of neutralizing antibody responses to Tisotumab Vedotin in human serum samples of clinical trial study GCT1015-04 by ECLIA	海外	社内資料	参考資料	無
5.3.1.4-34	[redacted]022UL-180227 A	INTERIM BIOANALYTICAL REPORT DETERMINATION OF MMAE IN HUMAN SODIUM CITRATE PLASMA SAMPLES BY LC-MS/MS (TRIPLE QUAD 5500)	海外	社内資料	参考資料	無
5.3.1.4-35	[redacted]022UL-180227 B	BIOANALYTICAL INTERIM REPORT DETERMINATION OF HUMAX-TF-ANTIBODY DRUG CONJUGATE (ADC) IN HUMAN K2-EDTA PLASMA SAMPLES BY ELISA	海外	社内資料	参考資料	無
5.3.1.4-36	[redacted]022UL-180227 C	BIOANALYTICAL INTERIM REPORT DETERMINATION OF TOTAL HUMAX-TF-ADC ANTIBODY IN HUMAN K2-EDTA PLASMA BY ELISA	海外	社内資料	参考資料	無
5.3.1.4-37	[redacted]022UL-180227 D	Immunoassay Sample Analysis Report for the Detection, Characterization, and Titration of Anti-Humax-TF-ADC Antibodies in Human Serum by an ECLA for Study SGNTV-001 Interim Report 3	海外	社内資料	参考資料	無

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5.3.1.4-38	23-10233-A	Immunoassay Sample Analysis Report for the Determination of Humax-TF-Antibody Drug Conjugate (ADC) in Human Plasma (K_2EDTA) by Quantitative ELISA for Study SGNTV-003	海外	社内資料	評価資料	無
5.3.1.4-39	976-R12549	Enzyme-Linked Immunosorbent Assay for the Quantitation of HuMax-TF-ADC Total Antibody in Human Plasma in Support of Clinical Protocol -Study Number SGNTV-003: A Randomized, Open-Label, Phase 3 Trial of Tisotumab Vedotin vs Investigator's Choice Chemotherapy in Second- or Third-Line Recurrent or Metastasic Cervical Cancer.	海外	社内資料	評価資料	無
5.3.1.4-40	976-R12516	Electrochemiluminescence Immunoassay for the Detection of Anti-HuMax-TF-ADC Antibodies in Human Serum for Study No. SGNTV-003: A Randomized, Open-Label, Phase 3 Trial of Tisotumab Vedotin vs Investigator's Choice Chemotherapy in Second or Third-Line Recurrent or Metastatic Cervical Cancer	海外	社内資料	評価資料	無
5.3.1.4-41	976-R12524	LC-MS/MS Determination of Unconjugated MMAE in Human Sodium Citrate and K_2EDTA Plasma Samples Originating from Seattle Genetics Inc. SGNTV-003 Study: A Randomized, Open-Label, Phase 3 Trial of Tisotumab Vedotin vs Invetigator's Choice Chemotherapy in Second- or Third-Line Recurrent or metastatic cervical Cancer	海外	社内資料	評価資料	無

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5.3.1.4-42	976-R13570	A Cell-Based Assay to Detect Neutralizing Antibodies against Humax-TF-ADC in Human Serum	海外	社内資料	参考資料	無
5.3.1.4-43	[redacted]012UL-170127-I	CROSS-VALIDATION OF A METHOD FOR THE DETERMINATION OF MMAE IN HUMAN SODIUM CITRATE PLASMA SAMPLES BY LC-MS/MS (TRIPLE QUAD 5500)	海外	社内資料	参考資料	無
5.3.1.4-44	[redacted]012UL-170127-J	CROSS VALIDATION OF A METHOD FOR THE DETERMINATION OF HUMAX-TF-ANTIBODY DRUG CONJUGATE (ADC) IN HUMAN K_2-EDTA PLASMA SAMPLES BY ELISA	海外	社内資料	参考資料	無
5.3.1.4-45	[redacted]012UL-170127-K	CROSS VALIDATION OF A METHOD FOR THE DETERMINATION OF TOTAL HUMAX-TF-ADC ANTIBODY IN HUMAN K_2-EDTA PLASMA BY ELISA	海外	社内資料	参考資料	無
5.3.1.4-46	[redacted]012UL-170127-L	CROSS-VALIDATION OF A METHOD FOR THE DETERMINATION OF MMAE IN HUMAN SODIUM CITRATE PLASMA SAMPLES BY LC-MS/MS (TRIPLE QUAD 5500)	海外	社内資料	参考資料	無

