プルヴィクト静注に関する資料

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略号一覧

略号	略していない表現（英）	略していない表現（日）
ADT	androgen deprivation therapy	アンドロゲン遮断療法
ARSI	novel androgen receptor signaling inhibitor	新規アンドロゲン受容体シグナル阻害薬
BSC/BSoC	best supportive care/standard of care	最良の支持療法／標準治療
CRPC	castration-resistant prostate cancer	去勢抵抗性前立腺癌
HPLC	high performance liquid chromatography	高速液体クロマトグラフィー
HRQoL	health-related quality of life	健康関連 QoL
mCRPC	metastatic castration-resistant prostate cancer	転移性去勢抵抗性前立腺癌
ORR	overall response rate	奏効率
OS	overall survival	全生存期間
PET	positron emission tomography	陽電子放出断層撮影
PSMA	prostate-specific membrane antigen	前立腺特異的膜抗原
QoL	quality of life	生活の質
rPFS	radiographic progression-free survival	画像診断による無増悪生存期間

1 起原又は発見の経緯

当該内容については，「2.3 品質に関する概括資料」，「2.4 非臨床試験の概括評価」，「2.5 臨床に関する概括評価」に記載した。

2 本剤の治療上の位置づけ

前立腺癌と治療の現状について

前立腺癌は世界的に多い男性の癌であり，本邦においても男性では前立腺癌が最も罹患率の高いがんである。ほとんどの前立腺癌は限局性であり，初期の段階では外科的治療や放射線治療による治療が行われた後に薬物療法としてホルモン療法であるアンドロゲン遮断療法（ADT）を受ける。初期の有効性は高いものの，ほぼすべての患者が ADT の実施中に進行を来し，最終的にホルモン療法抵抗性の転移性去勢抵抗性前立腺癌（mCRPC）に進行する。前立腺癌患者のうち約 10%～20%は 5 年以内に CRPC となり，その後 3 年以内に半数以上が死亡する。mCRPC 患者では約 90%で骨転移が認められ，このうち約半数で 2 年以内に骨関連事象が発現する。これらの症状は一般的に放射線療法又は骨手術を要し，生活の質を著しく損なう可能性がある。また，転移性前立腺癌の 5 年生存率は 32%，mCRPC の生存期間は 13～19 ヵ月と極めて予後不良である[2.5-1.1.1 項]。

現在，mCRPC の一次治療として最も一般的なのは，アビラテロン又はエンザルタミド等の新規アンドロゲン受容体シグナル阻害薬（ARSI）である。また，二次治療としての ARSI の変更は国内外の治療ガイドラインにも記載されている治療選択肢である。タキサン系薬剤であるドセタキセル及びカバジタキセルは，ARSI に次いで頻繁に用いられており，特に内臓転移を有する症候性の患者に用いられる。しかしながら，タキサン系薬剤には血液毒性や神経障害等，患者の日常生活動作に悪影響を及ぼす副作用の問題があり，患者の状態や副作用の懸念から投与には慎重な判断を要する[2.5-1.1.2 項]。

1 種類以上の ARSI による治療歴があり，かつ 2 種類のタキサン系薬剤による治療歴がある（又は 1 種類のタキサン系薬剤による治療歴があるが 2 種類目のタキサン系薬剤による治療が適さない）mCRPC 患者では，利用可能な治療法が存在しないか，現在利用可能な治療法の有効性に関する十分な知見が得られておらず確立された標準治療が存在しない。また，1 種類の ARSI による治療歴があり，かつタキサン系薬剤未治療の mCRPC 患者では，忍容性の観点から ARSI の切替え投与を考慮するものの，交差耐性によりその有効性は限定的である。mCRPC 患者に対する一次治療及び二次治療以降の治療選択肢は限られており，良好なリスクベネフィットバランスを有する新しい治療選択肢が求められている[2.5-1.1.2 項]。実際，新しい治療選択肢を求め，日本人患者が海外に渡航して ^{177}Lu-PSMA 標的療法を受ける事例もある。

セラノスティクス及び本剤について

セラノスティクス（Theranostics）は，治療（Therapy）と画像診断（Diagnostics）を融合させた新たな概念である。同じ標的分子に対して特異的な親和性を有する抗体やペプチド等の薬剤を，診断時には診断用放射性同位体（診断用 RI），治療時には治療用 RI で標識することで診断と治療を行う。セラノスティクスでは，診断用 RI で標識した薬剤を投与した後に画像診断により病巣を可視化し，標的分子を発現している患者を選択し，治療用 RI で標識した薬剤を投与することでより高い効果が得られる新たなタイプのプレシジョンメディシンとして期待される。また，ターゲット細胞で薬効を発揮する一方で，周囲の正常組織での傷害は限定的であることから，がん患者にとってより有効かつ安全な医療の実現につながると期待されている。

前立腺特異的膜抗原（PSMA）は葉酸加水分解酵素 I 又はグルタミン酸カルボキシペプチダーゼ II としても知られる II 型膜貫通タンパク質であり，前立腺癌に多く発現しているため，前立腺癌のセラノスティクスの新規標的タンパク質として注目されている。[^{177}Lu]Lu-PSMA-617（以下，本剤）は，PSMA 標的リガンドに放射性同位元素 ^{177}Lu をキレートさせた新規の放射性治療薬である。本剤は，PSMA に高い親和性をもって結合し内在化され，^{177}Lu から放出される放射線の直接的な DNA 損傷作用と DNA 周囲にある分子から誘発されるフリーラジカルを介した間接的な作用を誘発する。一方で，周囲の正常組織への損傷は限定的である[2.5-1.1.3 項, 2.4-1 項]。

なお，本剤により期待される効果を得るためには，対象となる前立腺癌の PSMA 陽性病変を適切な画像診断により確認することが極めて重要である。本邦では，PSMA 陽性病変を検出可能な画像検査は承認されていないが，PSMA 陽性病変を検出する PET 診断薬である[^{68}Ga]Ga-PSMA-11（以下，^{68}Ga-PSMA-11）と同時に承認取得をすることにより，本邦初の PSMA 陽性前立腺癌を対象としたセラノスティクスを提供できる見込みである。

3 開発の経緯

3.1 品質に関する開発の経緯

本剤の製造販売承認申請にあたり，20[redacted]年[redacted]月[redacted]日までに[redacted]相談（相談番号：[redacted]）が実施され，本剤の[redacted]について相談した。その結果，[redacted]との見解を得た。また，本剤の[redacted]として，[redacted]との見解を得た。

その他の品質に関する開発の経緯の詳細については「2.3 品質に関する概括資料」を参照のこと。

3.2 非臨床に関する開発の経緯

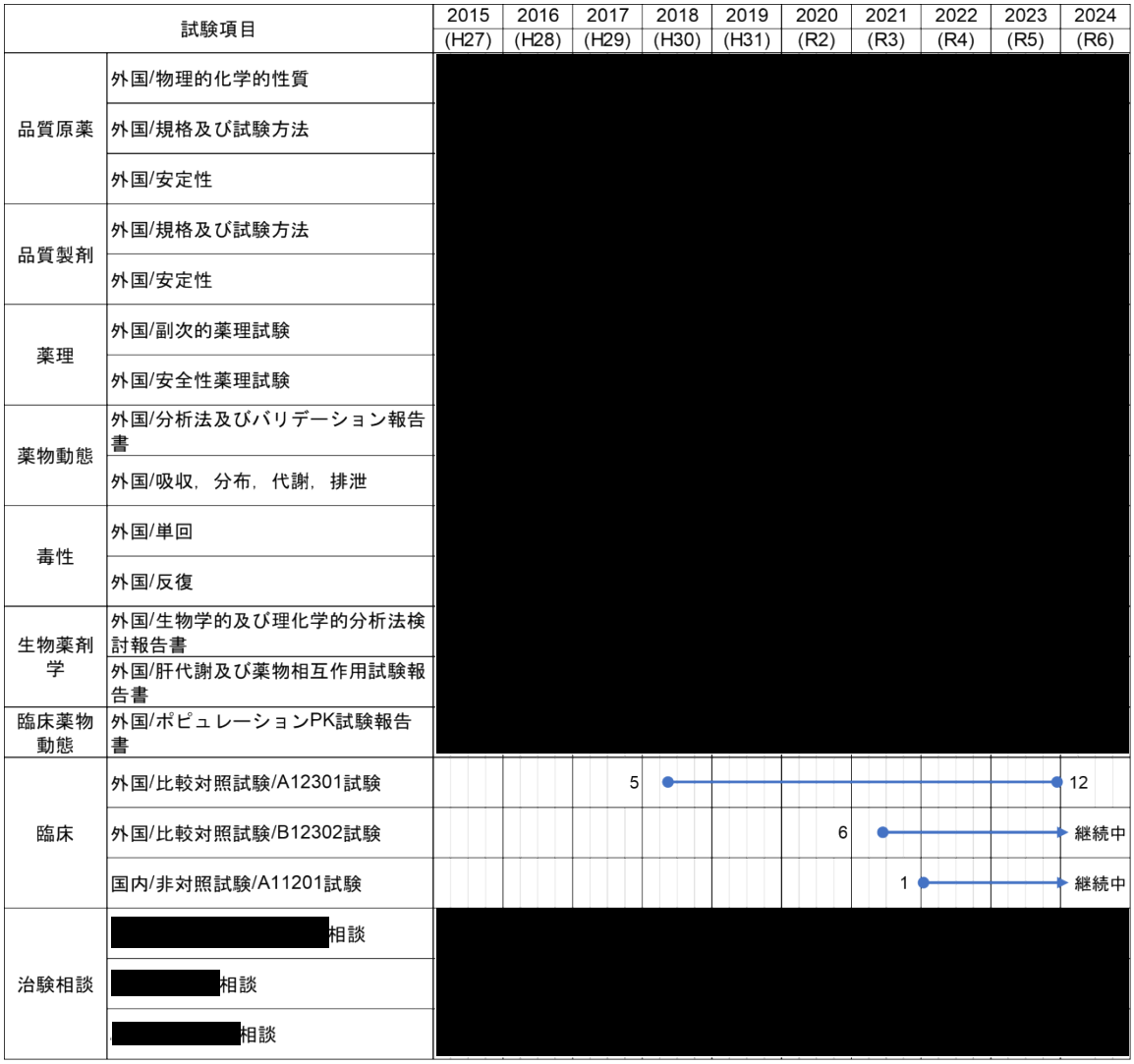
当該内容については，「2.4 非臨床試験の概括評価」に記載した。

3.3 臨床に関する開発の経緯

当該内容については，「2.5 臨床に関する概括評価」に記載した。

開発の経緯図を Figure 3-1 に示す。

Figure 3-1 開発の経緯図



4 特徴及び有用性

本剤は国内初の PSMA 標的リガンドに放射性同位元素 ^{177}Lu をキレートさせた放射性治療薬である

本剤の原薬 ^{177}Lu-PSMA-617 は，PSMA 標的部位とキレーター部位（DOTA）をリンカーで結合させた原薬前駆体ビピボチドテトラキセタン（PSMA-617）の，キレーター部位に放射性核種ルテチウム-177（^{177}Lu）を配位させることにより合成される薬物複合体である。放射性物質としての特性（崩壊）のため，原薬製造から製剤化まで自動化した連続の工程で製造される。製剤製造では，日本における投与予定時間に応じて薬液量を調整している。現在国内では，^{177}Lu により標識された放射性医薬品で，前立腺癌を対象とした治療薬は承認されていない。本剤は従来の前立腺癌に対する薬物治療とは創薬及び製造のプロセスが大きく異なる放射性治療薬である。

本剤は PSMA 陽性前立腺癌を対象とした国内初のセラノスティクスに用いる新規放射性治療薬である

セラノスティクスとは，標的分子に対して特異的な親和性を有する抗体やペプチド等の薬剤を，診断時には診断用 RI，治療時には治療用 RI で標識することで，ベースとなる薬剤を変えずに診断と治療を行うことである。診断用 RI で標識した薬剤で病巣を可視化することにより，腫瘍病変が標的分子を発現している患者のみに治療用 RI で標識した薬剤を投与することでより高い効果が期待される新たなタイプのプレシジョンメディシンである。また，ターゲット細胞で薬効を発揮する一方で，周囲の正常組織への損傷は限定的であることから，既存の治療方法では効果が不十分，あるいは安全性の理由で既存の治療方法が使用できないがん患者にとって理想的な医療の実現につながると期待される。

PSMA は，mCRPC を含む前立腺癌に多く発現しており，前立腺癌のセラノスティクスでの新規標的タンパク質として注目されている。本剤は，PSMA に高い親和性をもって結合し内在化され，^{177}Lu から放出される放射線の直接的な DNA 損傷作用と DNA 周囲にある分子から誘発されるフリーラジカルを介した間接的な作用を誘発する。一方で，周囲の正常組織への損傷は限定的である。本剤は，PSMA 陽性病変を適切な画像検査により確認された mCRPC 患者に対して，PSMA を標的として投与する新規放射性治療薬であり，従来の前立腺癌に対する薬物治療とは大きく異なる国内初のセラノスティクスとなる。

本剤は PSMA 陽性の mCRPC 患者において良好な QOL を維持しながら高い有効性を示す

タキサン既治療 mCRPC 患者を対象とした VISION 試験では，本剤と BSC/BSoC を併用投与したときの有効性が認められた。主要評価項目（alternate primary endpoints）の rPFS 及び OS はいずれも BSC/BSoC 群と比較して本剤+BSC/BSoC 群で有意に延長した。また，副次評価項目の新たな症候性骨関連事象発現までの期間及び各 HRQOL 指標の悪化までの期間はいずれも，BSC/BSoC 群と比較して本剤+BSC/BSoC 群で改善した。また，タキサン未治療の mCRPC 患者を対象とした

PSMAfore 試験では，本剤を投与したときの有効性が認められた。主要評価項目の rPFS は ARSI 群と比較して本剤群で有意に延長した。また，副次評価項目の新たな症候性骨関連事象発現までの期間及び各 HRQOL 指標の悪化までの期間はいずれも，ARSI 群と比較して本剤群で改善した。

さらに，タキサン既治療及びタキサン未治療の日本人 mCRPC 患者を対象とした国内試験 A11201 試験において，いずれも実施医療機関の判定に基づく ORR の 90% CI 下限は事前に設定した閾値を上回り，主要目的が達成され，日本人でも腫瘍縮小効果が確認された[2.5-4.6 項]。

ARSI であるアビラテロン及びエンザルタミドは，臨床現場では，mHSPC 及び mCRPC の一次治療として使用されることが多い。また，1 種類の ARSI による治療歴がある mCRPC 患者（タキサン系薬剤未治療）では，忍容性の観点から ARSI の切替え投与を考慮するものの，交差耐性によりその有効性は限定的である[2.5-1.1.2 項]。そのため，上記臨床試験の結果を踏まえ，ARSI 耐性となり，確立された標準治療が存在しない，若しくは治療選択肢が限られている一次治療及び二次治療以降の mCRPC において本剤は高い有効性を持つ，新規作用機序の非タキサン系治療選択肢として期待できる。

本剤は PSMA 陽性の mCRPC 患者において良好な安全性プロファイルを示す

本剤の前駆体分子である PSMA-617 は，PSMA に高い親和性をもって結合し内在化すると，^{177}Lu からの β 線がフリーラジカルを形成し PSMA 陽性細胞の DNA 損傷を誘発するが，周囲の正常組織への損傷は限定的であるという生物学的特性を有する。また，VISION 試験，PSMAfore 試験及び A11201 試験の結果から，骨髄抑制，腎毒性に注意する必要があるものの，PSMA 陽性 mCRPC 患者に対する AAA617 の安全性プロファイルは良好であることが確認された。さらに，日本人に特有の新たな安全性上の懸念は認められなかった[2.3-2.2.3 項, 2.5-5.9 項]。

5 まとめ

以上を踏まえ，以下のとおり本剤の製造販売承認申請を行う。

【申請品目】
プルヴィクト静注
【効能又は効果（案）】
前立腺特異的膜抗原（PSMA）陽性の遠隔転移を有する去勢抵抗性前立腺癌
【用法及び用量（案）】
通常、成人にはルテチウムビピボチドテトラキセタン(^{177}Lu)として 1 回 7.4 GBq (7,400 MBq) (200 mCi) を 6 週間間隔で 6 回静脈内投与する。

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2　外国の添付文書等の概要 3

1 外国における使用状況等

2025 年 6 月現在，本剤は，新規アンドロゲン受容体シグナル阻害薬（ARSI） 及びタキサン系薬剤による化学療法を含む治療歴があり，前立腺特異的膜抗原（PSMA） 陽性の転移性去勢抵抗性前立腺癌（mCRPC） を有する成人患者に対する治療薬として 2022 年 3 月に米国で最初の承認を取得し，欧州でも 2022 年 12 月に承認を取得した。現時点で本剤は世界 40 ヵ国以上で承認されている。さらに，ARSI による治療歴があり，タキサン系薬剤による化学療法を延期することが適切だと判断された PSMA 陽性の mCRPC を有する成人患者に対する治療薬として 2025 年 3 月に米国で追加承認された。主要国での承認状況を，Table 1-1 に示す。

Table 1-1 主要国での承認状況

国名	承認年月日	効能・効果
米国	2022 年 3 月 23 日	本剤は，ARSI 及びタキサン系薬剤による化学療法を含む治療歴がある PSMA 陽性の mCRPC を有する成人患者の治療を適応とする
	2025 年 3 月 28 日（適応追加）	本剤は，ARSI による治療歴があり，以下のいずれかの PSMA 陽性の mCRPC を有する成人患者の治療を適応とする， • タキサン系薬剤による化学療法を延期することが適切だと判断された • タキサン系薬剤による化学療法を含む治療歴がある
欧州	2022 年 12 月 9 日	本剤とアンドロゲン遮断療法（ADT）の併用，又は本剤と ADT 及び ARSI の併用は，ARSI 及びタキサン系薬剤による化学療法を含む治療歴がある PSMA 陽性の mCRPC を有する成人患者の治療を適応とする
英国	2022 年 8 月 10 日	本剤は，ARSI 及びタキサン系薬剤による化学療法を含む治療歴がある，又は，ARSI の治療歴があり，タキサン系薬剤による化学療法が医学的に適さない，PSMA 陽性の mCRPC を有する成人患者の治療を適応とする
カナダ	2022 年 8 月 25 日	本剤は，少なくとも 1 回の ARSI 及びタキサン系薬剤による化学療法を含む治療歴があり，PSMA 陽性の mCRPC を有する成人患者の治療を適応とする
豪州	2024 年 7 月 17 日	本剤は，ARSI 及びタキサン系薬剤による化学療法を含む治療歴があり，PSMA 陽性の mCRPC を有する成人患者の治療を適応とする

2 外国の添付文書等の概要

スイス・ノバルティスファーマ社の企業中核データシート（CCDS）を提出する。また 2025 年 6 月時点で最新の米国，欧州の添付文書を提出する。

２ページ目以降，非公表のため削除

NOVARTIS

[redacted]

PLUVICTO®/™ (lutetium (^{177}Lu) vipivotide tetraxetan)
1 GBq/mL (1,000 MBq/mL) solution for injection/infusion

Core Data Sheet (CDS)

[redacted]

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PLUVICTO safely and effectively. See full prescribing information for PLUVICTO.

PLUVICTO® (lutetium Lu 177 vipivotide tetraxetan) injection, for intravenous use
Initial U.S. Approval: 2022

----------RECENT MAJOR CHANGES----------

Indications and Usage (1)	3/2025
Dosage and Administration, Patient Selection (2.2)	3/2025
Dosage and Administration, Preparation and Administration (2.5)	3/2025
Warnings and Precautions, Myelosuppression (5.2)	3/2025
Warnings and Precautions, Renal Toxicity (5.3)	3/2025

----------INDICATIONS AND USAGE----------

PLUVICTO is a radioligand therapeutic agent indicated for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor pathway inhibitor (ARPI) therapy, and

- are considered appropriate to delay taxane-based chemotherapy, or
- have received prior taxane-based chemotherapy. (1)

----------DOSAGE AND ADMINISTRATION----------

- Select patients for treatment using LOCAMETZ® or another approved PSMA positron emission tomography (PET) product based on PSMA expression in tumors. (2.2)
- Recommended Dosage: Administer 7.4 GBq (200 mCi) every 6 weeks for 6 doses. (2.3)
- Dose interruption, reduction, or permanent discontinuation may be required due to adverse reactions. (2.4)

----------DOSAGE FORMS AND STRENGTHS----------

Injection: 1,000 MBq/mL (27 mCi/mL) in a single-dose vial. (3)

----------CONTRAINDICATIONS----------

None. (4)

----------WARNINGS AND PRECAUTIONS----------

- Risk From Radiation Exposure: Minimize radiation exposure during and after treatment with PLUVICTO consistent with institutional good radiation safety practices and patient treatment procedures. Ensure patients increase oral fluid intake and advise patients to void as often as possible to reduce bladder radiation. (5.1)
- Myelosuppression: Perform complete blood counts. Withhold, reduce dose, or permanently discontinue PLUVICTO based on severity. (2.4, 5.2)
- Renal Toxicity: Advise patients to remain well hydrated and to urinate frequently. Perform kidney function laboratory tests. Withhold, reduce dose, or permanently discontinue PLUVICTO based on severity. (2.4, 5.3)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise males with female partners of reproductive potential to use effective contraception. (5.4, 8.1, 8.3)
- Infertility: PLUVICTO may cause temporary or permanent infertility. (5.5, 8.3)

----------ADVERSE REACTIONS----------

Most common (≥ 20%) adverse reactions, including laboratory abnormalities, were decreased lymphocytes, decreased hemoglobin, fatigue, dry mouth, decreased platelets, decreased estimated glomerular filtration rate, nausea, decreased neutrophils, decreased calcium, decreased sodium, increased aspartate aminotransferase, increased alkaline phosphatase, arthralgia, decreased appetite, increased potassium, constipation, and back pain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Novartis Pharmaceuticals Corporation at 1-888-669-6682 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

PLUVICTO is indicated for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor pathway inhibitor (ARPI) therapy, and

- are considered appropriate to delay taxane-based chemotherapy, or
- have received prior taxane-based chemotherapy.

2 DOSAGE AND ADMINISTRATION

2.1 Important Safety Instructions

PLUVICTO is a radiopharmaceutical; handle with appropriate safety measures to minimize radiation exposure *[see Warnings and Precautions (5.1)]*. Use waterproof gloves and effective radiation shielding when handling PLUVICTO.

Radiopharmaceuticals, including PLUVICTO, should be used by or under the control of healthcare providers who are qualified by specific training and experience in the safe use and handling of radiopharmaceuticals, and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radiopharmaceuticals.

2.2 Patient Selection

Select patients with previously treated mCRPC for treatment with PLUVICTO using LOCAMETZ or another approved PSMA positron emission tomography (PET) product based on PSMA expression in tumors. Additional selection criteria were used in clinical studies *[see Clinical Studies (14)]*.

2.3 Recommended Dosage

The recommended PLUVICTO dosage is 7.4 GBq (200 mCi) intravenously every 6 weeks for 6 doses, or until disease progression, or unacceptable toxicity.

2.4 Dosage Modifications for Adverse Reactions

Recommended dosage modifications of PLUVICTO for adverse reactions are provided in Table 1. Management of adverse reactions may require temporary dose interruption, dose reduction or permanent discontinuation of treatment with PLUVICTO. If a treatment delay due to an adverse reaction persists for > 4 weeks, consider permanent discontinuation of PLUVICTO. The dose of PLUVICTO may be reduced by 20% to 5.9 GBq (160 mCi) once; do not re-escalate dose. If a patient has further adverse reactions that would require an additional dose reduction, treatment with PLUVICTO must be discontinued.

Table 1: Recommended Dosage Modifications of PLUVICTO for Adverse Reactions

Adverse reaction	Severity	Dosage modification
Myelosuppression (Anemia, thrombocytopenia, leukopenia, or neutropenia) *[see Warnings and Precautions (5.2)]*	Grade 2	Withhold PLUVICTO until improvement to Grade 1 or baseline.
	Grade ≥ 3	Withhold PLUVICTO until improvement to Grade 1 or baseline. Reduce PLUVICTO dose by 20% to 5.9 GBq (160 mCi).
	Recurrent Grade ≥ 3 myelosuppression after one dose reduction	Permanently discontinue PLUVICTO.

Adverse reaction	Severity	Dosage modification
Renal toxicity *[see Warnings and Precautions (5.3)]*	Defined as: • Confirmed serum creatinine increase (Grade ≥ 2) • Confirmed CLcr < 30 mL/min; calculate using Cockcroft-Gault with actual body weight	Withhold PLUVICTO until improvement.
	Defined as: • Confirmed ≥ 40% increase from baseline serum creatinine and • Confirmed > 40% decrease from baseline CLcr; calculate using Cockcroft-Gault with actual body weight	Withhold PLUVICTO until improvement or return to baseline. Reduce PLUVICTO dose by 20% to 5.9 GBq (160 mCi).
	Grade ≥ 3 renal toxicity	Permanently discontinue PLUVICTO.
	Recurrent renal toxicity after one dose reduction	Permanently discontinue PLUVICTO.
Dry mouth *[see Adverse Reactions (6.1)]*	Grade 2	Withhold PLUVICTO until improvement or return to baseline. Consider reducing PLUVICTO dose by 20% to 5.9 GBq (160 mCi).
	Grade 3	Withhold PLUVICTO until improvement or return to baseline. Reduce PLUVICTO dose by 20% to 5.9 GBq (160 mCi).
	Recurrent Grade 3 dry mouth after one dose reduction	Permanently discontinue PLUVICTO.
Gastrointestinal toxicity *[see Adverse Reactions (6.1)]*	Grade ≥ 3 (not amenable to medical intervention)	Withhold PLUVICTO until improvement to Grade 2 or baseline. Reduce PLUVICTO dose by 20% to 5.9 GBq (160 mCi).
	Recurrent Grade ≥ 3 gastrointestinal toxicity after one dose reduction	Permanently discontinue PLUVICTO.
Fatigue *[see Adverse Reactions (6.1)]*	Grade ≥ 3	Withhold PLUVICTO until improvement to Grade 2 or baseline.
Electrolyte or metabolic abnormalities *[see Adverse Reactions (6.1)]*	Grade ≥ 2	Withhold PLUVICTO until improvement to Grade 1 or baseline.
Other non-hematologic toxicity *[see Adverse Reactions (6.1)]*	Any unacceptable toxicity	Permanently discontinue PLUVICTO.
	Any adverse reaction that requires treatment delay of > 4 weeks	Permanently discontinue PLUVICTO.
	Any recurrent Grade 3 or 4 or persistent and intolerable Grade 2 adverse reaction after one dose reduction	Permanently discontinue PLUVICTO.

Abbreviations: CLcr, creatinine clearance; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ULN, upper limit of normal.
Grading according to most current Common Terminology Criteria for Adverse Events (CTCAE).

2.5 Preparation and Administration

Preparation Instructions

- Use aseptic technique and radiation shielding when handling or administering PLUVICTO, using tongs as needed to minimize radiation exposure.

- Inspect the product visually under a shielded screen for particulate matter and discoloration prior to administration. Discard the vial if particulates and/or discoloration are present.
- Do not inject the PLUVICTO solution directly into any other intravenous solution.
- Confirm the amount of radioactivity of PLUVICTO delivered to the patient with an appropriately calibrated dose calibrator prior to and after each PLUVICTO administration.
- Dispose of any unused medicinal product or waste material in accordance with local and federal laws.