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5.3.2 ヒト生体試料を用いた薬物動態関連の試験報告書：該当なし						
5.3.2.1 血漿蛋白結合試験報告書：該当なし						
5.3.2.2 肝代謝及び薬物相互作用試験報告書：該当なし						
5.3.2.3 他のヒト生体試料を用いた試験報告書：該当なし						
5.3.3 臨床薬物動態（PK）試験報告書						
5.3.3.1 健康被験者における PK 及び初期忍容性試験報告書：該当なし						
5.3.3.2 患者における PK 及び初期忍容性試験報告書：該当なし						
5.3.3.3 内因性要因を検討した PK 試験報告書：該当なし						
5.3.3.4 外因性要因を検討した PK 試験報告書：該当なし						
5.3.3.5 ポピュレーション PK 試験報告書						
5.3.3.5-1	[redacted]1015-248	Population PK Analysis for Tisotumab Vedotin in Patients with Locally Advanced and/or Metastatic Solid Tumors	海外	社内資料	評価資料	有

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5.3.3.5-2	[redacted]-7392	Population PK Analysis of Tisotumab Vedotin in Patients with Locally Advanced and/or Metastatic Solid Tumors	海外	社内資料	評価資料	有
5.3.3.5-3	[redacted]-7394	Exposure-Safety and Exposure-Efficacy Analyses for Tisotumab Vedotin in Patients with Locally Advanced and/or Metastatic Solid Tumors	海外	社内資料	参考資料	無
5.3.4 臨床薬力学（PD）試験報告書：該当なし						
5.3.4.1 健康被験者における PD 試験及び PK/PD 試験報告書：該当なし						
5.3.4.2 患者における PD 試験及び PK/PD 試験報告書：該当なし						

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5.3.5 有効性及び安全性試験報告書						
5.3.5.1 申請する適応症に関する比較対照試験報告書						
5.3.5.1-1	SGNTV-003 innovaTV 301	A Randomized, Open-Label, Phase 3 Trial of Tisotumab Vedotin vs Investigator's Choice Chemotherapy in Second- or Third-Line Recurrent or Metastatic Cervical Cancer	海外／国内	社内資料	評価資料	有
5.3.5.1-1	SGNTV-003 innovaTV 301 Japanese population	Japanese population of SGNTV-003 study	海外／国内	社内資料	評価資料	有
5.3.5.1-1	SGNTV-003 innovaTV 301 safety_ctd	Safety data of SGNTV-003 study for CTD	海外／国内	社内資料	評価資料	有
5.3.5.2 非対照試験報告書						
5.3.5.2-1	GCT1015-06 innovaTV 206	Open Label Phase 1/2 Trial of Tisotumab Vedotin in Japanese Subjects with Advanced Solid Malignancies	国内	社内資料	評価資料	無

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5.3.5.2-1	GCT1015-06 innovaTV 206	Open Label Phase 1/2 Trial of Tisotumab Vedotin in Japanese Subjects with Advanced Solid Malignancies Addendum	国内	社内資料	評価資料	有
5.3.5.2-1	GCT1015-06 innovaTV 206 safety_ctd	Safety data of GCT1015-06 study for CTD	国内	社内資料	評価資料	有
5.3.5.2-2	GEN701 innovaTV 201	First-In-Human, Dose Escalating Safety Study of Tissue Factor Specific Antibody-Drug Conjugate Tisotumab Vedotin (Humax®-TF-ADC) in Patients with Locally Advanced and/or Metastatic Solid Tumors Known to Express Tissue Factor.	海外	社内資料	評価資料	有
5.3.5.2-2	GEN701 innovaTV 201 safety_ctd (escalation part)	Safety data of GEN701 study escalation part for CTD	海外	社内資料	評価資料	有