Administration Instructions

Prior to administration, flush the intravenous catheter used exclusively for PLUVICTO administration with ≥ 10 mL of 0.9% Sodium Chloride Injection, USP to ensure patency and to minimize the risk of extravasation. Manage cases of extravasation as per institutional guidelines.

The recommended dosage of PLUVICTO may be administered intravenously as an injection using the syringe method, as an infusion using the gravity method, or as an infusion using the peristaltic pump method.

When using the gravity or peristaltic pump method, infuse PLUVICTO directly from its original container.

Use the syringe method or the peristaltic pump method when administering a reduced dose of PLUVICTO following a dosage modification for an adverse reaction. When using the gravity method for a reduced dose, adjust the PLUVICTO dose before the administration to avoid the delivery of an incorrect volume of PLUVICTO.

Intravenous Methods of Administration

Instructions for the Syringe Method

- Withdraw an appropriate volume of PLUVICTO solution to deliver the desired radioactivity by using a disposable syringe fitted with a syringe shield and a disposable sterile needle that is 9 cm, 18 gauge (long needle). To aid the withdrawal of the solution, a filtered 2.5 cm, 20 gauge needle (short venting needle) can be used to reduce the resistance from the pressurized vial. Ensure that the short needle does not touch the PLUVICTO solution in the vial.
- Administer PLUVICTO to the patient by slow intravenous push within approximately 1 to 10 minutes (either with a syringe pump or manually without a syringe pump) via an intravenous catheter that is primed with 0.9% Sodium Chloride Injection, USP and that is used exclusively for PLUVICTO administration to the patient.
- If using a syringe pump, fit the syringe into the shielded pump and include a 3-way stopcock valve between the syringe and an intravenous catheter primed with 0.9% Sodium Chloride Injection, USP and used for PLUVICTO administration to the patient.
- When the desired PLUVICTO radioactivity has been delivered, stop the syringe pump and then change the position of the 3-way stopcock valve to flush the syringe with 25 mL of 0.9% Sodium Chloride Injection, USP. Restart the syringe pump.
- After the flush of the syringe has been completed, perform an intravenous flush of ≥ 10 mL of 0.9% Sodium Chloride Injection, USP through the intravenous catheter to the patient.

Instructions for the Gravity Method

- Insert a 2.5 cm, 20 gauge needle (short needle) into the PLUVICTO vial and connect via a catheter to 500 mL 0.9% Sodium Chloride Injection, USP (used to transport the PLUVICTO solution during the infusion). Ensure that the short needle does not touch the PLUVICTO solution in the vial and do not connect the short needle directly to the patient. Do not allow the 0.9% Sodium Chloride Injection, USP to flow into the PLUVICTO vial prior to the initiation of the PLUVICTO infusion and do not inject the PLUVICTO solution directly into the 0.9% Sodium Chloride Injection, USP.
- Insert a second needle that is 9 cm, 18 gauge (long needle) into the PLUVICTO vial, ensuring that the long needle touches and is secured to the bottom of the PLUVICTO vial during the entire infusion. Connect the long needle to the patient by an intravenous catheter that is primed with 0.9% Sodium Chloride Injection, USP and that is used exclusively for the PLUVICTO infusion into the patient.
- Use a clamp or an infusion pump to regulate the flow of the 0.9% Sodium Chloride Injection, USP via the short needle into the PLUVICTO vial (the 0.9% Sodium Chloride Injection, USP entering the vial through the short needle

will carry the PLUVICTO solution from the vial to the patient via the intravenous catheter connected to the long needle within approximately 30 minutes).

- During the infusion, ensure that the level of solution in the PLUVICTO vial remains constant.
- Disconnect the vial from the long needle line and clamp the 0.9% Sodium Chloride Injection, USP line once the level of radioactivity is stable for at least five minutes.
- Follow the infusion with an intravenous flush of ≥ 10 mL of 0.9% Sodium Chloride Injection, USP through the intravenous catheter to the patient.

Instructions for the Peristaltic Pump Method

- Insert a filtered 2.5 cm, 20 gauge needle (short venting needle) into the PLUVICTO vial. Ensure that the short needle does not touch the PLUVICTO solution in the vial and do not connect the short needle directly to the patient or to the peristaltic pump.
- Insert a second needle that is 9 cm, 18 gauge (long needle) into the PLUVICTO vial, ensuring that the long needle touches and is secured to the bottom of the PLUVICTO vial during the entire infusion. Connect the long needle and a 0.9% Sodium Chloride Injection, USP to a 3-way stopcock valve via appropriate tubing.
- Connect the output of the 3-way stopcock valve to tubing installed on the input side of the peristaltic pump according to manufacturer's instructions.
- Prime the line by opening the 3-way stopcock valve and pumping the PLUVICTO solution through the tubing until it reaches the exit of the valve.
- Prime the intravenous catheter which will be connected to the patient by opening the 3-way stopcock valve to the 0.9% Sodium Chloride Injection, USP and pumping the 0.9% Sodium Chloride Injection, USP until it exits the end of the catheter tubing.
- Connect the primed intravenous catheter to the patient and set the 3-way stopcock valve such that the PLUVICTO solution is in line with the peristaltic pump.
- Infuse an appropriate volume of PLUVICTO solution at approximately 25 mL/h to deliver the desired radioactivity.
- When the desired PLUVICTO radioactivity has been delivered, stop the peristaltic pump and then change the position of the 3-way stopcock valve so that the peristaltic pump is in line with the 0.9% Sodium Chloride Injection, USP. Restart the peristaltic pump and infuse an intravenous flush of ≥ 10 mL of 0.9% Sodium Chloride Injection, USP through the intravenous catheter to the patient.

2.6 Radiation Dosimetry

Dosimetry of lutetium Lu 177 vipivotide tetraxetan was collected in 29 patients in the VISION sub-study, in order to calculate whole body and organ radiation dosimetry. The mean and standard deviation (SD) of the estimated radiation absorbed doses to different organs for adults receiving PLUVICTO are shown in Table 2. The organs with the highest radiation absorbed doses are lacrimal glands, salivary glands, large intestine (left and right colon), kidneys, and urinary bladder wall. The maximum penetration of lutetium-177 in tissue is approximately 2 mm and the mean penetration is 0.67 mm.

Table 2: Estimated Radiation Absorbed Dose[a] for PLUVICTO in VISION

	Absorbed dose per unit activity (Gy/GBq) N = 29		**Calculated absorbed dose for 7.4 GBq administration (Gy)**		**Calculated absorbed dose for 6 × 7.4 GBq (44.4 GBq cumulative activity) (Gy)**	
Organ*	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Adrenals	0.033	0.025	0.24	0.19	1.5	1.1
Brain	0.007	0.005	0.049	0.035	0.30	0.22
Esophagus	0.025	0.026	0.18	0.19	1.1	1.1
Eyes	0.022	0.024	0.16	0.18	0.99	1.1
Gallbladder wall	0.028	0.026	0.20	0.19	1.2	1.1
Heart wall	0.17	0.12	1.2	0.83	7.8	5.2
Kidneys	0.43	0.16	3.1	1.2	19	7.3

	Absorbed dose per unit activity (Gy/GBq) N = 29		Calculated absorbed dose for 7.4 GBq administration (Gy)		Calculated absorbed dose for 6 × 7.4 GBq (44.4 GBq cumulative activity) (Gy)	
Organ*	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Lacrimal glands	2.1	0.47	15	3.4	92	21
Left colon	0.58	0.14	4.1	1.0	26	6.0
Liver	0.090	0.044	0.64	0.32	4.0	2.0
Lungs	0.11	0.11	0.76	0.81	4.7	4.9
Pancreas	0.027	0.026	0.19	0.19	1.2	1.1
Prostate	0.027	0.026	0.19	0.19	1.2	1.1
Rectum	0.56	0.14	4.0	1.1	25	6.2
Right colon	0.32	0.078	2.3	0.58	14	3.4
Salivary glands	0.63	0.36	4.5	2.6	28	16
Small intestine	0.071	0.031	0.50	0.23	3.1	1.4
Spleen	0.067	0.027	0.48	0.20	3.0	1.2
Stomach wall	0.025	0.026	0.18	0.19	1.1	1.1
Testes	0.023	0.025	0.16	0.18	1.0	1.1
Thymus	0.025	0.026	0.18	0.19	1.1	1.1
Thyroid	0.26	0.37	1.8	2.7	11	16
Total body	0.037	0.027	0.27	0.20	1.6	1.2
Urinary bladder wall	0.32	0.025	2.3	0.19	14	1.1

[a]Radiation absorbed dose estimates were derived using OLINDA v2.2 radiation dosimetry software, using measured time-activity data from patient imaging as input.
*****Estimated radiation absorbed dose for bone marrow is not included given the wide expected variability based on location and burden of bone metastases between patients *[see Warnings and Precautions (5.2)]*.

3 DOSAGE FORMS AND STRENGTHS

Injection: 1,000 MBq/mL (27 mCi/mL) of lutetium Lu 177 vipivotide tetraxetan as a clear and colorless to slightly yellow solution in a single-dose vial.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Risk From Radiation Exposure

PLUVICTO contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk for cancer.

Minimize radiation exposure to patients, medical personnel, and others during and after treatment with PLUVICTO consistent with institutional good radiation safety practices, patient treatment procedures, Nuclear Regulatory Commission patient-release guidance, and instructions to the patient for follow-up radiation protection at home.

Ensure patients increase oral fluid intake and advise patients to void as often as possible to reduce bladder radiation.

Before the patient is released, inform patients about the necessary radioprotection precautions to follow to minimize radiation exposure to others *[see Patient Counseling Information (17)]*.

After each administration of PLUVICTO, advise patients to:

- Limit close contact (less than 3 feet) with others for 2 days or with children and pregnant women for 7 days.
- Refrain from sexual activity for 7 days.
- Sleep in a separate room from others for 3 days, from children for 7 days, or from pregnant women for 15 days.

5.2 Myelosuppression

PLUVICTO can cause severe and life-threatening myelosuppression, including anemia, thrombocytopenia, leukopenia, and neutropenia.

In the PSMAfore study, Grade 3 or 4 decreased hemoglobin (7%), decreased leukocytes (4.4%), decreased neutrophils (3.5%), and decreased platelets (2.7%) occurred in patients treated with PLUVICTO. One death occurred due to bone marrow failure during long-term follow-up in a patient who received PLUVICTO.

In the VISION study, Grade 3 or 4 decreased hemoglobin (15%), decreased platelets (9%), decreased leukocytes (7%), and decreased neutrophils (4.5%) occurred in patients treated with PLUVICTO. Grade ≥ 3 pancytopenia occurred in 1.1% (which includes two fatal events) of patients treated with PLUVICTO. Two deaths (0.4%) occurred due to intracranial hemorrhage and subdural hematoma in association with thrombocytopenia, one death (0.2%) occurred due to sepsis and concurrent neutropenia, and one death (0.2%) occurred due to bone marrow failure.

Perform complete blood counts before and during treatment with PLUVICTO. Withhold, reduce dose, or permanently discontinue PLUVICTO based on the severity of myelosuppression *[see Dosage and Administration (2.4)]*.

5.3 Renal Toxicity

PLUVICTO can cause severe renal toxicity.

In the PSMAfore study, Grade 3 or 4 acute kidney injury (1.3%) occurred in patients treated with PLUVICTO. In the VISION study, Grade 3 or 4 acute kidney injury (3.4%) occurred in patients treated with PLUVICTO.

Advise patients to remain well hydrated and to urinate frequently before and after administration of PLUVICTO. Perform kidney function laboratory tests, including serum creatinine and calculated creatinine clearance (CLcr), before and during treatment with PLUVICTO. Withhold, reduce dose, or permanently discontinue PLUVICTO based on the severity of renal toxicity *[see Dosage and Administration (2.4)]*.

5.4 Embryo-Fetal Toxicity

The safety and efficacy of PLUVICTO have not been established in females. Based on its mechanism of action, PLUVICTO can cause fetal harm *[see Clinical Pharmacology (12.1)]*. No animal studies using lutetium Lu 177 vipivotide tetraxetan have been conducted to evaluate its effect on female reproduction and embryo-fetal development; however, radioactive emissions, including those from PLUVICTO, can cause fetal harm. Advise males with female partners of reproductive potential to use effective contraception during treatment with PLUVICTO and for 14 weeks after the last dose *[see Use in Specific Populations (8.1, 8.3)]*.

5.5 Infertility

PLUVICTO may cause infertility in males. The recommended cumulative dose of 44.4 GBq of PLUVICTO results in a radiation absorbed dose to the testes within the range where PLUVICTO may cause temporary or permanent infertility *[see Use in Specific Populations (8.3)]*.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Myelosuppression *[see Warnings and Precautions (5.2)]*
- Renal Toxicity *[see Warnings and Precautions (5.3)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In the pooled safety population for the PSMAfore and VISION studies (N = 756), the most common (≥ 20%) adverse reactions, including laboratory abnormalities, were decreased lymphocytes (83%), decreased hemoglobin (65%), fatigue (49%), dry mouth (46%), decreased platelets (40%), decreased estimated glomerular filtration rate (37%), nausea (35%), decreased neutrophils (31%), decreased calcium (29%), decreased sodium (27%), increased aspartate aminotransferase (26%), increased alkaline phosphatase (24%), arthralgia (22%), decreased appetite (21%), increased potassium (21%), constipation (21%), and back pain (21%).

PSMAfore

The safety of PLUVICTO was evaluated in the PSMAfore study in patients with progressive, PSMA-positive mCRPC previously treated with ARPI therapy, for whom it was considered appropriate to delay taxane-based chemotherapy by the investigator *[see Clinical Studies (14.1)]*. Patients received at least one dose of either PLUVICTO 7.4 GBq (200 mCi) administered every 6 weeks (N = 227) or a change in ARPI (N = 232). The median duration of exposure to PLUVICTO was 8.4 months (range, 0.4 to 11.6), and the median number of doses of PLUVICTO received was 6 (range, 1 to 6). The median cumulative administered activity of PLUVICTO was 42.4 GBq (range, 7.0 to 45.4).

Serious adverse reactions occurred in 20% of patients who received PLUVICTO. Serious adverse reactions in > 1% of patients who received PLUVICTO included anemia (1.8%), urinary tract infection (1.8%), hemorrhage (1.3%), and sepsis (1.3%).

Fatal adverse reactions occurred in 1.8% of patients who received PLUVICTO, including COVID-19 pneumonia, cardiac arrest, intestinal ischemia, and sepsis (0.4% each).

PLUVICTO was permanently discontinued due to adverse reactions in 6% of patients. Adverse reactions leading to permanent discontinuation of PLUVICTO in ≥ 1% of patients who received PLUVICTO were thrombocytopenia (1.8%) and dry mouth (1.3%).

Adverse reactions leading to a dose interruption of PLUVICTO occurred in 12% of patients. The most frequent (≥ 1%) adverse reactions leading to a dose interruption of PLUVICTO in patients who received PLUVICTO were COVID-19 (3.1%) and anemia (1.8%).

Adverse reactions leading to a dose reduction of PLUVICTO occurred in 3.5% of patients. The most frequent (≥ 0.5%) adverse reaction leading to a dose reduction of PLUVICTO in patients who received PLUVICTO was dry mouth (0.9%).

Table 3 and Table 4 summarize the incidence of adverse reactions and laboratory abnormalities, respectively, in PSMAfore.

Table 3: Adverse Reactions (≥ 10%) in Patients With PSMA-Positive mCRPC Who Received PLUVICTO in PSMAfore

Adverse reactions	PLUVICTO (N = 227)		ARPI (N = 232)	
	All Grades (%)	Grades 3 or 4 (%)	All Grades (%)	Grades 3 or 4 (%)
Gastrointestinal disorders				
Dry mouth[a]	61	0.9	2.6	0
Nausea	32	0	12	0.4
Constipation	22	0.4	14	0
Diarrhea	17	0	9	0.4
Vomiting	11	0	4.7	0
General disorders				
Fatigue[a]	53	1.3	53	5
Metabolism and nutrition disorders				
Decreased appetite	22	0	19	0.4
Musculoskeletal and connective tissue disorders				
Arthralgia	20	0	23	0.4
Back pain	14	1.3	20	2.6

Abbreviation: ARPI, androgen receptor pathway inhibitor.
[a]Includes multiple similar terms.

Clinically relevant adverse reactions in < 10% of patients who received PLUVICTO included dysgeusia, abdominal pain, peripheral edema, headache, acute kidney injury, weight decreased, urinary tract infection, dry eye, dizziness, dry skin, oral fungal infection, gastroesophageal reflux disease, pyrexia, vertigo, stomatitis, dysphagia, esophagitis, pancytopenia, and bone marrow failure.

Table 4: Select Laboratory Abnormalities (≥ 10%) That Worsened From Baseline in Patients With PSMA-Positive mCRPC Who Received PLUVICTO or Change in ARPI (Between Arm Difference of ≥ 5% All Grades) in PSMAfore

Laboratory abnormalities	PLUVICTO[a]		ARPI[b]	
	All Grades (%)	Grades 3 or 4 (%)	All Grades (%)	Grades 3 or 4 (%)
Hematology				
Decreased lymphocytes	78	27	57	12
Decreased hemoglobin	67	7[c]	50	7[c]
Decreased neutrophils	38	3.5	18	1.3
Decreased platelets	30	2.7	11	1.7
Chemistry				
Increased alkaline phosphatase	31	8	50	10[c]
Decreased estimated glomerular filtration rate (eGFR)	23	0.9[c]	22	3.5
Increased magnesium	19	0.9[c]	28	0[c]
Decreased calcium	18	0.9	11	0.9
Decreased sodium	11	0[c]	18	0[c]
Decreased potassium	6	0.9[c]	18	2.6

Abbreviation: ARPI, androgen receptor pathway inhibitor.
[a]The denominator used to calculate the rate for each laboratory parameter was based on 226 patients with a baseline value and at least one post-treatment value.
[b]The denominator used to calculate the rate for each laboratory parameter varied from 231 to 232 based on the number of patients with a baseline value and at least one post-treatment value.
[c]No Grade 4 laboratory abnormalities worsening from baseline were reported.

VISION

The safety of PLUVICTO was evaluated in the VISION study in patients with progressive, PSMA-positive mCRPC previously treated with ARPI therapy and taxane-based chemotherapy *[see Clinical Studies (14.2)]*. Patients received at least one dose of either PLUVICTO 7.4 GBq (200 mCi) administered every 6 weeks plus BSoC (N = 529) or BSoC alone (N = 205). The median duration of exposure to PLUVICTO plus BSoC was 7.8 months (range, 0.3 to 36.5). Among patients who received PLUVICTO plus BSoC, the median number of doses of PLUVICTO received was 5 (range, 1 to 6). The median cumulative administered activity of PLUVICTO was 37.5 GBq (range, 7.0 to 48.3).

Serious adverse reactions occurred in 37% of patients who received PLUVICTO plus BSoC. Serious adverse reactions in > 1% of patients who received PLUVICTO plus BSoC included musculoskeletal pain (4%), hemorrhage (4%), sepsis (3.2%), urinary tract infection (3%), anemia (2.8%), acute kidney injury (1.9%), pneumonia (1.7%), pyrexia (1.5%), pancytopenia (1.3%), spinal cord compression (1.1%), and pulmonary embolism (1.1%).

Fatal adverse reactions occurred in 3% of patients who received PLUVICTO plus BSoC, including sepsis (0.9%), pancytopenia (0.6%), hepatic failure (0.4%), intracranial hemorrhage (0.2%), subdural hematoma (0.2%), ischemic stroke (0.2%), COVID-19 (0.2%), and aspiration pneumonia (0.2%).

PLUVICTO was permanently discontinued due to adverse reactions in 12% of patients. Adverse reactions leading to permanent discontinuation of PLUVICTO in ≥ 1% of patients who received PLUVICTO plus BSoC were anemia (2.8%), thrombocytopenia (2.8%), and leukopenia (including neutropenia) (1.7%).

Adverse reactions leading to a dose interruption of PLUVICTO occurred in 16% of patients. The most frequent (≥ 3%) adverse reactions leading to a dose interruption of PLUVICTO in patients who received PLUVICTO plus BSoC were anemia (5%) and thrombocytopenia (3.6%).

Adverse reactions leading to a dose reduction of PLUVICTO occurred in 6% of patients. The most frequent (≥ 1%) adverse reactions leading to a dose reduction of PLUVICTO in patients who received PLUVICTO plus BSoC were thrombocytopenia (1.9%) and anemia (1.3%).

Table 5 and Table 6 summarize the incidence of adverse reactions and laboratory abnormalities, respectively, in VISION.

Table 5: Adverse Reactions (≥ 10%) in Patients With PSMA-Positive mCRPC Who Received PLUVICTO Plus BSoC in VISION

Adverse reactions	PLUVICTO plus BSoC (N = 529)		BSoC (N = 205)	
	All Grades (%)	Grades 3 or 4 (%)	All Grades (%)	Grades 3 or 4 (%)
General disorders				
Fatigue[a]	48	7	29	2.4
Decreased appetite	21	1.9	15	0.5
Weight decreased	11	0.4	10	0.5
Peripheral edema[a]	10	0.4	7	1
Gastrointestinal disorders				
Dry mouth[a]	39	0	1	0
Nausea	36	1.3	17	0.5
Constipation	20	1.1	11	0.5
Vomiting[a]	19	0.9	6	0.5
Diarrhea	19	0.8	2.9	0.5
Abdominal pain[a]	12	1.3	6	0.5
Musculoskeletal and connective tissue disorders				
Back pain	24	3.6	15	3.9
Arthralgia	22	1.1	13	0.5
Bone pain	11	2.5	8	2.4
Renal and urinary disorders				
Urinary tract infection[a]	12	3.8	1	0.5

Abbreviation: BSoC, best standard of care.
[a]Includes multiple similar terms.

Clinically relevant adverse reactions in < 10% of patients who received PLUVICTO plus BSoC included acute kidney injury, dizziness, dysgeusia, headache, pyrexia, dry eye, oral fungal infection, vertigo, gastroesophageal reflux disease, stomatitis, pancytopenia, dry skin, dysphagia, esophagitis, and bone marrow failure.

Table 6: Select Laboratory Abnormalities (≥ 10%) That Worsened From Baseline in Patients With PSMA-Positive mCRPC Who Received PLUVICTO Plus BSoC (Between Arm Difference of ≥ 5% All Grades) in VISION

Laboratory abnormalities	PLUVICTO plus BSoC[a]		BSoC[b]	
	All Grades (%)	Grades 3 or 4 (%)	All Grades (%)	Grades 3 or 4 (%)
Hematology				
Decreased lymphocytes	85	47	51	18
Decreased hemoglobin	64	15[c]	34	7[c]
Decreased platelets	45	9	20	2.5
Decreased neutrophils	28	4.7	9	0.5
Chemistry				
Decreased estimated glomerular filtration rate (eGFR)	43	3.6	28	2.5
Decreased sodium	34	0.6[c]	23	1
Decreased calcium	34	1.9	18	1.5

Laboratory abnormalities	PLUVICTO plus BSoC[a]		BSoC[b]	
	All Grades (%)	Grades 3 or 4 (%)	All Grades (%)	Grades 3 or 4 (%)
Increased aspartate aminotransferase (AST)	29	1.1	18	1[c]
Increased potassium	24	0.6	18	0.5[c]
Increased sodium	11	0[c]	5	0[c]

Abbreviation: BSoC, best standard of care.

[a]The denominator used to calculate the rate for each laboratory parameter varied from 506 to 529 based on the number of patients with a baseline value and at least one post-treatment value.

[b]The denominator used to calculate the rate for each laboratory parameter varied from 194 to 198 based on the number of patients with a baseline value and at least one post-treatment value.

[c]No Grade 4 laboratory abnormalities worsening from baseline were reported.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

The safety and efficacy of PLUVICTO have not been established in females. Based on its mechanism of action, PLUVICTO can cause fetal harm *[see Clinical Pharmacology (12.1)]*. There are no available data on PLUVICTO use in pregnant females. No animal studies using lutetium Lu 177 vipivotide tetraxetan have been conducted to evaluate its effect on female reproduction and embryo-fetal development; however, all radioactive emissions, including those from PLUVICTO, can cause fetal harm.

8.2 Lactation

Risk Summary

The safety and efficacy of PLUVICTO have not been established in females. There are no data on the presence of lutetium Lu 177 vipivotide tetraxetan in human milk or its effects on the breastfed child or on milk production.

8.3 Females and Males of Reproductive Potential

Contraception

Males

Advise males with female partners of reproductive potential to use effective contraception during treatment with PLUVICTO and for 14 weeks after the last dose *[see Clinical Pharmacology (12.1), Nonclinical Toxicology (13.1)]*.

Infertility

The recommended cumulative dose of 44.4 GBq of PLUVICTO results in a radiation absorbed dose to the testes within the range where PLUVICTO may cause temporary or permanent infertility.

8.4 Pediatric Use

The safety and effectiveness of PLUVICTO in pediatric patients have not been established.

8.5 Geriatric Use

Of the 227 patients who received at least one dose of PLUVICTO in the PSMAfore study, 177 patients (78%) were 65 years of age or older and 83 patients (37%) were 75 years of age or older. No overall differences in effectiveness were observed between patients ≥ 75 years of age and younger patients. Serious adverse reactions occurred in 20% of patients ≥ 75 years of age and in 20% of younger patients. Grade ≥ 3 adverse reactions occurred in 39% of patients ≥ 75 years of age and in 34% of younger patients.

Of the 529 patients who received at least one dose of PLUVICTO plus BSoC in the VISION study, 387 patients (73%) were 65 years of age or older and 143 patients (27%) were 75 years of age or older. No overall differences in effectiveness were observed between patients ≥ 75 years of age and younger patients. Serious adverse reactions occurred in 41% of patients ≥ 75 years of age and in 35% of younger patients. Grade ≥ 3 adverse reactions occurred in 56% of patients ≥ 75 years of age and in 53% of younger patients.

8.6 Renal Impairment

Exposure of lutetium Lu 177 vipivotide tetraxetan is expected to increase with the degree of renal impairment *[see Clinical Pharmacology (12.3)]*. No dose adjustment is recommended for patients with mild (baseline CLcr 60 to 89 mL/min by Cockcroft-Gault) to moderate (CLcr 30 to 59 mL/min) renal impairment; however, patients with mild to moderate renal impairment may be at greater risk of toxicity. Frequently monitor renal function and adverse reactions in patients with mild to moderate renal impairment *[see Dosage and Administration (2.4)]*. The pharmacokinetics and safety of PLUVICTO have not been studied in patients with severe (CLcr 15 to 29 mL/min) renal impairment or end-stage renal disease.

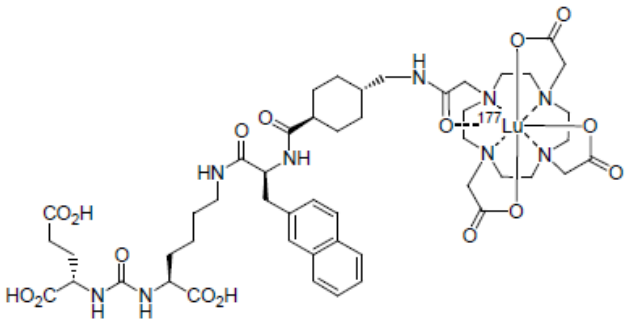
10 OVERDOSAGE

In the event of administration of a radiation overdosage with PLUVICTO, reduce the radiation absorbed dose to the patient by increasing the elimination of the radionuclide from the body by frequent micturition or by forced diuresis and frequent bladder voiding. Estimate the effective radiation dose that was applied and treat with additional supportive care measures as clinically indicated.

11 DESCRIPTION

PLUVICTO (lutetium Lu 177 vipivotide tetraxetan) is a radioligand therapeutic agent. Lutetium Lu 177 vipivotide tetraxetan is a PSMA-binding ligand bound to a DOTA chelator radiolabeled with lutetium-177.

The chemical name is 2-[4-[2-[[4-[[(2S)-1-[[(5S)-5-carboxy-5-[[(1S)-1,3-dicarboxy propyl]carbamoylamino]pentyl]amino]-3-naphthalen-2-yl-1-oxopropan-2-yl]carbamoyl]cyclohexyl]methylamino]-2-oxoethyl]-4,7,10-tris(carboxylatomethyl)-1,4,7,10-tetrazacyclododec-1-yl]acetate; lutetium-177(3+). The molecular mass is 1216.06 g/mol and the molecular formula is $C_{49}H_{68}{}^{177}LuN_9O_{16}$. The chemical structure for lutetium Lu 177 vipivotide tetraxetan is shown below:



PLUVICTO (lutetium Lu 177 vipivotide tetraxetan) 1,000 MBq/mL (27 mCi/mL) Injection is supplied as a sterile, clear, colorless to slightly yellow solution for intravenous use. Each single-dose vial contains acetic acid (0.30 mg/mL), sodium acetate (0.41 mg/mL), gentisic acid (0.39 mg/mL), sodium ascorbate (50.0 mg/mL), pentetic acid (0.10 mg/mL), and water for injection (q.s. to 1 mL). The pH range of the solution is 4.5 to 7.0.

11.1 Physical Characteristics

Lutetium-177 decays to a stable hafnium-177 with a physical half-life of 6.647 days by emitting beta-minus radiation with a maximum energy of 498 keV (79%) and photonic radiation (γ) of 208 keV (11%) and 113 keV (6.4%).

The main radiations of lutetium-177 are detailed in Table 7.

Table 7: Lutetium-177 Main Radiations

Radiation	Energy (keV)	Iβ-%	Iγ%
β^-	176.5	12.2	
β^-	248.1	0.05	
β^-	384.9	9.1	
β^-	497.8	78.6	
γ	71.6		0.15
γ	112.9		6.40
γ	136.7		0.05
γ	208.4		11.0

Radiation	Energy (keV)	Iβ-%	Iγ%
γ	249.7		0.21
γ	321.3		0.22

11.2 External Radiation

Table 8 summarizes the radioactive decay properties of lutetium-177.

Table 8: Physical Decay Chart: Lutetium-177 Physical Half-life = 6.647 days

Hours	Fraction remaining
0	1.000
1	0.996
2	0.991
5	0.979
10	0.958
24 (1 day)	0.901
48 (2 days)	0.812
72 (3 days)	0.731
120 (5 days)	0.594
168 (7 days)	0.482
336 (14 days)	0.232
720 (30 days)	0.044
1080 (45 days)	0.009

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Lutetium Lu 177 vipivotide tetraxetan is a radioligand therapeutic agent. The active moiety of lutetium Lu 177 vipivotide tetraxetan is the radionuclide lutetium-177 which is linked to a moiety that binds to PSMA, a transmembrane protein that is expressed in prostate cancer, including mCRPC. Upon binding of lutetium Lu 177 vipivotide tetraxetan to PSMA-expressing cells, the beta-minus emission from lutetium-177 delivers radiation to PSMA-expressing cells, as well as to surrounding cells, and induces DNA damage which can lead to cell death.

12.2 Pharmacodynamics

Lutetium Lu 177 vipivotide tetraxetan exposure-efficacy relationships and the time course of pharmacodynamic response have not been fully characterized.

Cardiac Electrophysiology

At the recommended dosage, PLUVICTO does not cause large mean increases (> 20 ms) in the QTc interval.

12.3 Pharmacokinetics

Pharmacokinetics of lutetium Lu 177 vipivotide tetraxetan are expressed as geometric mean (geometric mean coefficient of variation) unless otherwise specified.

The blood lutetium Lu 177 vipivotide tetraxetan area under the curve (AUC) is 52.3 ng.h/mL (31.4%) and the maximum blood concentration (C_{max}) is 6.58 ng/mL (43.5%) at the recommended dosage.

Distribution

Lutetium Lu 177 vipivotide tetraxetan volume of distribution is 123 L (78.1%).

Within 2.5 hours after administration, lutetium Lu 177 vipivotide tetraxetan distributes in gastrointestinal tract, liver, lungs, kidneys, heart wall, bone marrow, and salivary glands.

Vipivotide tetraxetan and non-radioactive lutetium vipivotide tetraxetan are 60% to 70% bound to human plasma proteins.

Elimination

The lutetium Lu 177 vipivotide tetraxetan terminal elimination half-life is 41.6 hours (68.8%) and the clearance (CL) is 2.04 L/h (31.5%).

Metabolism

Lutetium Lu 177 vipivotide tetraxetan does not undergo hepatic or renal metabolism.

Excretion

Lutetium Lu 177 vipivotide tetraxetan is primarily eliminated renally.

Specific Populations

Exposure (AUC) of lutetium Lu 177 vipivotide tetraxetan increased with decreasing creatinine clearance (CLcr). The effect of baseline CLcr < 54 mL/min on lutetium Lu 177 vipivotide tetraxetan pharmacokinetics has not been studied.

Drug Interaction Studies

In Vitro Studies

CYP450 enzymes: Vipivotide tetraxetan is not a substrate of cytochrome P450 (CYP450) enzymes. Vipivotide tetraxetan did not induce CYP1A2, 2B6 or 3A4; and did not inhibit CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6 or 3A in vitro.

Transporters: Vipivotide tetraxetan is not a substrate of BCRP, P-gp, MATE1, MATE2-K, OAT1, OAT3 or OCT2. Vipivotide tetraxetan did not inhibit BCRP, P-gp, MATE1, MATE2-K, OAT1, OAT3, OATP1B1, OATP1B3, OCT1 or OCT2 in vitro.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity and mutagenicity studies have not been conducted with lutetium Lu 177 vipivotide tetraxetan; however, radiation is a carcinogen and mutagen.

No animal studies were conducted to determine the effects of lutetium Lu 177 vipivotide tetraxetan on fertility.

14 CLINICAL STUDIES

14.1 PSMA-Positive mCRPC Previously Treated With ARPI Therapy

PSMAfore

The efficacy of PLUVICTO was evaluated in PSMAfore (NCT04689828), a randomized (1:1), multicenter, open-label trial that evaluated PLUVICTO (N = 234) versus a change in ARPI (N = 234) in patients with progressive, PSMA-positive mCRPC. Randomization was stratified by setting of prior ARPI use [castration-resistant prostate cancer (CRPC) vs. hormone-sensitive prostate cancer (HSPC)] and by symptomatology [asymptomatic or mildly symptomatic vs. symptomatic]. Patients were required to have a castrate level of serum/plasma testosterone by either medical castration or prior orchiectomy at study entry. Patients were required to have progressed only once on an ARPI (abiraterone acetate, enzalutamide, darolutamide, or apalutamide). Prior taxane-based chemotherapy was only allowed in the adjuvant or neoadjuvant setting greater than 12 months before enrollment. Patients were considered appropriate for delay of taxane-based chemotherapy by the investigator. Patients were required to have PSMA-positive mCRPC defined as having at least one tumor lesion (soft tissue or bone) with gallium Ga 68 gozetotide uptake greater than in normal liver. Patients were considered ineligible if any intraprostatic lesion or any one lesion larger than size criteria [organs ≥ 1 cm in longest diameter, lymph nodes ≥ 2.5 cm in short axis, bones (soft tissue component) ≥ 1 cm in longest diameter] had gallium Ga 68 gozetotide uptake less than or equal to uptake in normal liver.

Patients received PLUVICTO 7.4 GBq (200 mCi) every 6 weeks for 6 doses or a change in ARPI. Supportive care administered at the investigator's discretion included bone-targeted agents; androgen deprivation therapy (ADT); or palliative radiotherapy.

The median age was 72 years (range, 43 to 94 years); 91% were White; 2.6% Black or African American; 0.6% Asian; 6% were Hispanic or Latino; 99% had ECOG PS0-1.

The major efficacy outcome measure was radiographic progression-free survival (rPFS) as determined by blinded independent central review (BICR) per Prostate Cancer Working Group 3 (PCWG3)-modified Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 criteria. Additional efficacy outcome measures were Overall Survival (OS) and Overall Response Rate (ORR).

PSMAfore demonstrated a statistically significant improvement in rPFS for PLUVICTO compared to a change in ARPI.

Of patients that were randomized to receive a change in ARPI, 141 patients (60%) crossed over to receive PLUVICTO after confirmation of radiographic disease progression by BICR.

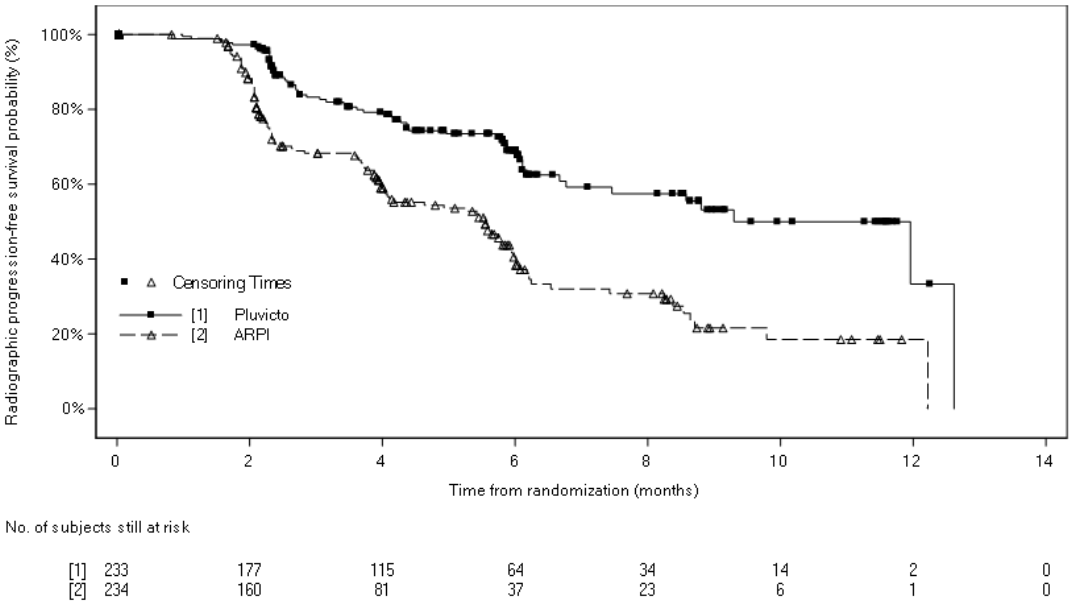
Efficacy results for PSMAfore are presented in Table 9 and Figure 1.

Table 9: Efficacy Results in PSMAfore

	PLUVICTO	ARPI
Radiographic progression-free survival (rPFS)[a]	N = 233[b]	N = 234
Events (progression or death), n (%)	60 (26)	106 (45)
Median, months (95% CI)[c]	9.3 (7, NE)	5.6 (4, 6)
Hazard ratio (95% CI)[d]	0.41 (0.29, 0.56)	
P-value[e]	<0.0001	
Overall survival (OS)	N = 234	N = 234
Deaths, n (%)	142 (61)	157 (67)
Median, months (95% CI)[c]	24.5 (19.5, 28.9)	23.1 (19.6, 25.5)
Hazard ratio (95% CI)[d]	0.91 (0.72, 1.14)	
P-value[e]	NS	
Overall response rate (ORR)[a,f]		
Patients with measurable disease at baseline	N = 72	N = 72
ORR (CR + PR), n (%) (95% CI)	35 (49) (37, 61)	10 (14) (7, 24)
Complete response (CR), n (%)	15 (21)	2 (2.8)
Partial response (PR), n (%)	20 (28)	8 (11)

ARPI=androgen receptor pathway inhibitor; NE=Not estimable; NS=Not statistically significant
[a]By BICR per PCWG3-modified RECIST v1.1 criteria.
[b]Excludes one patient in the PLUVICTO arm who was randomized after the data cut-off for the rPFS primary analysis.
[c]Based on Kaplan-Meier estimate.
[d]Hazard ratio based on the stratified Cox PH model.
[e]Stratified log-rank test one-sided p-value.
[f]Responses are based on soft tissue and bone lesion assessment.

Figure 1. Kaplan-Meier Plot of Radiographic Progression-Free Survival in PSMAfore



14.2 PSMA-Positive mCRPC Previously Treated With ARPI Therapy and Taxane-Based Chemotherapy

VISION

The efficacy of PLUVICTO was evaluated in VISION (NCT03511664), a randomized (2:1), multicenter, open-label trial of PLUVICTO plus BSoC (N = 551) versus BSoC alone (N = 280) in patients with progressive, PSMA-positive mCRPC. Randomization was stratified by baseline lactase dehydrogenase (LDH ≤ 260 IU/L vs. > 260 IU/L), presence of liver metastases (yes vs. no), ECOG PS score (0 or 1 vs. 2), and inclusion of an AR pathway inhibitor as part of BSoC (yes vs.

no) at the time of randomization. Patients were required to have a castrate level of serum/plasma testosterone by either medical castration or prior orchiectomy at study entry. Patients were required to have received at least one ARPI, and 1 or 2 prior taxane-based chemotherapy regimens. Eligible patients were required to have PSMA-positive mCRPC defined as having at least one tumor lesion (soft tissue or bone) with gallium Ga 68 gozetotide uptake greater than in normal liver. Patients were considered ineligible if any one lesion larger than size criteria [organs ≥ 1 cm in short axis, lymph nodes ≥ 2.5 cm in short axis, bones (soft tissue component) ≥ 1 cm in short axis] had gallium Ga 68 gozetotide uptake less than or equal to uptake in normal liver.

Patients received PLUVICTO 7.4 GBq (200 mCi) every 6 weeks for up to a total of 6 doses plus BSoC or BSoC alone. BSoC administered at the investigator's discretion included ketoconazole; radiation therapy to localized prostate cancer targets; bone-targeted agents; ADT; ARPIs. Patients continued treatment for up to 4-6 doses, or until disease progression or unacceptable toxicity. Patients with stable disease or partial response after 4 doses of PLUVICTO plus BSoC received up to 2 additional doses per investigator's discretion.

The median age was 71 years (range, 40 to 94 years); 87% White; 7% Black or African American; 2.4% Asian; 1.7% were Hispanic or Latino; 92% had ECOG PS0-1; 8% had ECOG PS2. All patients had received at least one prior taxane-based chemotherapy regimen and 41% of patients received two. One prior ARPI had been administered to 51% of patients, 41% of patients had received 2, and 8% of patients had received 3 or more. During the treatment period, 53% of patients in the PLUVICTO plus BSoC arm and 68% of patients in the BSoC alone arm received at least one ARPI.

The major efficacy outcome measures were OS and rPFS as determined by BICR per PCWG3-modified RECIST v1.1 criteria. An additional efficacy outcome measure was ORR.

VISION demonstrated a statistically significant improvement in both major efficacy outcome measures of OS and rPFS by BICR with PLUVICTO plus BSoC compared to treatment with BSoC alone. Interpretation of the magnitude of the rPFS effect was limited due to a high degree of censoring from early drop out in the control arm.

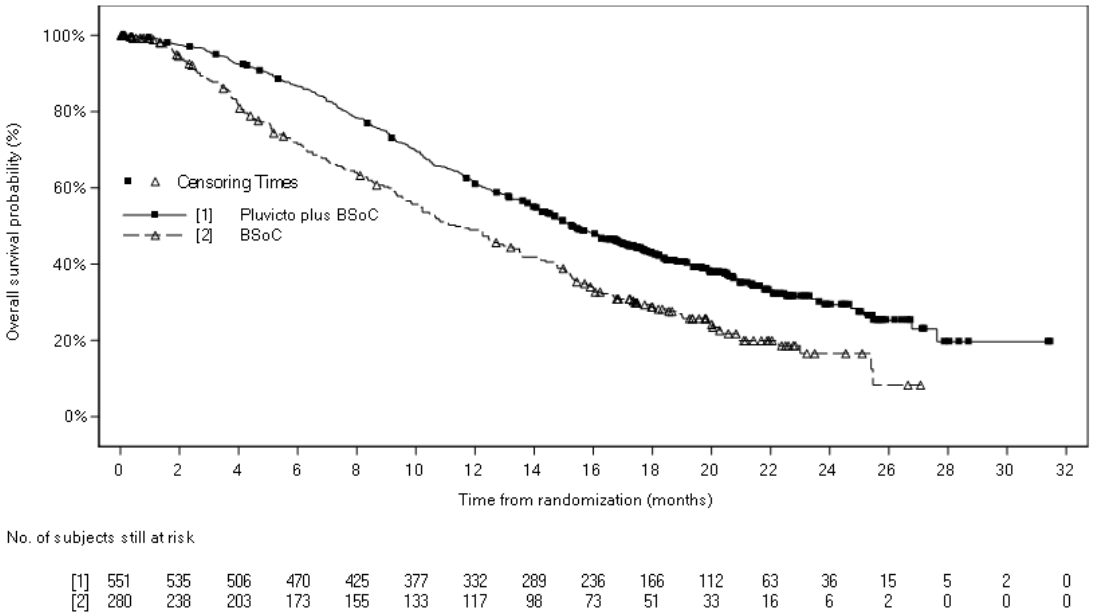
Efficacy results for VISION are presented in Table 10 and Figure 2.

Table 10: Efficacy Results in VISION

	PLUVICTO plus BSoC	**BSoC**
Overall survival (OS)	N = 551	N = 280
Deaths, n (%)	343 (62)	187 (67)
Median, months (95% CI)[a]	15.3 (14.2, 16.9)	11.3 (9.8, 13.5)
Hazard ratio (95% CI)[b]	0.62 (0.52, 0.74)	
P-value[c]	< 0.001	
Overall response rate (ORR)[d,e]		
Patients with measurable disease at baseline	N = 184	N = 64
ORR (CR + PR), n (%) (95% CI)	91 (49) (42, 57)	1 (1.6) (0, 8)
Complete response (CR), n (%)	17 (9)	0 (0)
Partial response (PR), n (%)	74 (40)	1 (1.6)
P-value[f]	< 0.001	

[a]Based on Kaplan-Meier estimate.
[b]Hazard ratio based on the stratified Cox PH model.
[c]Stratified log-rank test two-sided p-value.
[d]Responses are based on soft tissue and bone lesion assessment.
[e]By BICR per PCWG3-modified RECIST v1.1 criteria.
[f]Stratified Wald's Chi-square test two-sided p-value.

Figure 2. Kaplan-Meier Plot of Overall Survival in VISION



16 HOW SUPPLIED/STORAGE AND HANDLING

PLUVICTO Injection containing 1,000 MBq/mL (27 mCi/mL) of lutetium Lu 177 vipivotide tetraxetan is a sterile, preservative-free and clear, colorless to slightly yellow solution for intravenous use supplied in a clear, colorless Type I glass 30 mL single-dose vial containing 7.4 GBq (200 mCi) ± 10% of lutetium Lu 177 vipivotide tetraxetan at the date and time of administration (NDC# 69488-010-61). The solution volume in the vial can range from 7.5 mL to 12.5 mL in order to provide a total of 7.4 GBq (200 mCi) of radioactivity at the date and time of administration.

The product vial is enclosed within a lead shielded container (NDC# 69488-010-61) for protective shielding and placed in a plastic sealed container. The product is shipped in a type A package (NDC# 69488-010-61).

The shelf life is 120 hours (5 days) from the date and time of calibration.

Store below 30°C (86°F). Do not freeze. Store in the original package to protect from ionizing radiation (lead shielding).

Store PLUVICTO in accordance with local and federal laws on radioactive materials.

Do not use PLUVICTO after the expiration date and time which are stated on the label.

Dispose of any unused medicinal product or waste material in accordance with local and federal laws.

Lutetium-177 for PLUVICTO may be prepared using two different sources of stable nuclides (either lutetium-176 or ytterbium-176) that require different waste management. Lutetium-177 for PLUVICTO is prepared using ytterbium-176 (“non-carrier added”) unless otherwise communicated on the product batch release certificate.

17 PATIENT COUNSELING INFORMATION

Risk From Radiation Exposure

Ensure patients increase oral fluid intake and advise patients to void as often as possible to reduce bladder radiation.

Before the patient is released, inform patients about the necessary radioprotection precautions to follow to minimize radiation exposure to others.

After each administration of PLUVICTO, advise patients to:

- Limit close contact (less than 3 feet) with others for 2 days or with children and pregnant women for 7 days.
- Refrain from sexual activity for 7 days.
- Sleep in a separate room from others for 3 days, from children for 7 days, or from pregnant women for 15 days *[see Warnings and Precautions (5.1)]*.

Myelosuppression

Advise patients to contact their healthcare provider for any signs or symptoms of myelosuppression, such as tiredness, weakness, pale skin, shortness of breath, bleeding or bruising more easily than normal or difficulty to stop bleeding, or frequent infections with signs, such as fever, chills, sore throat or mouth ulcers *[see Warnings and Precautions (5.2)]*.

Renal Toxicity

Advise patients to remain well hydrated and to urinate frequently before and after administration of PLUVICTO. Advise patients to contact their healthcare provider for any signs or symptoms of renal toxicity, such as passing urine less often than usual or passing much smaller amounts of urine than usual *[see Warnings and Precautions (5.3)]*.

Embryo-Fetal Toxicity

Advise males that PLUVICTO can cause fetal harm *[see Warnings and Precautions (5.4), Use in Specific Populations (8.1)]*.

Advise male patients with female partners of reproductive potential to use effective contraception during treatment with PLUVICTO and for 14 weeks after the last dose *[see Warnings and Precautions (5.4), Use in Specific Populations (8.1, 8.3)]*.

Infertility

Advise males of reproductive potential that PLUVICTO may cause temporary or permanent infertility *[see Warnings and Precautions (5.5), Use in Specific Populations (8.3)]*.

Distributed by:
Novartis Pharmaceuticals Corporation
East Hanover, NJ 07936

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U.S. Patents 10398791; 10406240; 11318121; 12208102

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Pluvicto 1 000 MBq/mL solution for injection/infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One mL of solution contains 1 000 MBq of lutetium (^{177}Lu) vipivotide tetraxetan at the date and time of calibration.

The total amount of radioactivity per single-dose vial is 7 400 MBq ± 10% at the date and time of administration. Given the fixed volumetric activity of 1 000 MBq/mL at the date and time of calibration, the volume of the solution in the vial can range from 7.5 mL to 12.5 mL in order to provide the required amount of radioactivity at the date and time of administration.

Physical characteristics

Lutetium-177 decays to a stable hafnium-177 with a physical half-life of 6.647 days by emitting beta-minus radiation with a maximum energy of 0.498 MeV (79%) and photon radiation (γ) of 0.208 MeV (11%) and 0.113 MeV (6.4%).

Excipient with known effect

Each mL of solution contains up to 0.312 mmol (7.1 mg) of sodium. Each vial contains up to 88.75 mg of sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection/infusion.

Clear, colourless to slightly yellow solution, pH: 4.5 to 7.0.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Pluvicto in combination with androgen deprivation therapy (ADT) with or without androgen receptor (AR) pathway inhibition is indicated for the treatment of adult patients with progressive prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with AR pathway inhibition and taxane-based chemotherapy (see section 5.1).

4.2 Posology and method of administration

Important safety instructions

Pluvicto should be administered only by persons authorised to handle radiopharmaceuticals in designated clinical settings (see section 6.6) and after evaluation of the patient by a qualified physician.

Radiopharmaceuticals, including Pluvicto, should be used by or under the control of healthcare professionals who are qualified by specific training and experience in the safe use and handling of radiopharmaceuticals, and whose experience and training have been approved by the appropriate governmental agency authorised to license the use of radiopharmaceuticals.

Patient identification

Patients should be identified for treatment by PSMA imaging.

Posology

The recommended treatment regimen of Pluvicto is 7 400 MBq intravenously every 6 weeks (±1 week) for up to a total of 6 doses, unless there is disease progression or unacceptable toxicity.

Medical castration with a gonadotropin-releasing hormone (GnRH) analogue should be continued during treatment in patients not surgically castrated.

Treatment monitoring
Laboratory tests should be performed before and during treatment with Pluvicto. Dosing may need to be modified based on the test results (see Table 1).

- Haematology (haemoglobin, white blood cell count, absolute neutrophil count, platelet count)
- Kidney function (serum creatinine, calculated creatinine clearance [CLcr])
- Liver function (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, blood serum albumin, total blood bilirubin)

Dose modifications for adverse reactions
Recommended dose modifications of Pluvicto for adverse reactions are provided in Table 1. Management of severe or intolerable adverse reactions may require temporary dose interruption, dose reduction or permanent discontinuation of treatment with Pluvicto. If a treatment delay due to an adverse reaction persists for >4 weeks, treatment with Pluvicto must be discontinued. The dose of Pluvicto may be reduced by 20% to 5 900 MBq once; the dose should not be re-escalated. If a patient has further adverse reactions that would require an additional dose reduction, treatment with Pluvicto must be discontinued.

Table 1 Recommended dose modifications of Pluvicto for adverse reactions

Adverse reaction	Severity[a]	Dose modification
Dry mouth	Grade 3	Reduce Pluvicto dose by 20% to 5 900 MBq.
Gastrointestinal toxicity	Grade ≥3 (not amenable to medical intervention)	Withhold Pluvicto until improvement to grade 2 or baseline. Reduce Pluvicto dose by 20% to 5 900 MBq.
Myelosuppresion (anaemia, thrombocytopenia, leukopenia, neutropenia, pancytopenia)	Grade 2	Withhold Pluvicto until improvement to grade 1 or baseline. Manage as deemed appropriate. The use of growth factors is permitted but should be discontinued once improved to grade 1 or baseline. Checking haematinic levels (iron, B12 and folate) and providing supplementation is advocated. Transfusions may be given as clinically indicated.
	Grade ≥3	Withhold Pluvicto until improvement to grade 1 or baseline. Reduce Pluvicto dose by 20% to 5 900 MBq.
Renal toxicity	Defined as: • Confirmed serum creatinine increase (grade ≥2) • Confirmed CLcr <50 mL/min; calculate using Cockcroft-Gault with actual body weight	Withhold Pluvicto until improvement.
	Defined as: • Confirmed ≥40% increase from baseline serum creatinine and • Confirmed >40% decrease from baseline CLcr; calculate using Cockcroft-Gault with actual body weight	Withhold Pluvicto until improvement or return to baseline. Reduce Pluvicto dose by 20% to 5 900 MBq.
	Recurrent renal toxicity (grade ≥3)	Permanently discontinue Pluvicto.
Spinal cord compression	Any	Withhold Pluvicto until the compression has been adequately treated and any neurological sequela have stabilised and ECOG performance status has stabilised.
Fracture in weight-bearing bones	Any	Withhold Pluvicto until the fracture has been adequately stabilised/treated and ECOG performance status has stabilised.
Fatigue	Grade ≥3	Withhold Pluvicto until improvement to Grade 2 or baseline.
Electrolyte or metabolic abnormalities	Grade ≥2	Withhold Pluvicto until improvement to Grade 1 or baseline.
Non-haematological toxicity (clinically significant, not otherwise stated)	Grade ≥2	Withhold Pluvicto until improvement to Grade 1 or baseline.