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5.3.5.2-2	GEN701 innovaTV 201 safety_ctd (expansion part)	Safety data of GEN701 study expansion part for CTD	海外	社内資料	評価資料	有
5.3.5.2-3	GCT1015-04 innovaTV 204	A Single-arm, Multicenter, International Trial of Tisotumab Vedotin (HuMax®-TF-ADC) in Previously Treated, Recurrent or Metastatic Cervical Cancer	海外	社内資料	参考資料	無
5.3.5.2-3	GCT1015-04 innovaTV 204	A Single-arm, Multicenter, International Trial of Tisotumab Vedotin (HuMax®-TF-ADC) in Previously Treated, Recurrent or Metastatic Cervical Cancer Addendum	海外	社内資料	参考資料	無
5.3.5.2-4	GEN702 innovaTV 202	Dose-escalating and cohort expansion safety trial of tissue factor specific antibody drug conjugate tisotumab vedotin (HuMax®-TF-ADC) in patients with locally advanced and/or metastatic solid tumors known to express tissue factor	海外	社内資料	参考資料	無

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5.3.5.2-4	[redacted]361EL-153613-e	DETERMINATION OF CIRCULATING TISSUE FACTOR (CTF) IN HUMAN PLASMA SAMPLES FROM CLINICAL STUDY GEN702 BY ECLIA	海外	社内資料	参考資料	無
5.3.5.2-5	GCT1015-03 innovaTV 203	A multi-center, open-label trial investigating the efficacy and safety of continued treatment with tisotumab vedotin in patients with solid tumors known to express tissue factor	海外	社内資料	参考資料	無
5.3.5.2-6	SGNTV-001 innovaTV 207	Open Label Phase 2 Study of Tisotumab Vedotin for Locally Advanced or Metastatic Disease in Solid Tumors	海外	社内資料	参考資料	無
5.3.5.2-6	SGNTV-001 innovaTV 207	Open Label Phase 2 Study of Tisotumab Vedotin for Locally Advanced or Metastatic Disease in Solid Tumors Addendum	海外	社内資料	参考資料	無
5.3.5.3 複数の試験成績を併せて解析した報告書						

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5.3　試験報告書及び関連情報

添付資料番号	報告書番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別	申請電子データの提出有無
5.3.5.3-1	[redacted]1015-250	Evaluation of Concentration-QTc Relationship of Tisotumab Vedotin in Patients with Locally Advanced and/or Metastatic Solid Tumors (Studies SGNTV-001 and GCT1015-04; [redacted]/[redacted]/20[redacted] cutoff date)	海外	社内資料	参考資料	有
5.3.5.3-2	—	ISS	—	社内資料	—	有
5.3.5.3-3	—	SCE_appendix	—	社内資料	—	有
5.3.5.4 その他の臨床試験報告書						
5.3.5.4-1	—	OMP analysis	—	社内資料	参考資料	無
5.3.6 市販後の使用経験に関する報告書						

第5部（モジュール5）：臨床試験報告書　添付資料一覧
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5.3.6-1	PAER #1	(20Sep2021 to 19Dec2021) - 2022Jan12	海外	社内資料	—	—
5.3.6-2	PAER #2	(2021Dec20 to 2022Mar19) - 2022Apr08	海外	社内資料	—	—
5.3.6-3	PAER #3	(2022Mar20 to 2022Jun19) - 2022Jul11	海外	社内資料	—	—
5.3.6-4	PAER #4	(2022Jun20 to 2022Sep19) - 2022Oct11	海外	社内資料	—	—
5.3.6-5	PAER #5	(2022Sep20 to 2022Dec19) - 2023Jan11	海外	社内資料	—	—

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5.3　試験報告書及び関連情報

添付資料番号	報告書番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別	申請電子データの提出有無
5.3.6-6	PAER #6	(2022Dec20-2023Mar19) - 2023Apr11	海外	社内資料	—	—
5.3.6-7	PAER #7	(2023Mar20 - 2023Jun19) - 2023Jul12	海外	社内資料	—	—
5.3.6-8	PAER #8	(2023Jun20 - 2023Sep19) - 2023Oct12	海外	社内資料	—	—
5.3.6-9	PAER #9	(2023Sep20 - 2023Dec19) - 2024Jan12	海外	社内資料	—	—
5.3.7 患者データ一覧表及び症例記録						