AST or ALT elevation	AST or ALT >5 times ULN in the absence of liver metastases	Permanently discontinue Pluvicto.
Abbreviations: CLcr, creatinine clearance; ECOG, Eastern Cooperative Oncology Group; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ULN, upper limit of normal. Grading according to most current Common Terminology Criteria for Adverse Events (CTCAE). [a] The same thresholds are also applicable to baseline values at the time of treatment initiation with Pluvicto.		

Special populations

Elderly

No dose adjustment is recommended in patients aged 65 years or older.

Renal impairment

No dose adjustment is recommended for patients with mild to moderate renal impairment with baseline CLcr ≥50 mL/min by Cockcroft-Gault. Treatment with Pluvicto is not recommended in patients with moderate to severe renal impairment with baseline CLcr <50 mL/min or end-stage renal disease as the pharmacokinetic profile and safety of Pluvicto have not been studied in these patients (see sections 4.4 and 5.2).

Hepatic impairment

No dose adjustment is recommended for patients with hepatic impairment. Pluvicto has not been studied in patients with moderate or severe hepatic impairment (see section 5.2).

Paediatric population

There is no relevant use of Pluvicto in the paediatric population in the indication of treatment of PSMA-expressing prostate cancer.

Method of administration

Pluvicto is a ready-to-use solution for injection/infusion for single use only.

Administration instructions

The recommended dose of Pluvicto may be administered intravenously as an injection using the syringe method, as an infusion using the gravity method, or as an infusion using the peristaltic pump method.

When using the gravity or peristaltic pump method, Pluvicto should be infused directly from its original container.

The syringe method or the peristaltic pump method should be used when administering a reduced dose of Pluvicto following a dose modification for an adverse reaction. When using the gravity method for a reduced dose, the Pluvicto dose should be adjusted before the administration to avoid the delivery of an incorrect volume of Pluvicto.

Prior to administration, the intravenous catheter used exclusively for Pluvicto administration should be flushed with ≥10 mL of sterile sodium chloride 9 mg/mL (0.9%) solution for injection to ensure patency and to minimise the risk of extravasation. Cases of extravasation should be managed as per institutional guidelines. Patients should be advised to remain well hydrated and to urinate frequently before and after administration of Pluvicto (see section 4.4).

For instructions on the method of preparation and intravenous methods of administration, see section 12.

For patient preparation, see section 4.4.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Individual benefit/risk justification

For each patient, the radiation exposure must be justifiable by the likely benefit. The activity administered should in every case be as low as reasonably achievable to obtain the required therapeutic effect.

Risk from radiation exposure

Pluvicto contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk for cancer.

Radiation exposure to patients, medical personnel, and others should be minimised during and after treatment with Pluvicto consistent with institutional good radiation safety practices, patient management procedures, and instructions to the patient for follow-up radiation protection at home.

Patient preparation
Patients should be encouraged to increase oral fluids and urged to void as often as possible to reduce bladder radiation, especially after high activities, e.g. for radionuclide therapy.

After the procedure
Before the patient is released, the nuclear medicine physician or healthcare professional should explain the necessary radioprotection precautions that the patient should follow to minimise radiation exposure to others.

After each administration of Pluvicto, the following general recommendations for patients can be considered along with national, local and institutional procedures and regulations.

- Limit close contact (less than 1 metre) with others for 2 days or with children and pregnant women for 7 days.
- Refrain from sexual activity for 7 days.
- Sleep in a separate room from others for 3 days, from children for 7 days, or from pregnant women for 15 days.

Myelosuppression

In the VISION study, myelosuppression, including fatal cases, occurred more frequently in patients who received Pluvicto plus best standard of care (BSoC) compared to patients who received BSoC alone (see section 4.8).

Haematology laboratory tests, including haemoglobin, white blood cell count, absolute neutrophil count and platelet count, should be performed before and during treatment with Pluvicto. Pluvicto should be withheld, dose reduced or permanently discontinued and patients should be clinically managed as deemed appropriate based on the severity of myelosuppression (see section 4.2).

Renal toxicity

In the VISION study, renal toxicity occurred more frequently in patients who received Pluvicto plus BSoC compared to patients who received BSoC alone (see section 4.8).

Before and after administration of Pluvicto, patients should be encouraged to increase oral fluids and urged to void as often as possible, especially after high activities, e.g. for radionuclide therapy. Kidney function laboratory tests, including serum creatinine and calculated CLcr, should be performed before and during treatment with Pluvicto. Pluvicto should be withheld, dose reduced or permanently discontinued based on the severity of renal toxicity (see section 4.2).

Renal/Hepatic impairment

Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible.

Exposure (AUC) of lutetium (^{177}Lu) vipivotide tetraxetan is expected to increase with the degree of renal impairment (see section 5.2). Patients with mild or moderate renal impairment may be at greater risk of toxicity. Renal function and adverse reactions should be frequently monitored in patients with mild to moderate renal impairment (see section 4.2). Treatment with Pluvicto is not recommended in patients with moderate to severe renal impairment with baseline CLcr <50 mL/min or end-stage renal disease.

Fertility

Radiations of lutetium (^{177}Lu) vipivotide tetraxetan may potentially have toxic effects on male gonads and spermatogenesis. The recommended cumulative dose of 44 400 MBq of Pluvicto results in a radiation absorbed dose to the testes within the range where Pluvicto may cause infertility. Genetic consultation is recommended if the patient wishes to have children after treatment. Cryopreservation of sperm can be discussed as an option for male patients before treatment (see section 4.6).

Contraception in males

Male patients are advised not to father a child and to use a condom for intercourse during treatment with Pluvicto and for 14 weeks after the last dose (see section 4.6).

Specific warnings

Sodium content
This medicinal product contains up to 3.9 mmol (88.75 mg) sodium per vial, equivalent to 4.4% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Precautions with respect to environmental hazard see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

No clinical drug interaction studies were performed.

4.6 Fertility, pregnancy and lactation

Contraception in males

Because of potential effects on spermatogenesis associated with radiations of lutetium (^{177}Lu) vipivotide tetraxetan, male patients are advised not to father a child and to use a condom for intercourse during treatment with Pluvicto and for 14 weeks after the last dose (see section 4.4).

Pregnancy

Pluvicto is not indicated for use in females. No animal studies using lutetium (^{177}Lu) vipivotide tetraxetan have been conducted to evaluate its effect on female reproduction and embryo-foetal development. However, all radioactive emissions, including those from Pluvicto, can cause foetal harm when administered to a pregnant woman.

Breast-feeding

Pluvicto is not indicated for use in females. There are no data on the presence of lutetium (^{177}Lu) vipivotide tetraxetan in human milk or its effects on the breast-fed newborn/infant or on milk production.

Fertility

No studies were conducted to determine the effects of lutetium (^{177}Lu) vipivotide tetraxetan on fertility. Radiations of lutetium (^{177}Lu) vipivotide tetraxetan may potentially have toxic effects on male gonads and spermatogenesis. The recommended cumulative dose of 44 400 MBq of Pluvicto results in a radiation absorbed dose to the testes within the range where Pluvicto may cause infertility. Genetic consultation is recommended if the patient wishes to have children after treatment. Cryopreservation of sperm can be discussed as an option for male patients before treatment (see section 4.4).

4.7 Effects on ability to drive and use machines

Pluvicto may have a minor influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of safety profile

Unless otherwise stated, the frequency of listed adverse reactions is based on data from the VISION study in which 529 patients received at least one dose of 7 400 MBq (median number of doses was five).

The most common adverse reactions include: fatigue (48.0%), dry mouth (39.3%), nausea (35.7%), anaemia (31.9%), decreased appetite (21.4%) and constipation (20.2%). The most common grade 3 to 4 adverse reactions include: anaemia (12.9%), thrombocytopenia (7.9%), lymphopenia (7.8%) and fatigue (6.6%).

At the time of VISION final analysis, after a median follow-up duration of 14.2 months (range: 0.6 to 60.9 months), the overall safety profile remained consistent with that previously reported.

Tabulated list of adverse reactions

Adverse reactions (Table 2) are listed by MedDRA system organ class. Within each system organ class, the adverse reactions are ranked by frequency, with the most frequent reactions first. In addition, the corresponding frequency category for each adverse reaction is based on the following convention (CIOMS III): very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1 000 to <1/100); rare (≥1/10 000 to <1/1 000); very rare (<1/10 000).

Table 2 Adverse reactions occurring at a higher incidence in patients who received Pluvicto plus BSoC compared to BSoC alone in VISION[a]

System organ class Adverse reaction	Frequency category	All grades n (%)	Grades 3 to 4[b] n (%)
Infections and infestations			
Oral fungal infection[c]	Common	13 (2.5)	0 (0.0)
Blood and lymphatic system disorders			
Anaemia	Very common	169 (31.9)	68 (12.9)
Thrombocytopenia	Very common	91 (17.2)	42 (7.9)
Leukopenia[d]	Very common	83 (15.7)	22 (4.2)
Lymphopenia	Very common	75 (14.2)	41 (7.8)
Pancytopenia[e]	Common	9 (1.7)	7 (1.3)[b]
Bone marrow failure	Uncommon	1 (0.2)	1 (0.2)[b]
Nervous system disorders			
Dizziness	Common	44 (8.3)	5 (0.9)
Headache	Common	37 (7.0)	4 (0.8)
Dysgeusia[f]	Common	37 (7.0)	0 (0.0)
Eye disorders			
Dry eye	Common	16 (3.0)	0 (0.0)
Ear and labyrinth disorders			
Vertigo	Common	11 (2.1)	0 (0.0)
Gastrointestinal disorders			
Dry mouth[g]	Very common	208 (39.3)	0 (0.0)
Nausea	Very common	189 (35.7)	7 (1.3)
Constipation	Very common	107 (20.2)	6 (1.1)
Vomiting[h]	Very common	101 (19.1)	5 (0.9)
Diarrhoea	Very common	101 (19.1)	4 (0.8)
Abdominal pain[i]	Very common	61 (11.5)	7 (1.3)
Oesophageal disorder[j]	Common	18 (3.4)	1 (0.2)
Stomatitis	Common	9 (1.7)	1 (0.2)
Skin and subcutaneous tissue disorders			
Dry skin[k]	Common	8 (1.5)	0 (0.0)
Renal and urinary disorders			
Urinary tract infection[l]	Very common	63 (11.9)	20 (3.8)
Acute kidney injury[m]	Common	48 (9.1)	18 (3.4)

General disorders and administration site conditions			
Fatigue[n]	Very common	254 (48.0)	35 (6.6)
Decreased appetite	Very common	113 (21.4)	10 (1.9)
Weight decreased	Very common	58 (11.0)	2 (0.4)
Oedema peripheral[o]	Very common	53 (10.0)	2 (0.4)
Pyrexia	Common	37 (7.0)	2 (0.4)

Abbreviation: BSoC, best standard of care.

[a] National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.0.

[b] Only includes grades 3 to 4 adverse reactions, with the exception of pancytopenia and bone marrow failure. Grade 5 (fatal) pancytopenia was reported in 2 patients who received Pluvicto plus BSoC. Grade 5 (fatal) bone marrow failure was reported in 1 patient who received Pluvicto plus BSoC.

[c] Oral fungal infection includes oral candidiasis, candida infection, oral fungal infection, oropharyngitis fungal and tongue fungal infection.

[d] Leukopenia includes leukopenia and neutropenia.

[e] Pancytopenia includes pancytopenia and bicytopenia.

[f] Dysgeusia includes dysgeusia and taste disorder.

[g] Dry mouth includes dry mouth, lip dry, salivary hyposecretion and dry throat.

[h] Vomiting includes vomiting and retching.

[i] Abdominal pain includes abdominal pain, abdominal pain upper, abdominal discomfort, abdominal pain lower, abdominal tenderness and gastrointestinal pain.

[j] Oesophageal disorder includes gastrooesophageal reflux disease, dysphagia and oesophagitis.

[k] Dry skin includes dry skin and xeroderma.

[l] Urinary tract infection includes urinary tract infection, cystitis and cystitis bacterial.

[m] Acute kidney injury includes blood creatinine increased, acute kidney injury, renal failure and blood urea increased.

[n] Fatigue includes fatigue and asthenia.

[o] Oedema peripheral includes oedema peripheral, fluid retention and hypervolaemia.

Description of selected adverse reactions

Myelosuppression

In the VISION study, myelosuppression occurred more frequently in patients who received Pluvicto plus BSoC compared to patients who received BSoC alone (all grades/grade ≥3): anaemia (31.9%/12.9%) versus (13.2%/4.9%); thrombocytopenia (17.2%/7.9%) versus (4.4%/1.0%); leukopenia (12.5%/2.5%) versus (2.0%/0.5%); lymphopenia (14.2%/7.8%) versus (3.9%/0.5%); neutropenia (8.5%/3.4%) versus (1.5%/0.5%); pancytopenia (1.5%/1.1%) versus (0%/0%) including two fatal events of pancytopenia in patients who received Pluvicto plus BSoC; bicytopenia (0.2%/0.2%) versus (0%/0%); and bone marrow failure (0.2%/0.2%) versus (0%/0%) including one fatal event of bone marrow failure in a patient who received Pluvicto plus BSoC.

Myelosuppression adverse reactions that led to permanent discontinuation in ≥0.5% of patients who received Pluvicto plus BSoC included: anaemia (2.8%), thrombocytopenia (2.8%), leukopenia (1.3%), neutropenia (0.8%) and pancytopenia (0.6%). Myelosuppression adverse reactions that led to dose interruptions/dose reductions in ≥0.5% of patients who received Pluvicto plus BSoC included: anaemia (5.1%/1.3%), thrombocytopenia (3.6%/1.9%), leukopenia (1.5%/0.6%) and neutropenia (0.8%/0.6%).

Renal toxicity

In the VISION study, renal toxicity occurred more frequently in patients who received Pluvicto plus BSoC compared to patients who received BSoC alone (all grades/grades 3 to 4): blood creatinine increased (5.7%/0.2%) versus (2.4%/0.5%); acute kidney injury (3.8%/3.2%) versus (3.9%/2.4%); renal failure (0.2%/0%) versus (0%/0%); and blood urea increased (0.2%/0%) versus (0%/0%).

Renal adverse reactions that led to permanent discontinuation in ≥0.2% of patients who received Pluvicto plus BSoC included: blood creatinine increased (0.2%). Renal adverse reactions that led to dose interruptions/dose reductions in ≥0.2% of patients who received Pluvicto plus BSoC included: blood creatinine increased (0.2%/0.4%) and acute kidney injury (0.2%/0%).

Second primary malignancies
Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. The radiation dose resulting from therapeutic exposure may result in higher incidence of cancer and mutations. In all cases it is necessary to ensure that the risks of the radiation are less than from the disease itself. As Pluvicto contributes to a patient's overall long-term radiation exposure, which is associated with an increased risk for cancer (see section 4.4), a potential risk of second primary malignancies cannot be ruled out for radiopharmaceuticals such as Pluvicto. At the time of the VISION primary analysis (cut-off date 27-Jan-2021), cases of squamous cell carcinoma (4 patients; 0.8%) and basal cell carcinoma, malignant melanoma and squamous cell carcinoma of the skin (1 patient each; 0.2% each) were reported in patients who received Pluvicto plus BSoC.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

In the event of administration of a radiation overdose with Pluvicto, the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by frequent micturition or by forced diuresis and frequent bladder voiding. It might be helpful to estimate the effective dose that was applied.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Therapeutic radiopharmaceuticals, Other therapeutic radiopharmaceuticals, ATC code: V10XX05

Mechanism of action

The active moiety of Pluvicto is the radionuclide lutetium-177 which is linked to a small-molecule ligand that targets and binds with high affinity to PSMA, a transmembrane protein that is highly expressed in prostate cancer, including mCRPC. Upon the binding of Pluvicto to PSMA-expressing cancer cells, the beta-minus emission from lutetium-177 delivers therapeutic radiation to the targeted cell, as well as to surrounding cells, and induces DNA damage which can lead to cell death.

Pharmacodynamic effects

Vipivotide tetraxetan does not have any pharmacodynamic activity.

Clinical efficacy and safety

VISION
The efficacy of Pluvicto in patients with progressive, PSMA-positive mCRPC was evaluated in VISION, a randomised, multicentre, open-label phase III study. Eight hundred and thirty-one (N=831) adult patients were randomised (2:1) to receive either Pluvicto 7 400 MBq every 6 weeks for up to a total of 6 doses plus best standard of care (BSoC) (N=551) or BSoC alone (N=280). Patients who received 4 doses of Pluvicto were reassessed for evidence of response, signs of residual disease, and tolerability and could receive up to 2 additional doses per physician's discretion.

To maintain castration status, all patients continued to receive a GnRH analogue or had prior bilateral orchiectomy. Eligible patients were required to have progressive, PSMA-positive mCRPC, Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 to 2, at least one metastatic lesion present on computed tomography (CT), magnetic resonance imaging (MRI) or bone scan imaging, and adequate renal, hepatic and haematological function.

Eligible patients were also required to have received at least one AR pathway inhibitor, such as abiraterone acetate or enzalutamide, and 1 or 2 prior taxane-based chemotherapy regimens (with a regimen defined as a minimum exposure of 2 cycles of a taxane). Patients treated with only 1 prior taxane-based chemotherapy regimen were eligible if the patient was unwilling or the physician deemed the patient unsuitable to receive a second regimen. Patients with unstable symptomatic central nervous system metastases or symptomatic or clinically/radiologically impending spinal cord compression were not eligible for the study. Patients underwent a gallium (^{68}Ga) gozetotide positron emission tomography (PET) scan to evaluate PSMA expression in lesions defined by central read criteria. Eligible patients were required to have PSMA-positive mCRPC defined as having at least one tumour lesion with gallium (^{68}Ga) gozetotide uptake greater than in normal liver. Patients were excluded if any lesions exceeding size criteria in short axis (organs ≥1 cm, lymph nodes ≥2.5 cm, bones [soft-tissue component] ≥1 cm) had uptake less than or equal to uptake in normal liver.

BSoC administered at the physician's discretion included: supportive measures including pain management, hydration, blood transfusions, etc.; ketoconazole; radiation therapy (including seeded form or any external beam radiotherapy [including stereotactic body radiotherapy and palliative external beam]) to localised prostate cancer targets; bone-targeted agents including zoledronic acid, denosumab and any bisphosphonates; androgen-reducing agents including GnRH analogues, any corticosteroid, and 5-alpha reductases; AR pathway inhibitors. BSoC excluded investigational agents, cytotoxic chemotherapy, immunotherapy, other systemic radioisotopes and hemi-body radiotherapy treatment.

Patients continued randomised treatment until evidence of tumour progression (based on investigator assessment per Prostate Cancer Working Group 3 [PCWG3] criteria), unacceptable toxicity, use of prohibited treatment, non-compliance or withdrawal, or lack of clinical benefit.

The primary efficacy endpoints were overall survival (OS) and radiographic progression-free survival (rPFS) as determined by blinded independent central review (BICR) per PCWG3 criteria. Among the secondary efficacy endpoints were overall response rate (ORR) as determined by BICR per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 and time to first symptomatic skeletal event (SSE) defined as first new symptomatic pathological bone fracture, spinal cord compression, tumour-related orthopaedic surgical intervention, requirement for radiation therapy to relieve bone pain, or death from any cause, whichever occurred first. Radiographic imaging for tumour assessment (CT with contrast/MRI imaging and bone scan) was done every 8 weeks (±4 days) after the first dose for the first 24 weeks (independent of dose delays), then every 12 weeks (±4 days).

Demographic and baseline disease characteristics were balanced between the treatment arms. The median age was 71 years (range: 40 to 94 years); 86.8% White; 6.6% Black or African American; 2.4% Asian; 92.4% had ECOG PS0-1; 7.6% had ECOG PS2. Randomisation was stratified by baseline lactate dehydrogenase (LDH ≤260 IU/L vs. >260 IU/L), presence of liver metastases (yes vs. no), ECOG PS score (0 or 1 vs. 2), and inclusion of an AR pathway inhibitor as part of BSoC at the time of randomisation (yes vs. no). At randomisation, all patients (100.0%) had received at least one prior taxane-based chemotherapy regimen and 41.2% of patients had received two; 97.1% of patients had received docetaxel and 38.0% of patients had received cabazitaxel. At randomisation, 51.3% of patients had received one prior AR pathway inhibitor, 41.0% of patients had received 2, and 7.7% of patients had received 3 or more. During the randomised treatment period, 52.6% of patients in the Pluvicto plus BSoC arm and 67.8% of patients in the BSoC alone arm received at least one AR pathway inhibitor.

Efficacy results for VISION are presented in Table 3 and Figures 1 and 2. The final analyses of OS and rPFS were event-driven and conducted after the occurrence of 530 deaths and 347 events, respectively.

Table 3 Efficacy results in VISION

Efficacy parameters	**Pluvicto plus BsoC**	**BSoC**
Alternate primary efficacy endpoints		
Overall survival (OS)[a]	N=551	N=280
Deaths, n (%)	343 (62.3%)	187 (66.8%)
Median, months (95% CI)[b]	15.3 (14.2; 16.9)	11.3 (9.8; 13.5)
Hazard ratio (95% CI)[c]	0.62 (0.52; 0.74)	
P-value[d]	<0.001	
Radiographic progression-free survival (rPFS)[e,f]	N=385	N=196
Events (progression or death), n (%)	254 (66.0%)	93 (47.4%)
Radiographic progressions, n (%)	171 (44.4%)	59 (30.1%)
Deaths, n (%)	83 (21.6%)	34 (17.3%)
Median, months (99.2% CI)[b]	8.7 (7.9; 10.8)	3.4 (2.4; 4.0)
Hazard ratio (99.2% CI)[c]	0.40 (0.29; 0.57)	
P-value[d]	<0.001	
Secondary efficacy endpoints		
Time to first symptomatic skeletal event (SSE)[f]	N=385	N=196
Events (SSE or death), n (%)	256 (66.5%)	137 (69.9%)
SSEs, n (%)	60 (15.6%)	34 (17.3%)
Deaths, n (%)	196 (50.9%)	103 (52.6%)
Median, months (95% CI)[b]	11.5 (10.3; 13.2)	6.8 (5.2; 8.5)
Hazard ratio (95% CI)[c]	0.50 (0.40; 0.62)	
P-value[g]	<0.001	
Best overall response (BOR)		
Patients with evaluable disease at baseline	N=319	N=120
Complete response (CR), n (%)	18 (5.6%)	0 (0%)
Partial response (PR), n (%)	77 (24.1%)	2 (1.7%)
Overall response rate (ORR)[h,i]	95 (29.8%)	2 (1.7%)
P-value[j]	<0.001	
Duration of response (DOR)[h]		
Median, months (95% CI)[b]	9.8 (9.1; 11.7)	10.6 (NE; NE)[k]

BSoC: Best standard of care; CI: Confidence interval; NE: Not evaluable; BICR: Blinded independent central review; PCWG3: Prostate Cancer Working Group 3; RECIST: Response Evaluation Criteria in Solid Tumors.

[a] Analysed on an intent-to-treat (ITT) basis in all randomised patients.

[b] Based on Kaplan-Meier estimate.

[c] Hazard ratio based on the stratified Cox PH model. Hazard ratio <1 favours Pluvicto plus BSoC.

[d] Stratified log-rank test one-sided p-value.

[e] By BICR per PCWG3 criteria. The primary analysis of rPFS included censoring of patients who had ≥2 consecutive missed tumour assessments immediately prior to progression or death. Results for rPFS with and without censoring for missed assessments were consistent.

[f] Analysed on an ITT basis in all patients randomised on or after 05-Mar-2019, when actions were implemented to mitigate early drop-out from BSoC arm.

[g] Stratified log-rank test two-sided p-value.

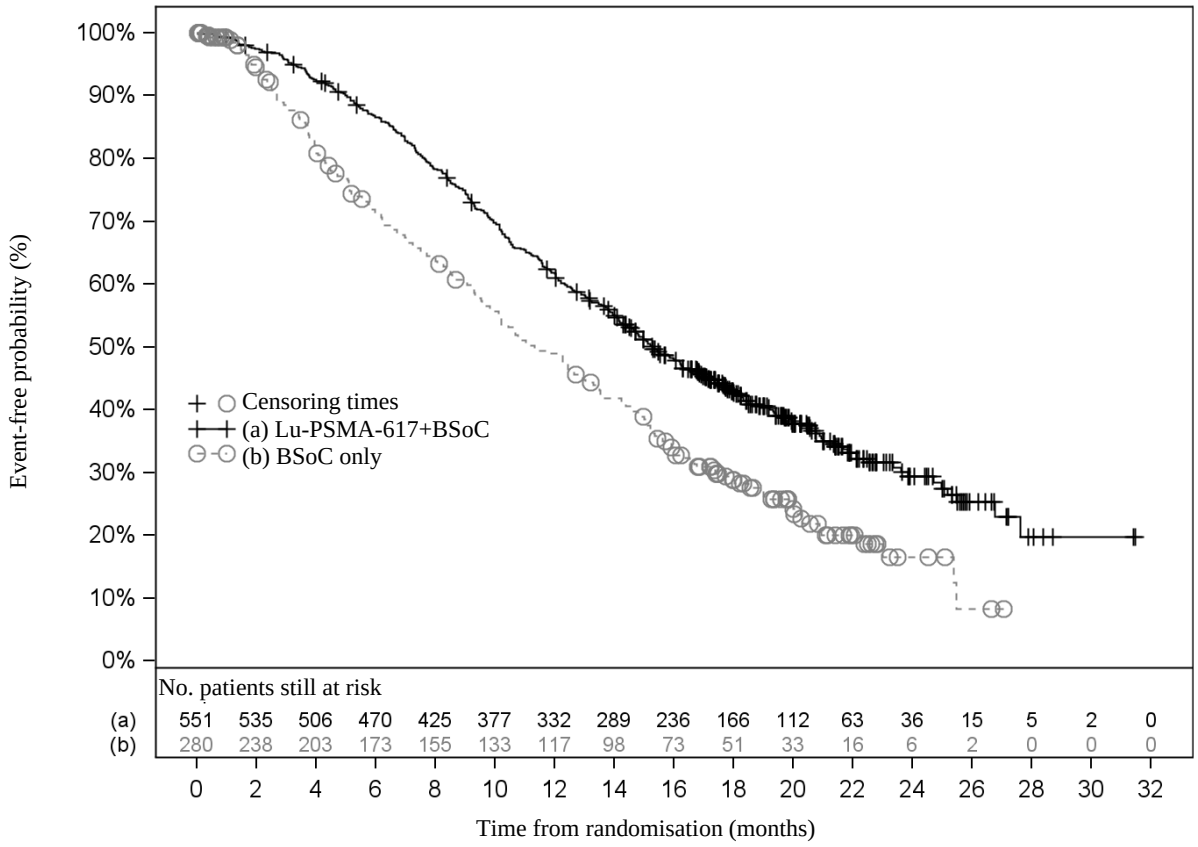
[h] By BICR per RECIST v1.1.

[i] ORR: CR+PR. Confirmed response for CR and PR.

[j] Stratified Wald's Chi-square test two-sided p-value.

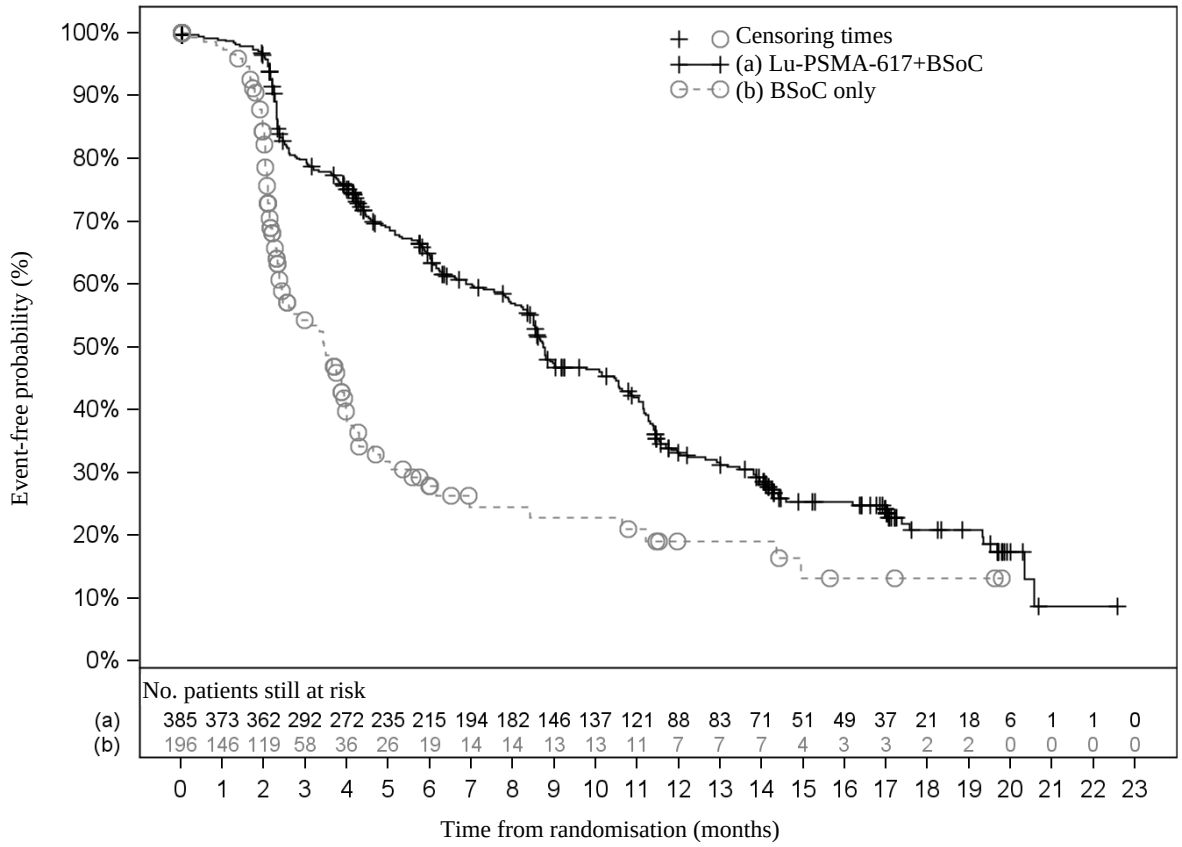
[k] Median DOR in the BSoC only arm was not reliable since only 1 of the 2 patients who responded had RECIST v1.1 radiographic progression or death.

Figure 1 Kaplan-Meier plot of OS in VISION



Stratified log-rank test and stratified Cox model using strata per Interactive Response Technology (IRT) defined by LDH level, presence of liver metastases, ECOG score and inclusion of an AR pathway inhibitor in BSoC at time of randomisation.
n/N: Number of events/number of patients in treatment arm.

Figure 2 Kaplan-Meier plot of BICR-assessed rPFS in VISION



Stratified log-rank test and stratified Cox model using strata per IRT defined by LDH level, presence of liver metastases, ECOG score and inclusion of an AR pathway inhibitor in BSoC at time of randomisation.
n/N: Number of events/number of patients in treatment arm.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Pluvicto in all subsets of the paediatric population in the treatment of PSMA-expressing prostate cancer (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

The pharmacokinetics of lutetium (^{177}Lu) vipivotide tetraxetan have been characterised in 30 patients in the phase III VISION sub-study.

Absorption

Pluvicto is administered intravenously and is immediately and completely bioavailable.

The geometric mean blood exposure (area under the curve [AUC_{inf}]) for lutetium (^{177}Lu) vipivotide tetraxetan at the recommended dose is 52.3 ng.h/mL (geometric mean coefficient of variation [CV] 31.4%). The geometric mean maximum blood concentration (C_{max}) for lutetium (^{177}Lu) vipivotide tetraxetan at the recommended dose is 6.58 ng/mL (CV 43.5%).

Distribution

The geometric mean volume of distribution (V_z) for lutetium (^{177}Lu) vipivotide tetraxetan is 123 L (CV 78.1%).

Vipivotide tetraxetan and non-radioactive lutetium (^{175}Lu) vipivotide tetraxetan are each 60% to 70% bound to human plasma proteins.

Organ uptake

The biodistribution of lutetium (^{177}Lu) vipivotide tetraxetan shows primary uptake in lacrimal glands, salivary glands, kidneys, urinary bladder wall, liver, small intestine and large intestine (left and right colon).

Elimination

The geometric mean clearance (CL) for lutetium (^{177}Lu) vipivotide tetraxetan is 2.04 L/h (CV 31.5%).

Lutetium (^{177}Lu) vipivotide tetraxetan is primarily eliminated renally.

Half-life

Pluvicto shows a bi-exponential elimination with a geometric mean terminal elimination half-life ($t_{½}$) of 41.6 hours (CV 68.8%).

Biotransformation

Lutetium (^{177}Lu) vipivotide tetraxetan does not undergo hepatic or renal metabolism.

In vitro evaluation of drug interaction potential

CYP450 enzymes
Vipivotide tetraxetan is not a substrate of cytochrome P450 (CYP450) enzymes. It does not induce cytochrome P450 (CYP) 1A2, 2B6 or 3A4, and it does not inhibit cytochrome P450 (CYP) 1A2, 2B6, 2C8, 2C9, 2C19, 2D6 or 3A4/5 *in vitro*.

Transporters
Vipivotide tetraxetan is not a substrate of BCRP, P-gp, MATE1, MATE2-K, OAT1, OAT3 or OCT2, and it is not an inhibitor of BCRP, P-gp, BSEP, MATE1, MATE2-K, OAT1, OAT3, OATP1B1, OATP1B3, OCT1 or OCT2 *in vitro*.

Special populations

Effects of age and body weight
No clinically significant effects on the pharmacokinetic parameters of lutetium (^{177}Lu) vipivotide tetraxetan were identified for the following covariates assessed in 30 patients in the phase III VISION sub-study: age (median: 67 years; range: 52 to 80 years) and body weight (median: 88.8 kg; range: 63.8 to 143.0 kg).

Renal impairment
Exposure (AUC) of lutetium (^{177}Lu) vipivotide tetraxetan increased by 20% in patients with mild renal impairment compared to normal renal function. Kidney dosimetry half-life also increased in patients with mild renal impairment compared to normal renal function, 51 hours vs. 37 hours, respectively. Patients with mild or moderate renal impairment may be at greater risk of toxicity (see section 4.4). No pharmacokinetic data are available for patients with moderate to severe renal impairment with baseline CLcr <50 mL/min or end-stage renal disease.

5.3 Preclinical safety data

No toxicological effects were observed in safety pharmacology or single-dose toxicity studies in rats and minipigs administered a non-radioactive formulation containing vipivotide tetraxetan and lutetium (^{175}Lu) vipivotide tetraxetan, or in repeat-dose toxicity studies in rats administered vipivotide tetraxetan.

Carcinogenicity and mutagenicity

Mutagenicity and long-term carcinogenicity studies have not been carried out with lutetium (^{177}Lu) vipivotide tetraxetan; however, radiation is a carcinogen and mutagen.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acetic acid
Sodium acetate
Gentisic acid
Sodium ascorbate
Pentetic acid
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in sections 4.2 and 12.

6.3 Shelf life

120 hours (5 days) from the date and time of calibration.

6.4 Special precautions for storage

Do not freeze.
Store in the original package in order to protect from ionising radiation (lead shielding).

Storage of radiopharmaceuticals should be in accordance with national regulations on radioactive materials.

6.5 Nature and contents of container

Clear, colourless type I glass vial, closed with a bromobutyl rubber stopper and aluminium seal.

Each vial contains a volume of solution that can range from 7.5 mL to 12.5 mL corresponding to a radioactivity of 7 400 MBq ±10% at the date and time of administration.

The vial is enclosed within a lead container for protective shielding.

6.6 Special precautions for disposal and other handling

General warning

Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the competent official organisation.

Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

For instructions on preparation of the medicinal product before administration, see section 12.

If at any time in the preparation of this medicinal product the integrity of the lead container or the vial is compromised it should not be used.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spill of urine, vomiting, etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

This preparation is likely to result in a relatively high radiation dose to most patients. The administration of Pluvicto may result in significant environmental hazard. This may be of concern to the immediate family of those individuals undergoing treatment or the general public depending on the level of activity administered. Suitable precautions in accordance with national regulations should be taken concerning the activity eliminated by the patients in order to avoid any contaminations.

Lutetium-177 for Pluvicto may be prepared using two different sources of stable nuclides (either lutetium-176 or ytterbium-176). Lutetium-177 for Pluvicto prepared using the stable isotope lutetium-176 (“carrier added”) requires special attention with regard to waste management due to the presence of the long-lived metastable lutetium-177 (^{177m}Lu) impurity with a half-life of 160.4 days. Lutetium-177 for Pluvicto is prepared using ytterbium-176 (“non-carrier added”) unless otherwise communicated on the product batch release certificate. The user must consult the product batch release certificate provided before using Pluvicto to ensure appropriate waste management.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1703/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09 December 2022

10. DATE OF REVISION OF THE TEXT

11. DOSIMETRY

Radiation dose to specific organs, which may not be the target organ of therapy, can be influenced significantly by pathophysiological changes induced by the disease process. This should be taken into consideration when using the following information.

Dosimetry of lutetium (^{177}Lu) vipivotide tetraxetan was collected in 29 patients in the phase III VISION sub-study, in order to calculate whole body and organ radiation dosimetry. The mean and standard deviation (SD) of the estimated absorbed doses to different organs for adult patients receiving Pluvicto are shown in Table 4. The organs with the highest absorbed doses are lacrimal glands and salivary glands.

The maximum penetration of lutetium-177 in tissue is approximately 2 mm and the mean penetration is 0.67 mm.

Table 4 Estimated absorbed dose[a] for Pluvicto in the VISION sub-study

	Absorbed dose per unit activity (mGy/MBq) (N=29)		Calculated absorbed dose for 7 400 MBq administration (Gy)		Calculated absorbed dose for 6 x 7 400 MBq (44 400 MBq cumulative activity) (Gy)	
Organ	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Adrenals	0.033	0.025	0.24	0.19	1.5	1.1
Brain	0.007	0.005	0.049	0.035	0.30	0.22
Eyes	0.022	0.024	0.16	0.18	0.99	1.1
Gallbladder wall	0.028	0.026	0.20	0.19	1.2	1.1
Heart wall	0.17	0.12	1.2	0.83	7.8	5.2
Kidneys	0.43	0.16	3.1	1.2	19	7.3
Lacrimal glands	2.1	0.47	15	3.4	92	21
Left colon	0.58	0.14	4.1	1.0	26	6.0
Liver	0.090	0.044	0.64	0.32	4.0	2.0
Lungs	0.11	0.11	0.76	0.81	4.7	4.9
Oesophagus	0.025	0.026	0.18	0.19	1.1	1.1
Osteogenic cells	0.036	0.028	0.26	0.21	1.6	1.3
Pancreas	0.027	0.026	0.19	0.19	1.2	1.1
Prostate	0.027	0.026	0.19	0.19	1.2	1.1
Red marrow	0.035	0.020	0.25	0.15	1.5	0.90
Rectum	0.56	0.14	4.0	1.1	25	6.2
Right colon	0.32	0.078	2.3	0.58	14	3.4
Salivary glands	0.63	0.36	4.5	2.6	28	16
Small intestine	0.071	0.031	0.50	0.23	3.1	1.4
Spleen	0.067	0.027	0.48	0.20	3.0	1.2
Stomach wall	0.025	0.026	0.18	0.19	1.1	1.1
Testes	0.023	0.025	0.16	0.18	1.0	1.1
Thymus	0.025	0.026	0.18	0.19	1.1	1.1
Thyroid	0.26	0.37	1.8	2.7	11	16
Total body	0.037	0.027	0.27	0.20	1.6	1.2
Urinary bladder wall	0.32	0.025	2.3	0.19	14	1.1
Effective dose[b]	0.120 mSv/MBq	0.043 mSv/MBq	0.886 Sv	0.315 Sv	5.319 Sv	1.892 Sv

[a] Absorbed dose estimates were derived using OLINDA v2.2. Values have been calculated based on dosimetry estimates at full precision and rounded to relevant digits.

[b] Derived according to ICRP Publication 103.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

The user must consult the product batch release certificate provided before using Pluvicto to ensure appropriate waste management (see section 6.6).

Withdrawals should be performed under aseptic conditions. The vials must not be opened before disinfecting the stopper, the solution should be withdrawn via the stopper using a single-dose syringe fitted with suitable protective shielding and a disposable sterile needle or using an authorised automated application system.

Preparation instructions

- Use aseptic technique and radiation shielding when handling or administering Pluvicto, using tongs as needed to minimise radiation exposure.
- Visually inspect the product under a shielded screen for particulate matter and discolouration prior to administration. Discard the vial if particulates and/or discolouration are present.
- Do not inject the Pluvicto solution directly into any other intravenous solution.
- Confirm the amount of radioactivity delivered to the patient with an appropriately calibrated dose calibrator prior to and after each Pluvicto administration.

Intravenous methods of administration

Instructions for the syringe method

- Withdraw an appropriate volume of Pluvicto solution to deliver the desired radioactivity by using a disposable syringe fitted with a syringe shield and a disposable sterile needle that is 9 cm, 18 gauge (long needle). To aid the withdrawal of the solution, a filtered 2.5 cm, 20 gauge needle (short venting needle) can be used to reduce the resistance from the pressurised vial. Ensure that the short needle does not touch the Pluvicto solution in the vial.
- If using a syringe pump, fit the syringe into the shielded pump and include a 3-way stopcock valve between the syringe and an intravenous catheter primed with sterile sodium chloride 9 mg/mL (0.9%) solution for injection and used for Pluvicto administration to the patient.
- Administer Pluvicto to the patient by slow intravenous push within approximately 1 to 10 minutes (either with a syringe pump or manually without a syringe pump) via an intravenous catheter that is primed with sterile sodium chloride 9 mg/mL (0.9%) solution for injection and that is used exclusively for Pluvicto administration to the patient.
- When the desired Pluvicto radioactivity has been delivered, stop the syringe pump and then change the position of the 3-way stopcock valve to flush the syringe with 25 mL of sterile sodium chloride 9 mg/mL (0.9%) solution for injection. Restart the syringe pump.
- After the flush of the syringe has been completed, perform an intravenous flush of ≥10 mL of sterile sodium chloride 9 mg/mL (0.9%) solution for injection through the intravenous catheter to the patient.

Instructions for the gravity method

- Insert a 2.5 cm, 20 gauge needle (short needle) into the Pluvicto vial and connect via a catheter to 500 mL sterile sodium chloride 9 mg/mL (0.9%) solution for injection (used to transport the Pluvicto solution during the infusion). Ensure that the short needle does not touch the Pluvicto solution in the vial and do not connect the short needle directly to the patient. Do not allow the sterile sodium chloride 9 mg/mL (0.9%) solution for injection to flow into the Pluvicto vial prior to the initiation of the Pluvicto infusion and do not inject the Pluvicto solution directly into the sterile sodium chloride 9 mg/mL (0.9%) solution for injection.
- Insert a second needle that is 9 cm, 18 gauge (long needle) into the Pluvicto vial, ensuring that the long needle touches and is secured to the bottom of the Pluvicto vial during the entire infusion. Connect the long needle to the patient by an intravenous catheter that is primed with sterile sodium chloride 9 mg/mL (0.9%) solution for injection and that is used exclusively for the Pluvicto infusion into the patient.
- Use a clamp or an infusion pump to regulate the flow of the sterile sodium chloride 9 mg/mL (0.9%) solution for injection via the short needle into the Pluvicto vial (the sterile sodium chloride 9 mg/mL (0.9%) solution for injection entering the vial through the short needle will carry the Pluvicto solution from the vial to the patient via the intravenous catheter connected to the long needle within approximately 30 minutes).
- During the infusion, ensure that the level of solution in the Pluvicto vial remains constant.
- Disconnect the vial from the long needle line and clamp the sterile sodium chloride 9 mg/mL (0.9%) solution for injection line once the level of radioactivity is stable for at least five minutes.
- Follow the infusion with an intravenous flush of ≥10 mL of sterile sodium chloride 9 mg/mL (0.9%) solution for injection through the intravenous catheter to the patient.

Instructions for the peristaltic pump method

- Insert a filtered 2.5 cm, 20 gauge needle (short venting needle) into the Pluvicto vial. Ensure that the short needle does not touch the Pluvicto solution in the vial and do not connect the short needle directly to the patient or to the peristaltic pump.
- Insert a second needle that is 9 cm, 18 gauge (long needle) into the Pluvicto vial, ensuring that the long needle touches and is secured to the bottom of the Pluvicto vial during the entire infusion. Connect the long needle and a sterile sodium chloride 9 mg/mL (0.9%) solution for injection to a 3-way stopcock valve via appropriate tubing.
- Connect the output of the 3-way stopcock valve to tubing installed on the input side of the peristaltic pump according to manufacturer's instructions.
- Prime the line by opening the 3-way stopcock valve and pumping the Pluvicto solution through the tubing until it reaches the exit of the valve.
- Prime the intravenous catheter which will be connected to the patient by opening the 3-way stopcock valve to the sterile sodium chloride 9 mg/mL (0.9%) solution for injection and pumping the sterile sodium chloride 9 mg/mL (0.9%) solution for injection until it exits the end of the catheter tubing.
- Connect the primed intravenous catheter to the patient and set the 3-way stopcock valve such that the Pluvicto solution is in line with the peristaltic pump.
- Infuse an appropriate volume of Pluvicto solution at approximately 25 mL/h to deliver the desired radioactivity.
- When the desired Pluvicto radioactivity has been delivered, stop the peristaltic pump and then change the position of the 3-way stopcock valve so that the peristaltic pump is in line with the sterile sodium chloride 9 mg/mL (0.9%) solution for injection. Restart the peristaltic pump and infuse an intravenous flush of ≥10 mL of sterile sodium chloride 9 mg/mL (0.9%) solution for injection through the intravenous catheter to the patient.

Quality control

The solution should be visually inspected for damage and contamination before use, and only clear solutions free of visible particles should be used. The visual inspection of the solution should be performed under a shielded screen for radioprotection purposes. The vial must not be opened.

If at any time in the preparation of this medicinal product the integrity of the lead container or the vial is compromised, it should not be used.

The amount of radioactivity in the vial must be measured prior to administration using a suitable radioactivity calibration system in order to confirm that the actual amount of radioactivity to be administered is equal to the planned amount at the administration time.

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Advanced Accelerator Applications (Italy) S.R.L.
Via Ribes 5
10010
Colleretto Giacosa (TO)
Italy

Advanced Accelerator Applications Ibérica, S.L.U.
Polígono Industrial la Cuesta – Sector 3
Parcelas 1 y 2 La Almunia de Doña Godina
50100 Zaragoza
Spain

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Additional risk minimisation measures**

Prior to launch of Pluvicto in each Member State, the Marketing Authorisation Holder (MAH) must agree about the content and format of the patient guide, including communication media, distribution modalities, and any other aspects of the programme, with the National Competent Authority (NCA).

The patient guide is aimed to reduce the risk of inadvertent radiation exposure.

The MAH shall ensure that, in each Member State where Pluvicto is marketed, patients have access to the patient guide.

The Pluvicto patient guide contains the following key elements:

- What Pluvicto is and how it works
- Description of risk guidance on:
    - Hydration
    - Close contacts
    - Care givers
    - Sexual activity and contraception
    - Toilet use
    - Showering and laundry
    - Waste disposal

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

LEAD SHIELDING CONTAINER

1. NAME OF THE MEDICINAL PRODUCT

Pluvicto 1 000 MBq/mL solution for injection/infusion
lutetium (^{177}Lu) vipivotide tetraxetan

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One mL contains 1 000 MBq of lutetium (^{177}Lu) vipivotide tetraxetan at calibration time.
Volumetric activity at calibration time: 1 000 MBq/mL - {DD/MM/YYYY hh:mm UTC}

3. LIST OF EXCIPIENTS

Acetic acid, sodium acetate, gentisic acid, sodium ascorbate, pentetic acid, water for injections. See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection/infusion

1 single-dose vial

Vial no.: {X}
Volume: {Y} mL
Activity at administration time: {Z} MBq - {DD/MM/YYYY hh:mm UTC}

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intravenous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY



8. EXPIRY DATE

EXP: {DD/MM/YYYY hh:mm UTC}

9. SPECIAL STORAGE CONDITIONS

Do not freeze.
Store in the original package in order to protect from ionising radiation (lead shielding).

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1703/001

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Pluvicto 1 000 MBq/mL solution for injection/infusion
lutetium (^{177}Lu) vipivotide tetraxetan
Intravenous use

2. METHOD OF ADMINISTRATION

Single-dose vial

3. EXPIRY DATE

EXP: {DD/MM/YYYY hh:mm UTC}

4. BATCH NUMBER

Lot:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Vial no.: {X}
Volume: {Y} mL
Volumetric activity at calibration time: 1 000 MBq/mL - {DD/MM/YYYY hh:mm UTC}
Activity at administration time: {Z} MBq - {DD/MM/YYYY hh:mm UTC}

6. OTHER



Manufacturer

Advanced Accelerator Applications (Italy) S.R.L.
Via Ribes 5
10010
Colleretto Giacosa (TO)
Italy

Advanced Accelerator Applications Ibérica, S.L.U.
Polígono Industrial la Cuesta – Sector 3
Parcelas 1 y 2 La Almunia de Doña Godina
50100 Zaragoza
Spain

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Pluvicto 1 000 MBq/mL solution for injection/infusion
lutetium (^{177}Lu) vipivotide tetraxetan

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Pluvicto is and what it is used for
2. What you need to know before Pluvicto is used
3. How Pluvicto is used
4. Possible side effects
5. How Pluvicto is stored
6. Contents of the pack and other information

1. What Pluvicto is and what it is used for

What Pluvicto is
Pluvicto contains lutetium (^{177}Lu) vipivotide tetraxetan. This medicine is a radiopharmaceutical product for therapy only.

What Pluvicto is used for
Pluvicto is used to treat adults with progressive castration-resistant prostate cancer that has spread to other parts of the body (metastatic) and has already been treated with other cancer treatments. Castration-resistant prostate cancer is a cancer of the prostate (a gland of the male reproductive system) that does not respond to treatment that reduces male hormones. Pluvicto is used if the prostate cancer cells have a protein on their surface called prostate-specific membrane antigen (PSMA).

How Pluvicto works
Pluvicto binds to PSMA found on the surface of the prostate cancer cells. Once bound, the radioactive substance in Pluvicto, lutetium-177, gives off radiation that causes the prostate cancer cells to die.

Your doctor will carry out tests to see if PSMA is present on the surface of the cancer cells. Your cancer is more likely to respond to treatment with Pluvicto if the test result is positive.

The use of Pluvicto involves exposure to amounts of radioactivity. Your doctor and the nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the radiopharmaceutical outweighs the risk due to radiation.

If you have any questions about how Pluvicto works or why this medicine has been prescribed for you, ask your nuclear medicine doctor.

2. What you need to know before Pluvicto is used

Follow all instructions given by your nuclear medicine doctor carefully. They may differ from the general information contained in this leaflet.

Pluvicto must not be used
- if you are allergic to lutetium (^{177}Lu) vipivotide tetraxetan or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
If any of these apply to you, tell your nuclear medicine doctor before receiving Pluvicto:
- if you have low levels of certain types of cells in the blood (red blood cells, white blood cells, neutrophils, platelets)
- if you have or have had tiredness, weakness, pale skin, shortness of breath, bleeding or bruising more easily than normal or bleeding for longer than normal, or frequent infections with signs such as fever, chills, sore throat or mouth ulcers (possible signs of myelosuppression [a condition in which the bone marrow cannot make enough blood cells])
- if you have or have had kidney problems
- if you have or have had any other type of cancer or treatment for cancer, as Pluvicto contributes to your overall long-term cumulative radiation exposure

Before administration of Pluvicto you should:
- drink plenty of water so that you remain hydrated and urinate as often as possible during the first hours after administration

Children and adolescents
The safety and efficacy of this medicine have not been established in children and adolescents under 18 years of age. This medicine should not be given to children or adolescents aged under 18 years because no data are available in this age group.

Pregnancy, breast-feeding and fertility
Pluvicto is not intended for use in women.

Before you receive Pluvicto, tell your nuclear medicine doctor if you are sexually active as all radioactive emissions, including those from Pluvicto, can cause harm to an unborn baby.

Fertility
Pluvicto may cause infertility. Please ask your nuclear medicine doctor how this may affect you, especially if you are planning to have children in the future. You may wish to seek advice on preservation of sperm before treatment starts.

Contraception in males
- You should avoid sexual activity for 7 days after administration of Pluvicto.
- You should not father a child and should use a condom during intercourse throughout treatment with Pluvicto and for 14 weeks after your last dose.
- Tell your nuclear medicine doctor immediately if you father a child at any time during this time period.

Driving and using machines
It is considered unlikely that Pluvicto will affect your ability to drive or use machines.

Pluvicto contains sodium
This medicine contains up to 88.75 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 4.4% of the recommended maximum daily dietary intake of sodium for an adult.

3. How Pluvicto is used

There are strict laws on the use, handling and disposal of radiopharmaceutical products. Pluvicto will only be used in special controlled areas. This radiopharmaceutical product will only be handled and given to you by people who are trained and qualified to use it safely. These persons will take special care for the safe use of this radiopharmaceutical product and will keep you informed of their actions.

How much Pluvicto is given
The recommended treatment regimen of Pluvicto is 7 400 MBq (megabecquerel, the unit used to express radioactivity), which is given approximately every 6 weeks for up to a total of 6 doses.

Administration of Pluvicto and conduct of the procedure
Pluvicto is administered directly into a vein.

Duration of the procedure
Your nuclear medicine doctor will inform you about the usual duration of the procedure.

If you have questions about how long you will receive Pluvicto, talk to your nuclear medicine doctor.

Treatment monitoring
Your nuclear medicine doctor will do blood tests before and during treatment to check your condition and to detect any side effects as early as possible. Based on the results, your nuclear medicine doctor may decide to delay, change or stop your treatment with Pluvicto if necessary.

After administration of Pluvicto, you should:
- drink plenty of water for 2 days so that you remain hydrated and urinate as often as possible to eliminate the radiopharmaceutical product from your body

Because this medicine is radioactive, you will have to follow the instructions described below to minimise radiation exposure to others unless otherwise instructed by your nuclear medicine doctor.