第5部（モジュール5）：臨床試験報告書　添付資料一覧
5.3　試験報告書及び関連情報

添付資料番号	報告書番号	タイトル	報種類（国内／海外）	掲載誌	評価資料・参考資料の別	申請電子データの提出有無
5.3.7-1	—	副作用が観察された症例の一覧表	—	社内資料	—	—
5.3.7-2	—	重篤な有害事象が観察された症例の一覧表	—	社内資料	—	—
5.3.7-3	—	臨床検査値異常変動が観察された症例の一覧表	—	社内資料	—	—

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添付資料番号	著者・タイトル・掲載誌
5.4-1	Abu-Rustum NR, Yashar CM, Bean S, et al. NCCN Guidelines Insights: Cervical Cancer, Version 1.2020. J Natl Compr Canc Netw. 2020;18(6):660-6.
5.4-2	Adegoke O, Kulasingam S, Virnig B. Cervical cancer trends in the United States: a 35-year population-based analysis. J Womens Health (Larchmt). 2012;21(10):1031-7.
5.4-3	Alberts DS, Blessing JA, Landrum LM, et al. Phase II trial of nab-paclitaxel in the treatment of recurrent or persistent advanced cervix cancer: a Gynecologic Oncology Group study. Gynecol Oncol. 2012;127(3):451-5.
5.4-4	Bookman MA, Blessing JA, Hanjani P, et al. Topotecan in squamous cell carcinoma of the cervix: a Phase II study of the Gynecologic Oncology Group. Gynecol Oncol. 2000;77(3):446-9.
5.4-5	Breij EC, de Goeij BE, Verploegen S, et al. An antibody-drug conjugate that targets tissue factor exhibits potent therapeutic activity against a broad range of solid tumors. Cancer Res. 2014;74(4):1214-26.
5.4-6	Bruni L, Albero G, Serrano B, et al. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in the World. Summary Report 10 March 2023. Date accessed: Mar 24, 2023.
5.4-7	Cerner Enviza. CancerMPact Treatment Architecture, Cervical Cancer 2023, Japan.
5.4-8	Chung HC, Ros W, Delord JP, et al. Efficacy and safety of pembrolizumab in previously treated advanced cervical cancer: results from the phase II KEYNOTE-158 study. J Clin Oncol. 2019;37(17):1470-8.
5.4-9	Cibula D, Raspollini MR, Planchamp F, et al. ESGO/ESTRO/ESP Guidelines for the management of patients with cervical cancer - update 2023. Int J Gynecol Cancer. 2023;33(5):649-66.
5.4-10	Cocco E, Varughese J, Buza N, et al. Expression of tissue factor in adenocarcinoma and squamous cell carcinoma of the uterine cervix: implications for immunotherapy with hI-con1, a factor VII-IgGFc chimeric protein targeting tissue factor. BMC Cancer. 2011;11:263.