<u>Contact with others, children, and/or pregnant women</u>
- Limit close contact (less than 1 metre) with:
  - others for 2 days
  - children and pregnant women for 7 days
- Sleep in a separate room from:
  - others for 3 days
  - children for 7 days
  - pregnant women for 15 days
- Avoid sexual activity for 7 days
- Do not father a child and do use a condom during intercourse throughout treatment with Pluvicto and for 14 weeks after your last dose

<u>Use of toilets</u>
Take special precautions to avoid contamination for 2 days after administration:
- You must always sit when using the toilet.
- It is essential that you use toilet paper every time you use the toilet.
- Always wash your hands well after using the toilet.
- Flush all wipes and/or toilet paper down the toilet immediately after use.
- Flush any tissues or any other items that contain bodily waste, such as blood, urine and faeces down the toilet. Items that cannot be flushed down the toilet, such as bandages, must be placed in separate plastic waste disposal bags (according to “Waste disposal recommendations” below).
- Any special medical equipment that could be contaminated by your bodily fluids (e.g. catheter bags, colostomy bags, bedpans, water nozzles) must be emptied immediately into the toilet and then cleaned.

Showering and laundry
- Take a shower every day for at least 7 days after administration.
- Wash your underwear, pyjamas, sheets and any clothes that contain sweat, blood or urine separately from the laundry of others in your household, using a standard washing cycle. You do not need to use bleach and you do not need extra rinses.

Care givers
For 2-3 days after administration:
- People who are confined to bed or have reduced mobility will preferably receive assistance from a care giver. It is recommended that when providing assistance in the bathroom, the care giver wears disposable gloves.
- Care givers who clean up vomit, blood, urine or faeces should wear plastic gloves, which should be disposed of in a separate plastic waste disposal bag (see "Waste disposal recommendations" below).

Waste disposal recommendations
- All items to be thrown away should be discarded in a separate plastic waste disposal bag to be used only for this purpose.
- Keep the plastic waste disposal bags separate from the other household waste and away from children and animals.
- A member of the hospital staff will tell you how and when to get rid of these waste disposal bags.

Hospitalisation and emergency care
- If for any reason you require emergency medical assistance or are unexpectedly admitted to the hospital during the first 7 days after administration, you should inform the healthcare professionals about the name, date and dose of your radioactive treatment.

Other precautions
- The nuclear medicine doctor will inform you if you need to take any other special precautions after receiving this medicine. Contact your nuclear medicine doctor if you have any questions.

If you have been given more Pluvicto than you should
An overdose is unlikely because you will only receive Pluvicto in doses that are precisely controlled by the nuclear medicine doctor supervising the procedure. However, in the event of an overdose, you will receive the appropriate treatment.

If you forget to receive Pluvicto
If you miss an appointment to receive Pluvicto, contact your nuclear medicine doctor as soon as possible to reschedule.

Should you have any further questions on the use of Pluvicto, please ask the nuclear medicine doctor who supervises the procedure.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Some side effects could be serious
If you experience any of the following serious side effects, **tell your nuclear medicine doctor right away**.

Very common: may affect more than 1 in 10 people
- tiredness, weakness, pale skin or shortness of breath (possible signs of low levels of red blood cells [*anaemia*])

- bleeding or bruising more easily than normal or bleeding for longer than normal (possible signs of low levels of platelets [*thrombocytopenia*])
- frequent infections with signs such as fever, sore throat or mouth ulcers (possible signs of low levels of white blood cells [*leukopenia, lymphopenia*])

Common: may affect up to 1 in every 10 people
- passing urine less often or in much smaller amounts than usual (possible sign of kidney problems [*acute kidney injury*])
- tiredness, weakness, pale skin, shortness of breath, bleeding or bruising more easily than normal or bleeding for longer than normal or frequent infections with signs such as fever, chills, sore throat or mouth ulcers (possible signs of low levels of blood cells [*pancytopenia*])

Uncommon: may affect up to 1 in every 100 people
- Weakness, pale skin, bleeding or bruising more easily than normal or difficulty to stop bleeding and frequent infections with signs such as fever, chills, sore throat or mouth ulcers (bone marrow failure)

Other possible side effects
Other side effects include the following listed below. If these side effects become severe, please tell your nuclear medicine doctor.

Very common: may affect more than 1 in 10 people
- tiredness (*fatigue*)
- dry mouth
- nausea
- loss of appetite
- changes in bowel movements (constipation or diarrhoea)
- vomiting
- frequent urination with pain or burning sensation (*urinary tract infection*)
- abdominal pain
- weight loss
- swollen hands, ankles or feet (*peripheral oedema*)

Common: may affect up to 1 in every 10 people
- dizziness
- headache
- disturbed sense of taste (*dysgeusia*)
- fever (*pyrexia*)
- trouble swallowing and/or heartburn (*oesophageal disorder*)
- dry eyes
- oral fungal infection
- dizziness, with a spinning sensation (*vertigo*)
- mouth sores (*stomatitis*)
- dry skin

Reporting of side effects
If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How Pluvicto is stored

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulations on radioactive materials.

The following information is intended for the specialist only:
- Keep this medicine out of the sight and reach of children.
- Do not freeze.
- Store in the original package in order to protect from ionising radiation (lead shielding).
- Pluvicto must not be used after the expiry date and time which are stated on the lead shielding container and vial labels after EXP.
- Any unused medicine or waste material should be disposed of in accordance with local requirements.

6. Contents of the pack and other information

What Pluvicto contains
- The active substance is lutetium (^{177}Lu) vipivotide tetraxetan. One mL of solution contains 1 000 MBq lutetium (^{177}Lu) vipivotide tetraxetan at the date and time of calibration.
- The other ingredients are: acetic acid, sodium acetate, gentisic acid, sodium ascorbate, pentetic acid, water for injections (see "Pluvicto contains sodium" in section 2).

What Pluvicto looks like and contents of the pack
Pluvicto is a clear, colourless to slightly yellow solution supplied in a clear, colourless type I glass vial, closed with a bromobutyl rubber stopper and aluminium seal.
Each vial contains a volume of solution that can range from 7.5 mL to 12.5 mL corresponding to a radioactivity of 7 400 MBq ±10% at the date and time of administration.
The vial is enclosed within a lead container for protective shielding.

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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu

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The following information is intended for healthcare professionals only:

The complete SmPC of Pluvicto is provided as a separate document in the product package, with the objective to provide healthcare professionals with other additional scientific and practical information about the administration and use of this radiopharmaceutical.

Please refer to the SmPC.

販売名	プルヴィクト静注	[ゾーフィゴ静注]	[リムパーザ錠 100mg リムパーザ錠 150mg]
一般名	無 放射性医薬品基準 ルテチウムビピボチドテトラキセタン(^{177}Lu)注射液	無 放射性医薬品基準　塩化ラジウム（^{223}Ra）注射液	オラパリブ
会社名	ノバルティスファーマ株式会社	バイエル薬品株式会社	アストラゼネカ株式会社
効能又は効果	前立腺特異的膜抗原（PSMA）陽性の遠隔転移を有する去勢抵抗性前立腺癌	骨転移のある去勢抵抗性前立腺癌	○白金系抗悪性腫瘍剤感受性の再発卵巣癌における維持療法 ○*BRCA* 遺伝子変異陽性の卵巣癌における初回化学療法後の維持療法 ○相同組換え修復欠損を有する卵巣癌におけるベバシズマブ（遺伝子組換え）を含む初回化学療法後の維持療法 ○がん化学療法歴のある *BRCA* 遺伝子変異陽性かつ HER2 陰性の手術不能又は再発乳癌 ○*BRCA* 遺伝子変異陽性かつ HER2 陰性で再発高リスクの乳癌における術後薬物療法 ○*BRCA* 遺伝子変異陽性の遠隔転移を有する去勢抵抗性前立腺癌 ○*BRCA* 遺伝子変異陽性の治癒切除不能な膵癌における白金系抗悪性腫瘍剤を含む化学療法後の維持療法 ○ミスマッチ修復機能正常（pMMR）の進行・再発の子宮体癌におけるデュルバルマブ（遺伝子組換え）を含む化学療法後の維持療法
添付文書改訂日		2025 年 3 月	2024 年 11 月

2025年３月改訂（第２版、再審査結果）
2022年11月改訂（第１版）

貯法：遮光して室温保存
有効期間：検定日より14日間

放射性医薬品・抗悪性腫瘍剤
劇薬、処方箋医薬品注）
放射性医薬品基準　塩化ラジウム（^{223}Ra）注射液

日本標準商品分類番号
874291

承認番号	販売開始
22800AMX00383000	2016年６月

ゾーフィゴ® 静注
Xofigo iv injection

注）注意―医師等の処方箋により使用すること

1. 警告
本剤は、緊急時に十分対応できる医療施設において、がん化学療法及び放射線治療に十分な知識・経験を持つ医師のもとで、本剤の投与が適切と判断される症例についてのみ投与すること。また、治療開始に先立ち、患者又はその家族に本剤の有効性及び危険性を十分説明し、同意を得てから投与すること。

3. 組成・性状
3.1 組成

販売名	ゾーフィゴ静注
有効成分	1バイアル（5.6mL）中 塩化ラジウム（^{223}Ra）としてラジウム223を6160kBq含有（検定日時において）
添加剤	1バイアル（5.6mL）中 塩化ナトリウム：35.3mg クエン酸ナトリウム水和物：46.5mg pH調整剤：適量

3.2 製剤の性状

販売名	ゾーフィゴ静注
色・性状	無色澄明の注射液
pH	6.0～8.0
浸透圧比	約1（生理食塩液に対する比）

4. 効能又は効果
骨転移のある去勢抵抗性前立腺癌

5. 効能又は効果に関連する注意
5.1 内臓転移のある前立腺癌における有効性及び安全性は確立していない。
5.2「17.臨床成績」の項の内容を熟知し、本剤の有効性及び安全性を十分に理解した上で、適応患者の選択を行うこと。［17.1.1、17.1.2 参照］

6. 用法及び用量
通常、成人には、1回55kBq/kgを4週間間隔で最大6回まで、緩徐に静脈内投与する。

7. 用法及び用量に関連する注意
7.1 外科的又は内科的去勢術と併用しない場合の有効性及び安全性は確立していない。
7.2 副作用があらわれた場合は、重症度等に応じて以下の基準を考慮して、本剤の投与を延期又は中止すること。

本剤の投与延期・中止の目安

副作用	処置
グレード3以上の好中球減少、貧血、血小板減少	グレード2以下に回復するまで投与を延期し、回復を確認後、投与を再開する。前回投与から6週間以内にグレード2以下に回復しない場合には、投与を中止する。
グレード3以上の下痢、悪心、嘔吐、便秘	グレード2以下に回復するまで投与を延期し、回復を確認後、投与を再開する。
グレード4のその他の事象	7日を超えて持続する場合は、投与を中止する。

グレードはCTCAE（Common Terminology Criteria for Adverse Events）v3.0に準じる。

7.3 化学療法未治療で無症候性又は軽度症候性の骨転移のある去勢抵抗性前立腺癌患者に対する本剤とアビラテロン酢酸エステル及びプレドニゾロンの併用投与は推奨されない。［15.1.2 参照］

8. 重要な基本的注意
骨髄抑制があらわれることがあるので、本剤投与開始前及び投与中は定期的に血液検査を行い、患者の状態を十分に観察すること。［9.1.1、11.1.1 参照］

9. 特定の背景を有する患者に関する注意
9.1 合併症・既往歴等のある患者
9.1.1 骨髄抑制のある患者
骨髄抑制が増強するおそれがある。［8.、11.1.1 参照］
9.1.2 炎症性腸疾患（クローン病、潰瘍性大腸炎等）の患者
本剤の主な排泄経路は糞中であるため、症状を増悪させるおそれがある。
9.1.3 脊髄圧迫のある患者又は脊髄圧迫の可能性のある患者
本剤投与前に適切な処置を行うこと。
9.4 生殖能を有する者
9.4.1 本剤投与中及び投与後6ヵ月間は適切な避妊を行うよう指導すること。本剤は放射性医薬品である。［9.4.2 参照］
9.4.2 生殖可能な年齢の患者に投与する場合には、性腺に対する影響を考慮すること。［9.4.1 参照］
9.7 小児等
小児等を対象とした臨床試験は実施していない。
9.8 高齢者
患者の状態を観察しながら慎重に投与すること。一般に生理機能が低下している。

11. 副作用
次の副作用があらわれることがあるので、観察を十分に行い、異常が認められた場合には投与を中止するなど適切な処置を行うこと。
11.1 重大な副作用
11.1.1 骨髄抑制
好中球減少（3.9%）、血小板減少（7.4%）、貧血（19.3%）、白血球減少（3.2%）、リンパ球減少（2.0%）、汎血球減少（1.7%）等があらわれることがある。［8.、9.1.1 参照］

11.2 その他の副作用

	5%以上	1～5%未満	1%未満
精神神経系		浮動性めまい、嗜眠、頭痛	
消化器	悪心、下痢、嘔吐、食欲減退	便秘、腹痛	上腹部痛
呼吸器		呼吸困難	咳嗽
肝臓			ＡＳＴ上昇、γ-GTP上昇
筋・骨格系	骨痛	関節痛	筋骨格痛
その他	疲労	発熱、体重減少、無力症、味覚異常、末梢性浮腫、脱水	全身健康状態低下、倦怠感、尿路感染、注射部位反応、悪寒

14. 適用上の注意

14.1 薬剤投与前の注意

14.1.1 希釈又は他剤と混合しないこと。

14.1.2 投与前に目視による確認を行い、注射液に変色や微粒子が認められる場合、容器に破損が認められる場合等、異常が認められる場合には使用しないこと。

14.2 薬剤投与時の注意

14.2.1 投与前後に、静脈ラインを生理食塩液でフラッシュすること。

14.2.2 投与量は以下の式で算出する。

$$\text{投与量(mL)} = \frac{\text{体重(kg)} \times \text{用量(55kBq/kg)}}{\text{減衰係数※} \times 1100\text{kBq/mL}}$$

※：「19.有効成分に関する理化学的知見」の項参照

14.2.3 投与速度：約1分間かけて緩徐に静脈内投与すること。

14.2.4 バイアルは一回限りの使用とすること。

15. その他の注意

15.1 臨床使用に基づく情報

15.1.1 放射線曝露により、二次発癌や遺伝子異常のリスクが増加する可能性がある。

15.1.2 化学療法未治療で無症候性又は軽度症候性[注)]の骨転移のある去勢抵抗性前立腺癌患者を対象に、アビラテロン酢酸エステル及びプレドニゾン(国内未承認)/プレドニゾロンとの併用で、本剤又はプラセボを投与する二重盲検無作為化国際共同第Ⅲ相試験の結果、本剤群ではプラセボ群と比較して、死亡率(本剤群38.5%、プラセボ群35.5%)及び骨折の発現率(本剤群28.6%、プラセボ群11.4%)が高い傾向が認められた[1)]。[7.3 参照]

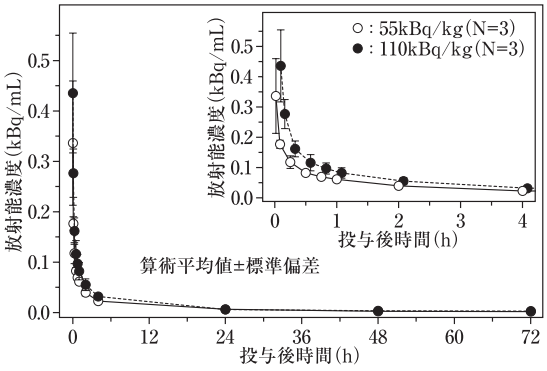
注)Brief Pain Inventory-Short Form(BPI-SF)の項目の3(過去24時間で最悪の疼痛)のスコア(0～10)が0(無症候性)又は1～3(軽度症候性)

16. 薬物動態

16.1 血中濃度

16.1.1 単回投与

日本人去勢抵抗性前立腺癌患者に本剤55kBq/kg又は110kBq/kg[注)]を単回投与後、血中放射能濃度は速やかに減少した(各々N=3)[2)]。



投与量	55kBq/kg (N=3)	110kBq/kg (N=3)
AUC(kBq・h/mL)	0.674/13.9	0.812/21.2
Cmax(kBq/mL)	0.323/35.6	0.425/28.3
$t_{1/2}$(h)	18.8/19.7	15.4/53.3

幾何平均値/幾何CV%

また、第Ⅰ相試験において検討された用量範囲(51～276kBq/kg)[注)]で薬物動態はおおむね線形性を示すと考えられた[3)](外国人データ)。

16.1.2 反復投与

第Ⅰ相試験の成績から反復投与による本薬の薬物動態への影響は認められず、蓄積性は臨床的に問題にならないと考えられた[4)](外国人データ)。

16.3 分布

16.3.1 本剤投与後、ラジウム223は主に骨及び骨転移部位に分布、又は腸管内に排出される。日本人去勢抵抗性前立腺癌患者に本剤55kBq/kg及び110kBq/kg[注)]を単回投与後、骨への放射能の取り込みは投与2時間後までに最大となり、骨中放射能の投与放射能に対する割合の平均値は52%であった。腸管内放射能は投与6時間後に最大となり、投与放射能に対する割合の平均値は64%であった。心臓、肝臓、腎臓、膀胱、脾臓等の臓器への特異的な取り込みは認められなかった(N=6)[2)]。

16.3.2 吸収線量

日本人去勢抵抗性前立腺癌患者に本剤55kBq/kg及び110kBq/kg[注)]を単回投与後の体内分布データから、MIRD法に基づき吸収線量を算出した(N=4)。

臓器・組織	平均値(mGy/MBq)	変動係数(%)
骨形成細胞	761	17
赤色骨髄	91.6	17
大腸壁上部	24.4	41
大腸壁下部	18.8	44
全身	14.0	20
小腸壁	5.42	34
腎臓	2.00	17
肝臓	1.87	17
膀胱壁	1.54	84
心臓壁	0.954	34
卵巣	0.269	36
胆のう壁	0.151	35
子宮	0.144	33
胃壁	0.0776	32
副腎	0.0637	20
筋肉	0.0606	25
膵臓	0.0605	26
脳	0.0498	17
脾臓	0.0440	26
精巣	0.0330	27
肺	1.17	－※

臓器・組織	平均値(mGy/MBq)	変動係数(%)
甲状腺	0.0319	17
皮膚	0.0313	21
胸腺	0.0224	17
胸部	0.0170	18

※：肺における吸収線量はモデルから推定した平均血中放射能濃度推移に基づき算出したため、変動係数については計算できない。

16.4 代謝

ラジウム223は二価陽イオン($^{223}Ra^{2+}$)の放射性同位元素であり、アクチニウム系列の壊変により消失し、代謝は受けない。

16.5 排泄

本剤投与後のラジウム223の主要排泄経路は糞中排泄である。日本人去勢抵抗性前立腺癌患者に本剤55kBq/kgを単回投与72時間後の累積糞中排泄率の平均値は56%、単回投与48時間後の累積尿中排泄率の平均値は1.5%であった(N=3)。肝胆道系排泄は認められなかった。日本人去勢抵抗性前立腺癌患者に本剤55kBq/kg及び110kBq/kg[注)]を単回投与7日後の全身放射能の残存率の平均値は22%であった(N=6)[2)]。

注)承認用法・用量：1回55kBq/kgを4週間間隔で最大6回まで、緩徐に静脈内投与する。

17. 臨床成績

17.1 有効性及び安全性に関する試験

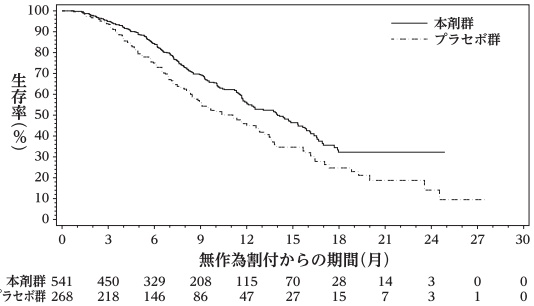
17.1.1 国内第Ⅱ相試験

ドセタキセル水和物に不応又は不耐で、内臓転移がなく、症候性の骨転移のある去勢抵抗性前立腺癌患者[※1]を対象に、標準的治療[※2]との併用で、本剤55kBq/kgを4週間間隔で6回投与する非盲検非対照試験を実施した。本剤が投与された49例において、主要評価項目である投与開始後12週時点における総ALPのベースラインからの変化率の平均値(95%信頼区間)は－19.3(－28.0～－10.7)%であった[5)]。

副作用は本剤が投与された49例中27例(55.1%)に認められた。主な副作用は、貧血15例(30.6%)、リンパ球減少12例(24.5%)、血小板減少6例(12.2%)、下痢5例(10.2%)、悪心5例(10.2%)等であった。[5.2 参照]

17.1.2 国外第Ⅲ相試験

ドセタキセル水和物に不応又は不耐で、内臓転移がなく、症候性の骨転移のある去勢抵抗性前立腺癌患者[※1]を対象に、標準的治療[※2]との併用で、本剤55kBq/kg又はプラセボを4週間間隔で6回投与する二重盲検無作為化比較試験を実施した。主要評価項目である全生存期間(OS)の中間解析(本剤群541例、プラセボ群268例)において、プラセボ群と比較して本剤群で統計学的に有意なOSの延長が認められた〔中央値(95%信頼区間)：本剤群14.0(12.0～15.8)ヵ月、プラセボ群11.1(8.8～12.9)ヵ月、ハザード比(95%信頼区間)：0.681(0.542～0.857)、p=0.00096(層別log-rank検定)、2010年10月14日データカットオフ〕[6)]。



※1：内臓転移又は短径3cmを超えるリンパ節腫脹のある患者、クローン病又は潰瘍性大腸炎の患者、半身外部放射線治療歴のある患者、切迫状態にある又は明らかな脊髄圧迫のある患者は除外した。

※2：局所的な外部放射線治療、鎮痛剤、コルチコステロイド製剤、LH-RHアゴニスト製剤、LH-RHアンタゴニスト製剤、抗アンドロゲン製剤、エストロゲン製剤、ビスホスホネート製剤、デノスマブ(遺伝子組換え)等。なお、デノスマブ(遺伝子組換え)は国内第Ⅱ相試験でのみ併用が許容された。

副作用は本剤が投与された600例中386例(64.3%)に認められた。主な副作用は、悪心125例(20.8%)、貧血110例(18.3%)、下痢100例(16.7%)、骨痛95例(15.8%)、疲労73例(12.2%)等であった。[5.2 参照]

18. 薬効薬理

18.1 作用機序

ラジウム223は、カルシウムに類似した性質を有しており、骨転移巣のように骨代謝が亢進している部位に集積し、高エネルギーのアルファ線を放出することにより、近接する腫瘍細胞等に対してDNA二重鎖切断等を誘発し、腫瘍増殖抑制作用を示すと考えられている[7)-9)]。

19. 有効成分に関する理化学的知見

一般的名称：塩化ラジウム(^{223}Ra)
(Radium(^{223}Ra)chloride)

化学名：塩化ラジウム(^{223}Ra)

分子式：$^{223}RaCl_2$

分子量：293.91

核物理学的特性(^{223}Raとして)：

物理的半減期：11.43日

アルファ線エネルギー：5.0～7.5MeV(95.3%)

ベータ線エネルギー(平均)：0.445MeV、0.492MeV(3.6%)

ガンマ線エネルギー：0.01～1.27MeV(1.1%)

減衰表

経過日数	減衰係数	経過日数	減衰係数
−14	2.39	1	0.96
−13	2.24	2	0.90
−12	2.11	3	0.85
−11	1.99	4	0.80
−10	1.87	5	0.75
−9	1.76	6	0.71
−8	1.66	7	0.67
−7	1.56	8	0.63
−6	1.47	9	0.59
−5	1.38	10	0.56
−4	1.30	11	0.52
−3	1.22	12	0.49
−2	1.15	13	0.46
−1	1.08	14	0.44
0	1.02		

注)経過日数は、検定日の前(−)又は後の日数を示す。

20. 取扱い上の注意

本剤は、医療法その他の放射線防護に関する法令、関連する告示及び通知(患者退出等を含む)等を遵守し、適正に使用すること。

22. 包装

1バイアル

23. 主要文献

1) 社内資料: アビラテロン酢酸エステル及びプレドニゾン(国内未承認)/プレドニゾロンとの併用に関する二重盲検無作為化国際共同第Ⅲ相試験
2) 社内資料: 去勢抵抗性前立腺癌患者を対象とした国内第Ⅰ相臨床試験(2016年3月28日承認、CTD2.7.6.4)
3) 社内資料: 骨転移を有する進行性がん患者を対象とした国外第Ⅰ相臨床試験(2016年3月28日承認、CTD2.7.6.1)
4) 社内資料: 去勢抵抗性前立腺癌患者を対象とした国外第Ⅰ相臨床試験(2016年3月28日承認、CTD2.7.6.2)
5) 社内資料: 症候性去勢抵抗性前立腺癌患者を対象とした国内第Ⅱ相臨床試験(2016年3月28日承認、CTD2.7.6.12)
6) 社内資料: 症候性去勢抵抗性前立腺癌患者を対象とした国外第Ⅲ相臨床試験(2016年3月28日承認、CTD2.7.6.6)
7) Bruland OS, et al.: Clin Cancer Res. 2006; 12: 6250s-6257s
8) Kassis AI, et al.: J Nucl Med. 2005; 46: 4S-12S
9) 社内資料: 塩化ラジウム(^{223}Ra)のDNA分子二重鎖切断誘発作用(2016年3月28日承認、CTD2.6.2.2.1.1.4)

24. 文献請求先及び問い合わせ先

文献請求先
バイエル薬品株式会社・メディカルインフォメーション
〒530-0001大阪市北区梅田二丁目4番9号
バイエル医療用医薬品のお問い合わせ先
電話0120-106-398

26. 製造販売業者等

26.1 製造販売元

バイエル薬品株式会社
大阪市北区梅田二丁目4番9号

**2024年11月改訂（第6版、効能変更、用法変更）
*2023年8月改訂（第5版、用法変更）

日本標準商品分類番号
874291

抗悪性腫瘍剤／
ポリアデノシン5'二リン酸リボースポリメラーゼ（PARP）阻害剤
オラパリブ錠

貯　　法：室温保存
有効期間：4年

劇薬、処方箋医薬品注）

リムパーザ®錠100mg
リムパーザ®錠150mg
Lynparza®Tablets 100mg・150mg

	錠100mg	錠150mg
承認番号	23000AMX00022	23000AMX00023
販売開始	2018年4月	

注）注意－医師等の処方箋により使用すること

1. 警告

本剤は、緊急時に十分対応できる医療施設において、がん化学療法に十分な知識・経験を持つ医師のもとで、本剤の使用が適切と判断される症例についてのみ投与すること。また、治療開始に先立ち、患者又はその家族に有効性及び危険性を十分説明し、同意を得てから投与すること。

2. 禁忌（次の患者には投与しないこと）

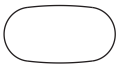
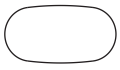
本剤の成分に対し過敏症の既往歴のある患者

3. 組成・性状

3.1 組成

販売名	リムパーザ錠100mg	リムパーザ錠150mg
有効成分	1錠中 オラパリブ 100mg	1錠中 オラパリブ 150mg
添加剤	コポビドン、軽質無水ケイ酸、D-マンニトール、フマル酸ステアリルナトリウム、ヒプロメロース、マクロゴール400、酸化チタン、黄色三二酸化鉄	コポビドン、軽質無水ケイ酸、D-マンニトール、フマル酸ステアリルナトリウム、ヒプロメロース、マクロゴール400、酸化チタン、黄色三二酸化鉄、黒酸化鉄