第5部（モジュール5）：臨床試験報告書　添付資料一覧
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添付資料番号	著者・タイトル・掲載誌
5.4-11	Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976;16(1):31-41.
5.4-12	Coleman RE, Harper PG, Gallagher C, et al. A phase II study of ifosfamide in advanced and relapsed carcinoma of the cervix. Cancer Chemother Pharmacol. 1986;18(3):280-3.
5.4-13	Collett D. Interval-censored survival data. Modelling survival data in medical research. London, Chapman & Hall. 1994:237-51.
5.4-14	de Goeij BECG, Satijn D, Freitag CM, et al. High turnover of tissue factor enables efficient intracellular delivery of antibody-drug conjugates. Mol Cancer Ther. 2015;14(5):1130-40.
5.4-15	Dillman RO. Infusion reactions associated with the therapeutic use of monoclonal antibodies in the treatment of malignancy. Cancer Metastasis Rev. 1999;18(4):465-71.
5.4-16	Ferlay J, Colombet M, Soerjomataram I, et al. Cancer statistics for the year 2020: an overview. Int J Cancer. 2021:778-89.
5.4-17	Garcia AA, Blessing JA, Vaccarello L, et al. Gynecologic Oncology Group. Phase II clinical trial of docetaxel in refractory squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study. Am J Clin Oncol. 2007;30(4):428-31.
5.4-18	Han TH, Gopal AK, Ramchandren R, et al. CYP3A-mediated drug-drug interaction potential and excretion of brentuximab vedotin, an antibody-drug conjugate, in patients with CD30-positive hematologic malignancies. J Clin Pharmacol. 2013;53(8):866-77.
5.4-19	Hanley SJB. Towards the elimination of cervical cancer in Japan. J Gynecol Oncol. 2021;32(4):e76.
5.4-20	Holt HK, Peterson CE, MacLaughlan David S, et al. Mediation of racial and ethnic inequities in the diagnosis of advanced-stage cervical cancer by insurance status. JAMA Netw Open. 2023;6(3):e232985.

第5部（モジュール5）：臨床試験報告書　添付資料一覧
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添付資料番号	著者・タイトル・掲載誌
5.4-21	Hong DS, Concin N, Vergote I, et al. Tisotumab vedotin in previously treated recurrent or metastatic cervical cancer. Clin Cancer Res. 2020;26(6):1220-8.
5.4-22	Kagedal M, Claret L, Marchand M, et al. Herceptin in HER2-positive gastric cancer: evaluation of exposure-response with two dose levels. Proceedings of the 26th Annual Meeting of the Population Approach Group in Europe. 2017:Abstract 7329.
5.4-23	Kasthuri RS, Taubman MB, Mackman N. Role of tissue factor in cancer. J Clin Oncol. 2009;27(29):4834-8.
5.4-24	Kraynov E, Kamath AV, Walles M, et al. Current approaches for absorption, distribution, metabolism, and excretion characterization of antibody-drug conjugates: an industry white paper. Drug Metab Dispos. 2016;44(5):617-23.
5.4-25	Li C, Wang B, Chen SC, et al. Exposure-response analyses of trastuzumab emtansine in patients with HER2-positive advanced breast cancer previously treated with trastuzumab and a taxane. Cancer Chemother Pharmacol. 2017;80(6):1079-90.
5.4-26	Li C, Zhang C, Li Z, et al. Clinical pharmacology of vc-MMAE antibody-drug conjugates in cancer patients: learning from eight first-in-human phase 1 studies. MAbs. 2020;12(1):1699768.
5.4-27	Li N, Franceschi S, Howell-Jones R, et al . Human papillomavirus type distribution in 30,848 invasive cervical cancers worldwide: variation by geographical region, histological type and year of publication. Int J Cancer. 2011;128(4):927-35.
5.4-28	Libtayo. Summary of Product Characteristics. Regeneron Ireland Designated Activity Company. July 2022.
5.4-29	Look KY, Blessing JA, Gallup DG, et al. A phase II trial of 5-fluorouracil and high-dose leucovorin in patients with recurrent squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study. Am J Clin Oncol. 1996;19(5):439-41.
5.4-30	Lorusso D, Ferrandina G, Pignata S, et al. Evaluation of pemetrexed (Alimta, LY231514) as second-line chemotherapy in persistent or recurrent carcinoma of the cervix: the CERVIX 1 study of the MITO (Multicentre Italian Trials in Ovarian Cancer and Gynecologic Malignancies) Group. Ann Oncol. 2010;21(1):61-6.