3.2 製剤の性状

販売名	リムパーザ錠100mg	リムパーザ錠150mg
剤形	黄色～暗黄色のフィルムコーティング錠	緑色～灰緑色のフィルムコーティング錠
外形（表面）		
外形（裏面）		
外形（側面）		
大きさ（長径）	約14.7mm	約14.7mm
大きさ（短径）	約7.6mm	約7.6mm
大きさ（厚さ）	約4.7mm	約6.8mm
質量	約0.41g	約0.62g
識別コード	OP 100	OP 150

**4. 効能又は効果

○白金系抗悪性腫瘍剤感受性の再発卵巣癌における維持療法
○*BRCA* 遺伝子変異陽性の卵巣癌における初回化学療法後の維持療法
○相同組換え修復欠損を有する卵巣癌におけるベバシズマブ（遺伝子組換え）を含む初回化学療法後の維持療法
○がん化学療法歴のある*BRCA* 遺伝子変異陽性かつHER2陰性の手術不能又は再発乳癌
○*BRCA* 遺伝子変異陽性かつHER2陰性で再発高リスクの乳癌における術後薬物療法
○*BRCA* 遺伝子変異陽性の遠隔転移を有する去勢抵抗性前立腺癌
○*BRCA* 遺伝子変異陽性の治癒切除不能な膵癌における白金系抗悪性腫瘍剤を含む化学療法後の維持療法
○ミスマッチ修復機能正常（pMMR）の進行・再発の子宮体癌におけるデュルバルマブ（遺伝子組換え）を含む化学療法後の維持療法

5. 効能又は効果に関連する注意

〈白金系抗悪性腫瘍剤感受性の再発卵巣癌における維持療法〉

5.1 再発時の白金系抗悪性腫瘍剤を含む化学療法で奏効が維持されている患者を対象とすること。

5.2 臨床試験に組み入れられた患者における白金系抗悪性腫瘍剤を含む化学療法終了後から再発までの期間（PFI）等について、「17. 臨床成績」の項の内容を熟知し、本剤の有効性及び安全性を十分に理解した上で、適応患者の選択を行うこと。[17.1.1、17.1.2参照]

〈*BRCA* 遺伝子変異陽性の卵巣癌における初回化学療法後の維持療法〉

5.3 国際産婦人科連合（FIGO）進行期分類III期又はIV期の卵巣癌と診断され、白金系抗悪性腫瘍剤を含む初回化学療法で奏効が維持されている患者を対象とすること。

5.4 承認された体外診断用医薬品又は医療機器注）を用いた検査により、*BRCA* 遺伝子変異を有することが確認された患者に投与すること。

5.5 臨床試験に組み入れられた患者における前治療歴等について、「17.臨床成績」の項の内容を熟知し、本剤の有効性及び安全性を十分に理解した上で、適応患者の選択を行うこと。[17.1.1参照]

〈相同組換え修復欠損を有する卵巣癌におけるベバシズマブ（遺伝子組換え）を含む初回化学療法後の維持療法〉

5.6 国際産婦人科連合（FIGO）進行期分類III期又はIV期の卵巣癌と診断され、白金系抗悪性腫瘍剤及びベバシズマブ（遺伝子組換え）を含む初回化学療法で奏効が維持されている患者を対象とすること。

5.7 承認された体外診断用医薬品又は医療機器注）を用いた検査により、相同組換え修復欠損を有することが確認された患者に投与すること。

〈がん化学療法歴のある*BRCA* 遺伝子変異陽性かつHER2陰性の手術不能又は再発乳癌〉

5.8 本剤の投与を行う場合には、アントラサイクリン系抗悪性腫瘍剤及びタキサン系抗悪性腫瘍剤を含む化学療法歴のある患者を対象とすること。

**5.9 承認された体外診断用医薬品又は医療機器注）を用いた検査により、*BRCA* 遺伝子変異を有することが確認された患者に投与すること。

〈*BRCA* 遺伝子変異陽性かつHER2陰性で再発高リスクの乳癌における術後薬物療法〉

5.10 本剤の術前薬物療法としての有効性及び安全性は確立していない。

5.11 臨床試験に組み入れられた患者の再発高リスクの定義、前治療歴等について、「17.臨床成績」の項の内容を熟知し、本剤の有効性及び安全性を十分に理解した上で、適応患者の選択を行うこと。[17.1.6参照]

5.12 承認された体外診断用医薬品又は医療機器注）を用いた検査により、*BRCA* 遺伝子変異を有することが確認された患者に投与すること。

〈*BRCA* 遺伝子変異陽性の遠隔転移を有する去勢抵抗性前立腺癌〉

5.13 本剤の術後補助療法としての有効性及び安全性は確立していない。

5.14 承認された体外診断用医薬品又は医療機器注）を用いた検査により、*BRCA* 遺伝子変異を有することが確認された患者に投与す

ること。

*5.15 臨床試験に組み入れられた患者の前治療歴等について、「17.臨床成績」の項の内容を熟知し、本剤の有効性及び安全性を十分に理解した上で、適応患者の選択を行うこと。[17.1.7、17.1.8参照]

〈*BRCA* 遺伝子変異陽性の治癒切除不能な膵癌における白金系抗悪性腫瘍剤を含む化学療法後の維持療法〉

5.16 本剤の手術の補助療法としての有効性及び安全性は確立していない。

5.17 白金系抗悪性腫瘍剤を含む化学療法で疾患進行が認められていない患者を対象とすること。

5.18 臨床試験に組み入れられた患者の病期、白金系抗悪性腫瘍剤を含む化学療法の投与期間等について、「17.臨床成績」の項の内容を熟知し、本剤の有効性及び安全性を十分に理解した上で、適応患者の選択を行うこと。[17.1.9参照]

5.19 承認された体外診断用医薬品又は医療機器[注)]を用いた検査により、生殖細胞系列の*BRCA* 遺伝子変異（病的変異又は病的変異疑い）を有することが確認された患者に投与すること。

〈ミスマッチ修復機能正常（pMMR）の進行・再発の子宮体癌におけるデュルバルマブ（遺伝子組換え）を含む化学療法後の維持療法〉

**5.20 デュルバルマブ（遺伝子組換え）及び白金系抗悪性腫瘍剤を含む化学療法で疾患進行が認められていない患者を対象とすること。

**5.21 十分な経験を有する病理医又は検査施設における検査により、pMMRが確認された患者に投与すること。検査にあたっては、承認された体外診断用医薬品又は医療機器[注)]を用いること。

注）承認された体外診断用医薬品又は医療機器に関する情報については、以下のウェブサイトから入手可能である：
https://www.pmda.go.jp/review-services/drug-reviews/review-information/cd/0001.html

**6. 用法及び用量

〈白金系抗悪性腫瘍剤感受性の再発卵巣癌における維持療法、*BRCA* 遺伝子変異陽性の卵巣癌における初回化学療法後の維持療法、*BRCA* 遺伝子変異陽性の治癒切除不能な膵癌における白金系抗悪性腫瘍剤を含む化学療法後の維持療法〉

通常、成人にはオラパリブとして1回300mgを1日2回、経口投与する。なお、患者の状態により適宜減量する。

〈相同組換え修復欠損を有する卵巣癌におけるベバシズマブ（遺伝子組換え）を含む初回化学療法後の維持療法〉

ベバシズマブ（遺伝子組換え）との併用において、通常、成人にはオラパリブとして1回300mgを1日2回、経口投与する。なお、患者の状態により適宜減量する。

〈がん化学療法歴のある*BRCA* 遺伝子変異陽性かつHER2陰性の手術不能又は再発乳癌、*BRCA* 遺伝子変異陽性かつHER2陰性で再発高リスクの乳癌における術後薬物療法〉

通常、成人にはオラパリブとして1回300mgを1日2回、経口投与する。ただし、術後薬物療法の場合、投与期間は1年間までとする。なお、患者の状態により適宜減量する。

〈*BRCA* 遺伝子変異陽性の遠隔転移を有する去勢抵抗性前立腺癌〉

通常、成人にはオラパリブとして1回300mgを1日2回、経口投与する。他の薬剤と併用する場合は、アビラテロン酢酸エステル及びプレドニゾロンと併用すること。なお、患者の状態により適宜減量する。

〈ミスマッチ修復機能正常（pMMR）の進行・再発の子宮体癌におけるデュルバルマブ（遺伝子組換え）を含む化学療法後の維持療法〉

デュルバルマブ（遺伝子組換え）との併用において、通常、成人にはオラパリブとして1回300mgを1日2回、経口投与する。なお、患者の状態により適宜減量する。

7. 用法及び用量に関連する注意

〈効能共通〉

7.1 100mg錠と150mg錠の生物学的同等性は示されていないため、300mgを投与する際には100mg錠を使用しないこと。

**7.2 本剤投与により副作用が発現した場合には、以下の基準を考慮して、休薬・減量・中止すること。

副作用発現時の用量調節基準

副作用	程度[注]	処置	再開時の投与量
貧血	ヘモグロビン値がGrade 3又は4の場合	ヘモグロビン値≧9g/dLに回復するまで最大4週間休薬する。	・1回目の再開の場合、減量せずに投与する。 ・2回目の再開の場合、1回250mgを1日2回で投与する。 ・3回目の再開の場合、1回200mgを1日2回で投与する。
好中球減少	Grade 3又は4の場合	Grade 1以下に回復するまで休薬する。	
血小板減少	Grade 3又は4の場合	Grade 1以下に回復するまで最大4週間休薬する。	減量せずに投与する。
間質性肺疾患	Grade 2の場合	Grade 1以下に回復するまで休薬する。	減量せずに投与する。
	Grade 3又は4の場合	中止する。	再開しない。
** デュルバルマブ（遺伝子組換え）との併用投与下の赤芽球癆	全Grade	本剤及びデュルバルマブ（遺伝子組換え）の投与を中止する。	再開しない。
** デュルバルマブ（遺伝子組換え）との併用投与下の自己免疫性溶血性貧血	全Grade	本剤及びデュルバルマブ（遺伝子組換え）の投与を中止する。	再開しない。
上記以外の副作用	Grade 3又は4の場合	Grade 1以下に回復するまで休薬する。	減量せずに投与する。

注：GradeはNCI-CTCAE ver4.0に準じる。

〈白金系抗悪性腫瘍剤感受性の再発卵巣癌における維持療法、がん化学療法歴のある*BRCA* 遺伝子変異陽性かつHER2陰性の手術不能又は再発乳癌、*BRCA* 遺伝子変異陽性の治癒切除不能な膵癌における白金系抗悪性腫瘍剤を含む化学療法後の維持療法〉

7.3 他の抗悪性腫瘍剤との併用について、有効性及び安全性は確立していない。

〈*BRCA* 遺伝子変異陽性の卵巣癌における初回化学療法後の維持療法〉

7.4 他の抗悪性腫瘍剤との併用について、有効性及び安全性は確立していない。

7.5 本剤の投与開始後2年が経過した時点で完全奏効が得られている患者においては、本剤の投与を中止すること。

〈相同組換え修復欠損を有する卵巣癌におけるベバシズマブ（遺伝子組換え）を含む初回化学療法後の維持療法〉

7.6 本剤の投与開始後2年が経過した時点で完全奏効が得られている患者においては、本剤の投与を中止すること。

7.7 ベバシズマブ（遺伝子組換え）の投与期間等について、「17.臨床成績」の項の内容を熟知し、本剤の有効性及び安全性を十分に理解した上で投与すること。[17.1.4参照]

〈*BRCA* 遺伝子変異陽性かつHER2陰性で再発高リスクの乳癌における術後薬物療法〉

7.8 他の抗悪性腫瘍剤との併用について、有効性及び安全性は確立していない。

7.9 内分泌療法剤との併用の必要性について、「17.臨床成績」の項の内容を熟知し、ホルモン受容体の発現状態等を考慮した上で判断すること。[17.1.6参照]

〈*BRCA* 遺伝子変異陽性の遠隔転移を有する去勢抵抗性前立腺癌〉

*7.10 アビラテロン酢酸エステル又はエンザルタミドによる治療歴のない患者における本剤単独投与の有効性及び安全性は確立して

いない。

7.11 他の抗悪性腫瘍剤との併用について、有効性及び安全性は確立していない。

7.12 外科的又は内科的去勢術と併用しない場合の有効性及び安全性は確立していない。

8. 重要な基本的注意

8.1 骨髄抑制があらわれることがあるので、本剤投与開始前及び投与中は定期的に血液検査を行い、患者の状態を十分に観察すること。[11.1.1参照]

9. 特定の背景を有する患者に関する注意

9.2 腎機能障害患者

減量を考慮するとともに、患者の状態をより慎重に観察し、有害事象の発現に十分注意すること。本剤の血中濃度が上昇するおそれがある。なお、重度の腎機能障害又は末期腎不全(クレアチニンクリアランス(CrCL):30mL/min以下)患者を対象とした有効性及び安全性を指標とした臨床試験は実施していない。[16.6.2参照]

9.3 肝機能障害患者

9.3.1 重度の肝機能障害のある患者

本剤の血中濃度が上昇するおそれがある。また、重度の肝機能障害(Child-Pugh分類C)患者を対象とした有効性及び安全性を指標とした臨床試験は実施していない。[16.6.1参照]

*9.4 生殖能を有する者

9.4.1 妊娠する可能性のある女性には、本剤投与中及び最終投与後6カ月間において避妊する必要性及び適切な避妊法について説明すること。また、妊娠中に本剤を投与するか、本剤投与中の患者が妊娠した場合は、胎児に異常が生じる可能性があることを患者に十分説明すること。[9.5、15.2参照]

9.4.2 男性には、本剤投与中及び最終投与後3カ月間においてバリア法(コンドーム)を用いて避妊する必要性について説明すること。[15.2参照]

9.5 妊婦

妊婦又は妊娠している可能性のある女性には、治療上の有益性が危険性を上回ると判断される場合にのみ投与すること。ラットを用いた動物実験において、臨床曝露量を下回る用量で胚・胎児死亡及び催奇形性(眼球異常、椎骨及び肋骨の欠損等)が報告されている。[9.4.1参照]

9.6 授乳婦

治療上の有益性及び母乳栄養の有益性を考慮し、授乳の継続又は中止を検討すること。本剤の乳汁中への移行は不明である。

9.7 小児等

小児等を対象とした臨床試験は実施していない。

9.8 高齢者

患者の状態を観察しながら慎重に投与すること。一般に高齢者では、生理機能が低下している。

10. 相互作用

本剤は、主にCYP3Aにより代謝される。[16.4参照]

10.2 併用注意(併用に注意すること)

薬剤名等	臨床症状・措置方法	機序・危険因子
強いCYP3A阻害剤 イトラコナゾール リトナビル ボリコナゾール等 中程度のCYP3A阻害剤 シプロフロキサシン ジルチアゼム エリスロマイシン フルコナゾール ベラパミル等 [16.7.1参照]	副作用の発現率及び重症度が増加するおそれがあるので、CYP3A阻害作用のない又は弱い薬剤への代替を考慮すること。やむを得ず中程度又は強いCYP3A阻害剤を併用する際には本剤の減量を考慮するとともに、患者の状態を慎重に観察し、副作用発現に十分注意すること。	これらの薬剤等のCYP3A阻害作用により、本剤の代謝が阻害され、血中濃度が上昇する可能性がある。
グレープフルーツ含有食品	本剤投与時はグレープフルーツ含有食品を摂取しないよう注意すること。	
CYP3A誘導剤 リファンピシン カルバマゼピン フェノバルビタール フェニトイン セイヨウオトギリソウ(St. John's Wort)含有食品等 [16.7.2参照]	本剤の有効性が減弱するおそれがあるので、CYP3A誘導作用のない薬剤への代替を考慮すること。	これらの薬剤等のCYP3A誘導作用により、本剤の代謝活性が誘導されるため、本剤の血中濃度が低下する可能性がある。

11. 副作用

次の副作用があらわれることがあるので、観察を十分に行い、異常が認められた場合には投与を中止するなど適切な処置を行うこと。

11.1 重大な副作用

**11.1.1 骨髄抑制

貧血(30.2%)、好中球減少(13.7%)、白血球減少(12.0%)、リンパ球減少(7.0%)、血小板減少(6.8%)等があらわれることがある。[8.1参照]

**11.1.2 間質性肺疾患(0.7%)

*11.1.3 静脈血栓塞栓症

肺塞栓症(0.4%)、深部静脈血栓症(0.1%)等の静脈血栓塞栓症があらわれることがある。

*11.1.4 感染症

肺炎(0.4%)等の重篤な感染症があらわれることがある。

**11.1.5 赤芽球癆(1.6%)注)

本剤とデュルバルマブ(遺伝子組換え)との併用において、赤芽球癆があらわれることがある。

**11.1.6 溶血性貧血(1.6%)注)

本剤とデュルバルマブ(遺伝子組換え)との併用において、溶血性貧血があらわれることがある。

注)発現頻度は、国際共同第III相試験(DUO-E試験)における、本剤及びデュルバルマブ(遺伝子組換え)併用投与時から集計した。

**11.2 その他の副作用

	10%以上	1%～10%未満	1%未満	頻度不明
皮膚		発疹	過敏症、皮膚炎、結節性紅斑	血管性浮腫
精神神経系		頭痛、浮動性めまい		
呼吸器		咳嗽、呼吸困難		
** 消化器	悪心(47.4%)、嘔吐、下痢、食欲減退、味覚異常	消化不良、腹痛、便秘、口内炎、上腹部痛		
** 全身	疲労・無力症(36.6%)			
その他		クレアチニン増加	平均赤血球容積(MCV)増加	

14. 適用上の注意

14.1 薬剤交付時の注意

PTP包装の薬剤はPTPシートから取り出して服用するよう指導すること。PTPシートの誤飲により、硬い鋭角部が食道粘膜へ刺入し、更には穿孔を起こして縦隔洞炎等の重篤な合併症を併発することが報告されている。

15. その他の注意

15.1 臨床使用に基づく情報

国内外の臨床試験等において、骨髄異形成症候群、急性骨髄性白血病等の二次性悪性腫瘍が発生したとの報告がある。

15.2 非臨床試験に基づく情報

遺伝毒性試験において、細菌を用いる復帰突然変異試験で遺伝子突然変異誘発性は認められなかったが、チャイニーズハムスター卵巣細胞を用いる*in vitro*染色体異常試験では染色体異常誘発作用がみられ、ラット骨髄小核試験で経口投与後に小核誘発作用が

認められた[1]。[9.4.1、9.4.2参照]

16. 薬物動態

16.1 血中濃度

16.1.1 単回投与

日本人固形癌患者(7例)に本剤300mgを単回経口投与したときのオラパリブの血漿中濃度推移及び薬物動態パラメータは以下のとおりであった[2]。

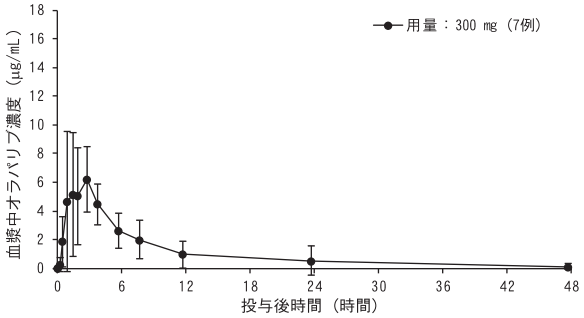


図　日本人固形癌患者に本剤300mgを単回経口投与したときの血漿中オラパリブ濃度推移(算術平均値±標準偏差)

表　日本人固形癌患者に本剤300mgを単回経口投与したときのオラパリブの薬物動態パラメータ(算術平均値±標準偏差)

例数	C_{max}(μg/mL)	t_{max}(h)※	AUC (μg・h/mL)	$t_{1/2}$(h)
7例	8.14±2.91	1.98(1.00～3.00)	54.4±37.5	9.43±2.86

※中央値(範囲)

16.1.2 反復投与

日本人固形癌患者(9例)に本剤200mg[注1)]及び300mgを1日2回反復経口投与したときの第15日目におけるオラパリブの血漿中濃度推移及び薬物動態パラメータは以下のとおりであった。また、300mg投与時における$AUC_{(0\text{-}12時間)}$の累積係数は約1.8であった[2]。

注1)本剤の承認用法・用量は300mgの1日2回投与である。

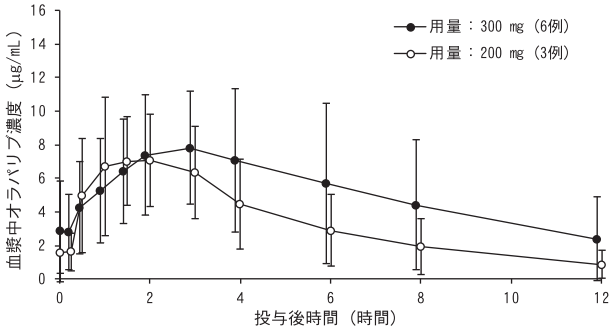


図　日本人固形癌患者に本剤200mg及び300mgを1日2回反復経口投与したときの第15日目における血漿中オラパリブ濃度推移(算術平均値±標準偏差)

表　日本人固形癌患者に本剤200mg及び300mgを1日2回反復経口投与したときの第15日目におけるオラパリブの薬物動態パラメータ(算術平均値±標準偏差)

用量	例数	C_{max}(μg/mL)	t_{max}(h)※	$AUC_{(0\text{-}12時間)}$ (μg・h/mL)
200mg	3例	8.16±3.34	1.50(1.00～3.00)	41.1±20.9
300mg	6例	8.86±3.14	3.00(1.50～3.93)	61.9±40.5

※中央値(範囲)

16.2 吸収

16.2.1 食事の影響

固形癌患者(56例)に本剤300mgを食後投与したとき、空腹時投与と比較して、オラパリブのC_{max}は21%(90%信頼区間：14%～28%)低下し、AUCは8%(90%信頼区間：1%～16%)増加した[3](外国人データ)。

16.3 分布

オラパリブの血漿蛋白結合率はヒトでのC_{max}付近(10μg/mL)で82%であった。オラパリブの主要な結合蛋白は血清アルブミンであり(結合率：56%)、α1-酸性糖蛋白質との結合率は10μg/mLで29%であった[4](*in vitro* 試験成績)。

16.4 代謝

In vitro 試験から、オラパリブの主代謝酵素はCYP3A4/5であることが示された[5]。

固形癌患者に^{14}C標識オラパリブ100mgをカプセル剤[注2)]で単回経口投与したとき、投与12時間後までの血漿中において主成分はオラパリブであった(血漿中放射能の70%)。血漿中の主代謝物はM12(ピペラジン開環体の3位水酸化体)、M15(フルオロベンジル環のメチレン基水酸化体)及びM18(ピペラジン環の3位水酸化体)であった(血漿中放射能の9～14%)。投与48時間後までの尿及び糞便中において主代謝物はM15であった(尿及び糞便中放射能のそれぞれ5～6%)[6](外国人データ)。[10.参照]

注2)カプセル剤は本邦未承認である。

16.5 排泄

固形癌患者に^{14}C標識オラパリブ100mgをカプセル剤[注3)]で単回経口投与したとき、投与後7日間で投与放射能量の44%が尿中に、42%が糞便中に主に代謝物として排泄された。未変化体の尿中排泄率は15%であった[6](外国人データ)。

注3)カプセル剤は本邦未承認である。

16.6 特定の背景を有する患者

16.6.1 肝機能障害のある患者

肝機能の正常な固形癌患者並びに軽度(Child-Pugh分類A)又は中等度(Child-Pugh分類B)の肝機能障害を有する固形癌患者を対象に本剤300mgを単回経口投与した。軽度肝機能障害者(9例)では肝機能正常者(13例)に比べオラパリブのC_{max}は13%(90%信頼区間：-18%～56%)、AUCは15%(-28%～83%)高値を示した。中等度肝機能障害者(8例)では肝機能正常者(13例)に比べオラパリブのC_{max}は13%(90%信頼区間：-22%～37%)低値を示したが、AUCは8%(-34%～74%)高値を示した。軽度及び中等度の肝機能障害により臨床上問題となる影響は認められなかった[7](外国人データ)。[9.3.1参照]

16.6.2 腎機能障害のある患者

腎機能の正常な固形癌患者並びに軽度(CrCL：51～80mL/min)又は中等度(CrCL：31～50mL/min)の腎機能障害を有する固形癌患者を対象に本剤300mgを単回経口投与した。軽度腎機能障害者(13例)では腎機能正常者(12例)に比べオラパリブのC_{max}は15%(90%信頼区間：4%～27%)、AUCは24%(6%～47%)高値を示した。中等度腎機能障害者(13例)では、腎機能正常者(12例)に比べオラパリブのC_{max}は26%(90%信頼区間：6%～48%)、AUCは44%(90%信頼区間：10%～89%)高値を示した[8](外国人データ)。[9.2参照]

16.7 薬物相互作用

16.7.1 イトラコナゾール

固形癌患者(57例)に強いCYP3A阻害剤であるイトラコナゾール200mgを1日1回7日間投与し、投与5日目に本剤100mg[注4)]を併用投与したとき、オラパリブのC_{max}は1.4倍(90%信頼区間：1.3～1.5倍)に増加し、AUCは2.7倍(90%信頼区間：2.4～3.0倍)に増加した[9](外国人データ)。また、生理学的薬物動態モデルによるシミュレーションから、本剤100mgと弱いCYP3A阻害剤であるフルボキサミンとの併用ではオラパリブのC_{max}及び$AUC_{(0\text{-}t)}$に影響はないと推定されたものの、中程度のCYP3A阻害剤であるフルコナゾールとの併用ではオラパリブのC_{max}及び$AUC_{(0\text{-}t)}$はそれぞれ平均1.14倍及び2.21倍増加すると推定された[10]。[10.2参照]

注4)本剤の承認用法・用量は300mgの1日2回投与である。

16.7.2 リファンピシン

固形癌患者(22例)に強いCYP3A誘導剤であるリファンピシン600mgを1日1回13日間投与し、投与10日目に本剤300mgを併用投与したとき、オラパリブのC_{max}は71%(90%信頼区間：67%～76%)、AUCは87%(90%信頼区間：84%～89%)低下した[9](外国人データ)。[10.2参照]

16.7.3 その他

オラパリブはCYP3Aに対し阻害作用を示し[10]、CYP2B6に対し誘導作用を示した[11](*in vitro* 試験成績)。

オラパリブはUDPグルクロン酸転移酵素(UGT)1A1に対し阻害作用を示した[12](*in vitro* 試験成績)。

固形癌患者(76例)を対象に、本剤300mgとタモキシフェン(20mg1日1回)、アナストロゾール(1mg1日1回)又はレトロゾール(2.5mg1日1回)との併用投与を行ったところ(例数はそれぞれ29例、22例及び25例)、臨床上問題となる相互作用は認められなかった[13](外国人データ)。

オラパリブはP-糖蛋白質(P-gp)の基質であった[14]。また、オラパリブはP-gp、OATP1B1、OCT1及びMATE1を阻害した[15](*in vitro* 試験成績)。

***17. 臨床成績

17.1 有効性及び安全性に関する試験

〈白金系抗悪性腫瘍剤感受性の再発卵巣癌における維持療法〉

17.1.1 国際共同第III相試験(SOLO2試験)[16]