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添付資料番号	著者・タイトル・掲載誌
5.4-31	Lu T, Gibiansky L, Li X, et al. Exposure-safety and exposure-efficacy analyses of polatuzumab vedotin in patients with relapsed or refractory diffuse large B-cell lymphoma. Leuk Lymphoma. 2020;61(12):2905-14.
5.4-32	Miller DS, Blessing JA, Bodurka DC, et al. Evaluation of pemetrexed (Alimta, LY231514) as second line chemotherapy in persistent or recurrent carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. Gynecol Oncol. 2008;110(1):65-70.
5.4-33	Monk BJ, Colombo N, Tewari KS, et al. KEYNOTE-826: Final overall survival results from a randomized, double-blind, phase 3 study of pembrolizumab + chemotherapy vs placebo + chemotherapy for first-line treatment of persistent, recurrent, or metastatic cervical cancer. J Clin Oncol. 2023;41(Suppl 16):Abstract 5500.
5.4-34	Monk BJ, Sill MW, Burger RA, et al. Phase II trial of bevacizumab in the treatment of persistent or recurrent squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study. J Clin Oncol. 2009;27(7):1069-74.
5.4-35	Muderspach LI, Blessing JA, Levenback C, et al. A phase II study of topotecan in patients with squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study. Gynecol Oncol. 2001;81(2):213-5.
5.4-36	Muggia FM, Blessing JA, Method M, et al. Evaluation of vinorelbine in persistent or recurrent squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study. Gynecol Oncol. 2004;92(2):639-43.
5.4-37	Nitori N, Ino Y, Nakanishi Y, et al. Prognostic significance of tissue factor in pancreatic ductal adenocarcinoma. Clin Cancer Res. 2005;11(7):2531-9.
5.4-38	Olusola P, Banerjee HN, Philley JV, et al. Human papilloma virus-associated cervical cancer and health disparities. Cells. 2019;8(6):622.
5.4-39	Perkins R, Mitchell E. Cervical cancer disparities. J Natl Med Assoc. 2023;115(2S):S19-25.
5.4-40	Regina S, Valentin JB, Lachot S, et al. Increased tissue factor expression is associated with reduced survival in non-small cell lung cancer and with mutations of TP53 and PTEN. Clin Chem. 2009;55(10):1834-42.

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添付資料番号	著者・タイトル・掲載誌
5.4-41	Rondon AMR, Kroone C, Kapteijn MY, et al. Role of tissue factor in tumor progression and cancer-associated thrombosis. Semin Thromb Hemost. 2019;45(4):396-412.
5.4-42	Sampson HA, Munoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report--Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol. 2006;117(2):391-7.
5.4-43	Schilder RJ, Blessing J, Cohn DE. Evaluation of gemcitabine in previously treated patients with non-squamous cell carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. Gynecol Oncol. 2005;96(1):103-7.
5.4-44	Singh D, Vignat J, Lorenzoni V, et al. Global estimates of incidence and mortality of cervical cancer in 2020: a baseline analysis of the WHO Global Cervical Cancer Elimination Initiative. Lancet Glob Health. 2023;11(2):e197-206.
5.4-45	Smith-Gagen J, White LL, Santos A, et al. Scope-of-practice laws and expanded health services: the case of underserved women and advanced cervical cancer diagnoses. J Epidemiol Community Health. 2019;73(3):278-84.
5.4-46	Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-49.
5.4-47	Suri A, Mould DR, Liu Y, et al. Population PK and exposure-response relationships for the antibody-drug conjugate brentuximab vedotin in CTCL patients in the phase III ALCANZA study. Clin Pharmacol Ther. 2018;104(5):989-99.
5.4-48	Sutton GP, Blessing JA, McGuire WP, et al. Phase II trial of ifosfamide and mesna in patients with advanced or recurrent squamous carcinoma of the cervix who had never received chemotherapy: a Gynecologic Oncology Group study. Am J Obstet Gynecol. 1993;168(3 Pt 1):805-7.
5.4-49	Tewari KS, Monk BJ, Vergote I, et al. Survival with cemiplimab in recurrent cervical cancer. N Engl J Med. 2022;386(6):544-55.
5.4-50	Tewari KS, Sill MW, Long HJ 3rd, et al. Improved survival with bevacizumab in advanced cervical cancer. N Engl J Med. 2014;370(8):734-43.

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添付資料番号	著者・タイトル・掲載誌
5.4-51	Turner DC, Kondic AG, Anderson KM, et al. Pembrolizumab exposure-response assessments challenged by association of cancer cachexia and catabolic clearance. Clin Cancer Res. 2018;24(23):5841-9.
5.4-52	Vergote I, Monk BJ, Coleman RL, et al. Tisotumab vedotin versus investigator's choice chemotherapy in second- or third-line recurrent or metastatic cervical cancer (innovaTV 301/ENGOT cx12/GOG 3057, trial in progress). J Clin Oncol. 2021;39(15 Suppl):Abstract TPS5596.
5.4-53	Verschraegen CF, Levy T, Kudelka AP, et al. Phase II study of irinotecan in prior chemotherapy-treated squamous cell carcinoma of the cervix. J Clin Oncol. 1997;15(2):625-31.
5.4-54	Wagenaar HC, Pecorelli S, Mangioni C, et al. Phase II study of mitomycin-C and cisplatin in disseminated, squamous cell carcinoma of the uterine cervix. A European Organization for Research and Treatment of Cancer (EORTC) Gynecological Cancer Group study. Eur J Cancer. 2001;37(13):1624-8.
5.4-55	Walboomers JM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. J Pathol. 1999;189(1):12-9.
5.4-56	Wang Y, Booth B, Rahman A, et al. Toward greater insights on pharmacokinetics and exposure-response relationships for therapeutic biologics in oncology drug development. Clin Pharmacol Ther. 2017;101(5):582-4.
5.4-57	Younes A, Bartlett NL, Leonard JP, et al. Brentuximab vedotin (SGN-35) for relapsed CD30-positive lymphomas. N Engl J Med. 2010;363(19):1812-21.
5.4-58	Han TH, Gopal AK, Ramchandren R, et al. CYP3A mediated drug drug interaction potential and excretion of brentuximab vedotin, an antibody drug conjugate, in patients with CD30 positive hematologic malignancies. J Clin Pharmacol. 2013;53(8):866–77.
5.4-59	Donaghy H. Effects of antibody, drug and linker on the preclinical and clinical toxicities of antibody-drug conjugates. MAbs. 2016;8(4):659-71.
5.4-60	Moskowitz CH, Nademanee A, Masszi T, et al. Brentuximab vedotin as consolidation therapy after autologous stem-cell transplantation in patients with Hodgkin's lymphoma at risk of relapse or progression (AETHERA): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2015;385(9980):1853-62.

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添付資料番号	著者・タイトル・掲載誌
5.4-61	Kagedal M, Samineni D, Gillespie WR, et al. Time-to-event modeling of peripheral neuropathy: platform analysis of eight valine-citrulline-monomethylauristatin E antibody-drug conjugates. CPT Pharmacometrics Syst Pharmacol. 2019;8(8):606-15.
5.4-62	Dahlmann-Noor, A.H., Cosgrave, E., Lowe, S., Bailly, M., Vivian, A.J. (2009) Brimonidine and apraclonidine as vasoconstrictors in adjustable strabismus surgery. J AAPOS. 13, 123-126.
5.4-63	Desco, M.C., Navea, A., Ferrer, E., Menezo, J.L. (2005) Effect of prophylactic brimonidine on bleeding complications after cataract surgery. Eur J Ophthalmol. 15, 228-232.
5.4-64	McLaurin, E., Cavet, M.E., Gomes, P.J., Ciolino, J.B. (2018) Brimonidine ophthalmic solution 0.025% for reduction of ocular redness: a randomized clinical trial. Optom Vis Sci. 95, 264-271.
5.4-65	Torkildsen, G.L., Sanfilippo, C.M., DeCory, H.H., Gomes, P.J. (2018) Evaluation of efficacy and safety of brimonidine tartrate ophthalmic solution, 0.025% for treatment of ocular redness. Curr Eye Res. 43, 43-51.
5.4-66	Ucar, F., Cetinkaya, S. (2020) The results of preoperative topical brimonidine usage of pterygium surgery. J Ocul Pharmcol Ther. 36, 234-237.
5.4-67	Wikberg-Matsson, A., Simonsen, U. (2001) Potent α_{2A}-adrenoceptor-mediated vasoconstriction by brimonidine in porcine ciliary arteries. Invest Ophthalmol Vis Sci. 42: 2049-2055.