BRCA 遺伝子変異陽性で、白金系抗悪性腫瘍剤を含む化学療法による少なくとも2回以上の治療歴があり、白金系抗悪性腫瘍剤感受性[注1)]かつ直近の白金系抗悪性腫瘍剤を含む化学療法で奏効(画像診断による完全奏効又は部分奏効)が維持されている再発高異型度漿液性卵巣癌(原発性腹膜癌及び卵管癌を含む)又は再発高異型度類内膜卵巣癌患者295例(本剤群196例、プラセボ群99例、うち日本人は本剤群8例、プラセボ群6例)を対象として、本剤(錠剤)300mg1日2回投与の有効性及び安全性をプラセボと比較する無作為化二重盲検プラセボ対照多施設共同第III相試験を実施した。主要評価項目である治験担当医師判定による無増悪生存期間において、本剤はプラセボに対し統計学的に有意な延長を示した(ハザード比0.30、95%信頼区間0.22～0.41、p<0.0001)。無増悪生存期間の中央値は本剤群で19.1カ月、プラセボ群で5.5カ月であった。(2016年9月19日データカットオフ)

注1)PFI(platinum free interval)が6カ月以上であること。

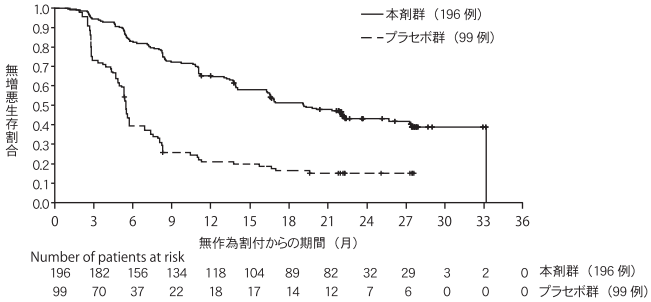


図　SOLO2試験：無増悪生存期間のKaplan-Meier曲線(最大解析対象集団、治験担当医師による評価)

本剤が投与された195例(日本人8例を含む)中192例(98.5%)に有害事象が認められ、主な有害事象は、悪心148例(75.9%)、貧血84例(43.1%)、疲労74例(37.9%)、嘔吐73例(37.4%)、下痢64例(32.8%)、無力症61例(31.3%)であった。(2016年9月19日データカットオフ)

17.1.2 海外第II相試験(D0810C00019試験)[17]

白金系抗悪性腫瘍剤を含む化学療法による少なくとも2回以上の治療歴があり、白金系抗悪性腫瘍剤感受性[注2)]かつ直近の白金系抗悪性腫瘍剤を含む化学療法で奏効(画像診断による完全奏効又は部分奏効)が維持されている再発漿液性卵巣癌(原発性腹膜癌及び卵管

癌を含む）患者265例（本剤群136例、プラセボ群129例）を対象として、本剤（カプセル剤）400mg[注3)]1日2回投与の有効性及び安全性をプラセボと比較する無作為化二重盲検プラセボ対照多施設共同第II相試験を実施した。主要評価項目である治験担当医師判定による無増悪生存期間において、プラセボに対する本剤の優越性の評価で事前に設定した有効性判断基準を満たした（ハザード比0.35、95%信頼区間0.25～0.49、p<0.00001［両側］）。無増悪生存期間の中央値は本剤群で8.4カ月、プラセボ群で4.8カ月であった。（2010年6月30日データカットオフ）

注2）PFI（platinum free interval）が6カ月以上であること。

注3）本剤の承認用法・用量は錠剤300mgの1日2回投与である。

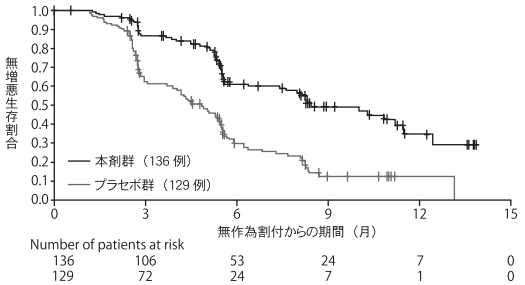


図　D0810C00019試験：無増悪生存期間のKaplan-Meier曲線（最大解析対象集団、治験担当医師による評価）

本剤が投与された136例中132例（97.1%）に有害事象が認められ、主な有害事象は、悪心96例（70.6%）、疲労73例（53.7%）、嘔吐48例（35.3%）であった。（2016年5月9日データカットオフ）

〈*BRCA* 遺伝子変異陽性の卵巣癌における初回化学療法後の維持療法〉

17.1.3 国際共同第III相試験（SOLO1試験）[18)]

BRCA 遺伝子変異陽性（病的変異又は病的変異疑い）で、新たに進行卵巣癌（FIGO進行期分類III期又はIV期）であると診断され、白金系抗悪性腫瘍剤を含む初回化学療法[注4)]で奏効（画像診断による完全奏効又は部分奏効）が維持されている高異型度漿液性又は高異型度類内膜卵巣癌（原発性腹膜癌及び卵管癌を含む）患者391例（本剤群260例、プラセボ群131例、うち日本人は本剤群11例、プラセボ群3例）を対象として、本剤（錠剤）300mg1日2回投与[注5)]の有効性及び安全性をプラセボと比較する無作為化二重盲検プラセボ対照多施設共同第III相試験を実施した。主要評価項目である治験担当医師判定による無増悪生存期間において、本剤はプラセボに対し統計学的に有意な延長を示した（ハザード比0.30、95%信頼区間0.23～0.41、p<0.0001［両側］）。無増悪生存期間の中央値は本剤群では未到達、プラセボ群で13.8カ月であった。（2018年5月17日データカットオフ）

注4）初回化学療法との併用又は初回化学療法後の維持療法としてベバシズマブ（遺伝子組換え）の投与を受けた患者は除外した。

注5）最長2年間又は原疾患の病勢進行が認められるまで投与した。投与開始2年後の時点で完全奏効（画像診断で病変なし）が維持されている場合は投与を中止し、投与開始2年後の時点で病変が確認され、治験担当医師が治療継続によりさらなるベネフィットが期待できると判断する場合は2年後以降も投与継続可能とした。

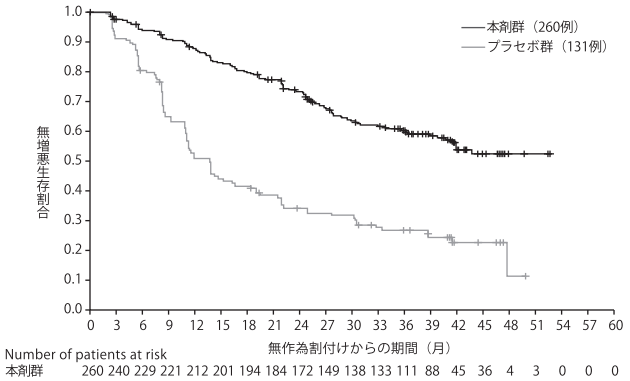


図　SOLO1試験：無増悪生存期間のKaplan-Meier曲線（最大解析対象集団、治験担当医師による評価）

本剤が投与された260例（日本人11例を含む）中256例（98.5%）に有害事象が認められ、主な有害事象は、悪心201例（77.3%）、疲労106例（40.8%）、嘔吐104例（40.0%）、貧血99例（38.1%）、下痢89例（34.2%）であった。（2018年5月17日データカットオフ）

〈相同組換え修復欠損を有する卵巣癌におけるベバシズマブ（遺伝子組換え）を含む初回化学療法後の維持療法〉

17.1.4 国際共同第III相試験（PAOLA-1試験）[19)]

新たに進行卵巣癌（FIGO進行期分類III期又はIV期）であると診断され、白金系抗悪性腫瘍剤、タキサン系抗悪性腫瘍剤及びベバシズマブによる初回化学療法[注6)]で奏効（画像診断による無病状態、完全奏効又は部分奏効）が維持されている高異型度漿液性又は類内膜卵巣癌（原発性腹膜癌及び卵管癌を含む）患者806例（本剤/ベバシズマブ群537例、プラセボ/ベバシズマブ群269例、うち日本人は本剤/ベバシズマブ群15例、プラセボ/ベバシズマブ群9例）を対象として、本剤（錠剤）300mg1日2回及びベバシズマブ併用投与[注7)]の有効性及び安全性をプラセボ及びベバシズマブ併用投与と比較する無作為化二重盲検プラセボ対照多施設共同第III相試験を実施した。主要評価項目である治験担当医師判定による無増悪生存期間において、本剤/ベバシズマブ群はプラセボ/ベバシズマブ群に対し統計学的に有意な延長を示した（ハザード比0.59、95%信頼区間0.49～0.72、p<0.0001［両側］）。（2019年3月22日データカットオフ）

また、腫瘍検体が入手可能であった755例のうち664例において相同組換え修復欠損に関する検査結果が得られ、探索的に実施された陽性・陰性[注8)]別の解析結果は下表のとおりであった。

注6）白金系抗悪性腫瘍剤とタキサン系抗悪性腫瘍剤との併用投与が6～9サイクル行われ、少なくとも最後の3サイクルはベバシズマブも併用投与された患者を対象とした。

注7）最長2年間又は原疾患の病勢進行が認められるまで投与した。治験担当医師が治療継続によりさらなるベネフィットが期待できると判断する場合は2年後以降も投与継続可能とした。ベバシズマブは、無作為化前と無作為化後の合計で15カ月間まで投与可能とした。

注8）Myriad社の「Myriad myChoice HRD CDx」を用いた検査により、ゲノム不安定性スコア（GIS）が42以上、又は*BRCA* 遺伝子変異陽性の場合に陽性と判定した。

表　PAOLA-1試験：相同組換え修復欠損陽性・陰性別の無増悪生存期間（相同組換え修復欠損に関する検査結果を有する患者集団、治験担当医師による評価）

相同組換え修復欠損	投与群	例数	中央値（カ月）［95%信頼区間］	ハザード比［95%信頼区間］※
陽性	本剤/ベバシズマブ群	255	37.2［36.0, －］	0.33［0.25, 0.45］
	プラセボ/ベバシズマブ群	132	17.7［15.8, 19.9］	
陰性	本剤/ベバシズマブ群	192	16.6［14.9, 18.0］	1.00［0.75, 1.35］
	プラセボ/ベバシズマブ群	85	16.2［13.8, 18.6］	

－：推定不可、※：投与群、相同組換え修復欠損（陽性・陰性）、投与群と相同組換え修復欠損の交互作用項を含めたCox比例ハザードモデルにより算出

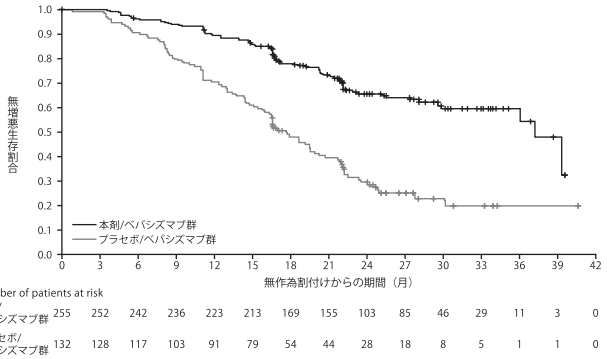


図　PAOLA-1試験：無増悪生存期間のKaplan-Meier曲線（相同組換え修復欠損陽性集団、治験担当医師による評価）

本剤が投与された535例（日本人15例を含む）中531例（99.3%）に有害事象が認められ、主な有害事象は、悪心285例（53.3%）、疲労283例（52.9%）、高血圧245例（45.8%）、貧血219例（40.9%）であった。（2019年3月22日データカットオフ）

〈がん化学療法歴のある*BRCA* 遺伝子変異陽性かつHER2陰性の手術不能又は再発乳癌〉

17.1.5 国際共同第III相試験（OlympiAD試験）[20)]

生殖細胞系列の*BRCA* 遺伝子変異（病的変異又は病的変異疑い）陽性かつHER2陰性であり、アントラサイクリン系抗悪性腫瘍剤（禁忌でない場合）及びタキサン系抗悪性腫瘍剤による治療歴を有する手術不能又は再発乳癌患者302例（本剤群205例、化学療法群97例、うち日本人は本剤群15例、化学療法群9例）を対象として、本剤300mg1日2回投与の有効性及び安全性を、医師が選択した化学療法（カペシタビン、エリブリン、又はビノレルビンのいずれかを選択）と比較する非盲検無作為化多施設共同第III相試験を実施した。主要評価項目である盲検下での独立中央評価に基づく無増悪生存期間において、本剤は医師が選択した化学療法に対し統計学的に有意な延長を示した（ハザード比0.58、95%信頼区間0.43～0.80、p=0.0009［両側］）。無増悪生存期間の中央値は本剤群で7.0カ月、化学療法群で4.2カ月であった。（2016年12月9日データカットオフ）

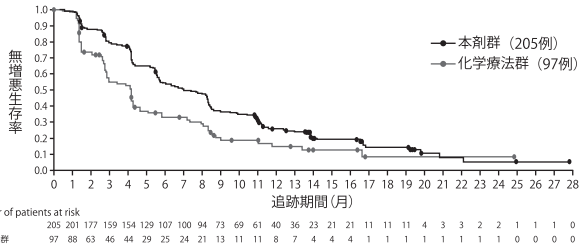


図　無増悪生存期間のKaplan-Meier曲線（OlympiAD試験：最大解析対象集団、盲検下での独立中央評価）

本剤が投与された205例（日本人15例を含む）中200例（97.6%）に有害事象が認められ、主な有害事象は、悪心119例（58.0%）、貧血81例（39.5%）、嘔吐66例（32.2%）であった。（2017年9月25日データカットオフ）

〈*BRCA* 遺伝子変異陽性かつHER2陰性で再発高リスクの乳癌における術後薬物療法〉

17.1.6 国際共同第III相試験（OlympiA試験）[21)]

術前又は術後化学療法[注9)]歴のある生殖細胞系列の*BRCA* 遺伝子変異（病的変異又は病的変異疑い）陽性かつHER2陰性で再発高リスク[注10)]の乳癌患者[注11)]1,836例（本剤群921例、プラセボ群915例、うち日本人は本剤群64例、プラセボ群76例）を対象として、本剤（錠剤）300mg1日2回投与の術後薬物療法としての有効性及び安全性を、プラセボと比較する無作為化二重盲検多施設共同第III相試験を実施した。本剤又はプラセボは最長1年間、又は疾患の再発若しくは許容できない毒性が認められるまで投与された。また、エストロゲン受容体（ER）及び／又はプロゲステロン受容体（PgR）陽性患者の場合、診療ガイドラインに従い、内分泌療法が併用された。主要評価項目である治験担当医師判定による浸潤性疾患のない生存期間（IDFS）において、本剤はプラセボに対して統計学的に有意な延長を示した（ハザード比0.581、95%信頼区間0.455～0.737、p=0.0000073）。2年IDFS率は本剤群で89.2%、プラセボ群で81.5%であった。（2020年3月27日データカットオフ）

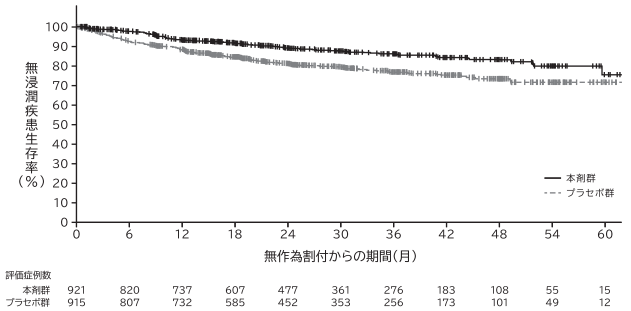


図　浸潤性疾患のない生存期間のKaplan-Meier曲線（OlympiA試験：最大解析対象集団、治験担当医師による評価）

本剤が投与された911例（日本人64例を含む）中836例（91.8%）に有害事象が認められ、主な有害事象は、悪心519例（57.0%）、疲労366例（40.2%）、貧血215例（23.6%）、嘔吐206例（22.6%）であった。（2021年7月12日データカットオフ）

注9）アントラサイクリン系抗悪性腫瘍剤若しくはタキサン系抗悪性腫瘍剤、又はその両剤を含む術前又は術後化学療法が少なくとも6サイクル実施された患者が対象とされた。

注10）以下の①又は②に該当する患者が再発高リスクの患者と定義された。

① 術前化学療法歴のある場合

- 乳房及び／又は切除リンパ節に残存浸潤性乳癌があるER及びPgR陰性かつHER2陰性乳癌患者（トリプルネガティブ乳癌患者）。
- 乳房及び／又は切除リンパ節に残存浸潤性乳癌があり、CPS+EGスコア（臨床病期[CS]、ERの発現状態[E]、核グレード[G]及び治療後の病理学的病期[PS]－疾患スコア評価システム）が3以上であるER及び／又はPgR陽性かつHER2陰性乳癌患者。

② 術後化学療法歴のある場合

- 腋窩リンパ節転移陽性（≧pN1、腫瘍径は問わない）又は腋窩リンパ節転移陰性（pN0）であるが浸潤性原発腫瘍の病理学的サイズが2cmを超える（≧pT2）トリプルネガティブ乳癌患者。
- 病理学的に確認した陽性リンパ節が4個以上あるER及び／又はPgR陽性かつHER2陰性乳癌患者。

注11）以下に該当する患者が対象とされた。

- 乳房温存手術が施行された場合には、乳房に対する放射線療法が実施された患者。
- 腋窩のセンチネルリンパ節転移陽性の場合には、腋窩リンパ節郭清術又は腋窩への放射線療法が実施された患者。
- 放射線療法が実施された場合には、放射線療法終了後の患者。

〈*BRCA* 遺伝子変異陽性の遠隔転移を有する去勢抵抗性前立腺癌〉

17.1.7 国際共同第III相試験（PROfound試験）[22)]

アビラテロン若しくはエンザルタミド又はその両剤の治療歴のある相同組換え修復関連遺伝子変異陽性[注12)]の遠隔転移を有する去勢抵抗性前立腺癌患者387例（本剤群256例、対照群131例、うち日本人は本剤群34例、対照群23例）を対象として、本剤（錠剤）300mg1日2回投与の有効性及び安全性を、治験担当医師が選択した治療（エンザルタミド又はアビラテロン酢酸エステル）と比較する無作為化非盲検多施設共同第III相試験を実施した。なお、両側精巣摘除術を受けていない患者は、性腺刺激ホルモン放出ホルモン（GnRH）アゴニスト又はアンタゴニスト療法が継続された。主要評価項目であるコホートAにおける盲検下での独立中央評価による画像診断に基づく無増悪生存期間において、本剤群は、対照群に対し統計学的に有意な延長を示した（ハザード比0.34、95%信頼区間0.25～0.47、p<0.0001［両側］）。（2019年6月4日データカットオフ）

また、探索的に実施された*BRCA1*、*BRCA2*、*ATM* 遺伝子変異別（該当する遺伝子変異のみが認められた患者集団）及び*BRCA* 遺伝子変異陽性集団（少なくとも*BRCA1* 又は*BRCA2* 遺伝子変異が認められた患者集団）の解析結果はそれぞれ下表①及び②のとおりであった。

注12）コホートAでは*BRCA1*、*BRCA2* 又は*ATM* 遺伝子に変異を有する患者、コホートBでは*BARD1*、*BRIP1*、*CDK12*、*CHEK1*、*CHEK2*、*FANCL*、*PALB2*、*PPP2R2A*、*RAD51B*、*RAD51C*、*RAD51D*、又は*RAD54L* に変異を有する患者を対象とした。

表①　PROfound試験：*BRCA1*、*BRCA2*、*ATM* 遺伝子変異別の画像診断に基づく無増悪生存期間（単一の相同組換え修復関連遺伝子変異を有する患者集団、盲検下での独立中央評価）

遺伝子変異	本剤群		対照群		ハザード比[95%信頼区間]※
	例数	中央値（カ月）[95%信頼区間]	例数	中央値（カ月）[95%信頼区間]	
BRCA1	8	2.07 [1.38, 5.52]	5	1.84 [1.71, 3.71]	0.41 [0.13, 1.39]
BRCA2	81	10.84 [9.17, 13.08]	47	3.48 [1.74, 3.65]	0.21 [0.13, 0.32]
ATM	62	5.36 [3.61, 6.21]	24	4.70 [1.84, 7.26]	1.04 [0.61, 1.87]

※：投与群、各遺伝子変異（あり・なし）、投与群と各遺伝子変異の交互作用項を含めたCox比例ハザードモデルにより算出

表②　PROfound試験：*BRCA* 遺伝子変異陽性集団における画像診断に基づく無増悪生存期間（最大解析対象集団、盲検下での独立中央評価）

	本剤群	対照群
例数	102	58
イベント数（%）	62（60.8）	51（87.9）
中央値（カ月）[95%信頼区間]	9.79[7.62, 11.30]	2.96[1.81, 3.55]
ハザード比[95%信頼区間]※	0.22[0.15, 0.32]	

※：投与群、*BRCA* 遺伝子変異（陽性・陰性）、投与群と*BRCA* 遺伝子変異の交互作用項を含めたCox比例ハザードモデルにより算出

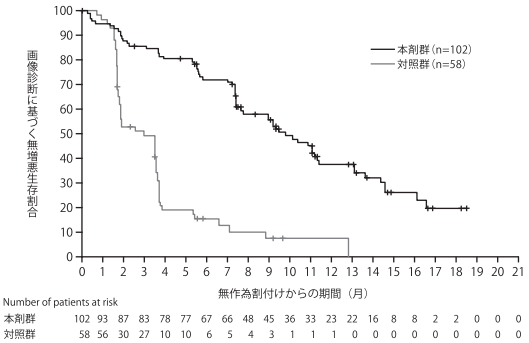


図　PROfound試験：画像診断に基づく無増悪生存期間のKaplan-Meier曲線（*BRCA* 遺伝子変異陽性集団、盲検下での独立中央評価）

本剤が投与された256例（日本人34例を含む）中244例（95.3%）に有害事象が認められ、主な有害事象は、貧血118例（46.1%）、悪心106例（41.4%）、食欲減退77例（30.1%）であった。（2019年6月4日データカットオフ）

∗17.1.8 国際共同第III相試験（PROpel試験）[23)]

遠隔転移を有する去勢抵抗性前立腺癌（mCRPC）に対する薬物療法歴のない[注13)] mCRPC患者796例（本剤群399例、対照群397例、うち日本人は本剤群36例、対照群41例）を対象として、本剤300mg1日2回とアビラテロン酢酸エステル1000mg1日1回[注14)]併用投与の有効性及び安全性を、プラセボ1日2回とアビラテロン酢酸エステル1000mg1日1回併用投与と比較する無作為化二重盲検プラセボ対照多施設共同第III相試験を実施した。なお、両側精巣摘除術を受けていない患者は、性腺刺激ホルモン放出ホルモン（GnRH）アゴニスト又はアンタゴニスト療法が継続された。主要評価項目である治験担当医師の評価による画像診断に基づく無増悪生存期間（rPFS）において、本剤群は、プラセボ群に対して統計学的に有意な延長を示した（ハザード比0.66、95%信頼区間0.54～0.81、p<0.0001［両側］）。rPFSの中央値は本剤群で24.8カ月、プラセボ群で16.6カ月であった。（2021年7月30日データカットオフ）

また、探索的に実施された*BRCA* 遺伝子（*BRCA1* 又は*BRCA2* 遺伝子）変異の有無別のrPFS及び全生存期間（OS）の解析結果はそれぞれ下表のとおりであった。（2021年7月30日データカットオフ）

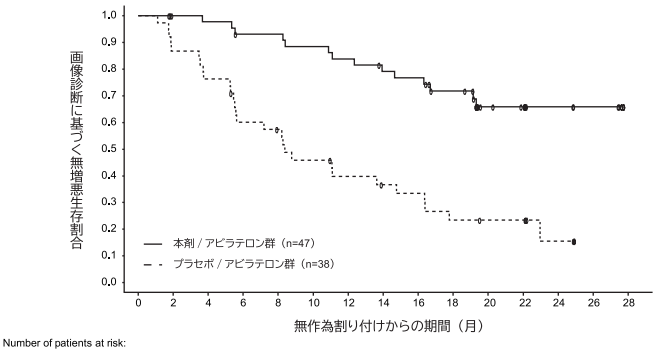
注13）無作為割付け4週間前までのビカルタミド、フルタミド等の抗アンドロゲン剤の使用は許容された。また、mCRPCとなる前のエンザルタミド、アパルタミド、又はダロルタミドの使用については、それらの治療中に病勢進行がなく、無作為割付け12カ月間以上前に投与が終了している場合に限り許容された。限局性前立腺癌に対する術前・術後薬物療法中及び遠隔転移を有するホルモン感受性前立腺癌におけるドセタキセルの使用は、それらの治療中又は治療直後に治療無効又は病勢進行の徴候が認められていなければ許容された。

注14）アビラテロン酢酸エステルは、プレドニゾロン又はprednisone（国内未承認）（いずれも5mg1日2回経口投与）と併用された。

表　PROpel試験：*BRCA* 遺伝子変異の有無別のrPFS（治験担当医師による評価）及びOS

	遺伝子変異	投与群	例数	中央値（カ月）[95%信頼区間]	ハザード比※1[95%信頼区間]
rPFS	*BRCA* 陽性※2	本剤群	47	－[－, －]	0.23 [0.12, 0.43]
		プラセボ群	38	8.4[5.5, 14.8]	
	BRCA 陰性※3	本剤群	214	21.9[16.6, 25.2]	0.86 [0.66, 1.12]
		プラセボ群	213	16.7[13.8, 19.4]	
OS	*BRCA* 陽性※2	本剤群	47	－[－, －]	0.39 [0.16, 0.86]
		プラセボ群	38	23.6[17.8, －]	
	BRCA 陰性※3	本剤群	214	－[－, －]	1.10 [0.78, 1.57]
		プラセボ群	213	－[－, －]	

－：推定不可、※1：投与群、*BRCA* 遺伝子変異の有無、投与群と*BRCA* 遺伝子変異の有無との交互作用項を含めた非層別Cox比例ハザードモデルにより算出、※2：腫瘍組織検体又は血漿検体の少なくとも一方において*BRCA* 遺伝子変異陽性の患者、※3：腫瘍組織検体及び血漿検体の両方において*BRCA* 遺伝子変異陰性の患者



Number of patients at risk:

本剤 / アピラテロン群	47	44	43	40	40	38	36	33	32	27	16	14	7	5	0
プラセボ / アピラテロン群	38	33	29	22	20	16	13	11	10	7	6	6	2	0	0

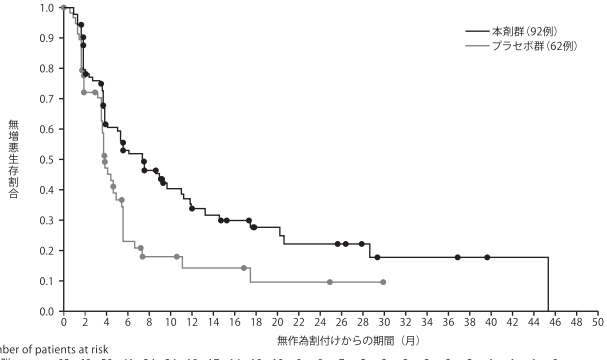
図　PROpel試験：rPFSのKaplan-Meier 曲線（腫瘍組織検体又は血漿検体の少なくとも一方における*BRCA* 遺伝子変異陽性集団、治験担当医師による評価）

本剤が投与された398例（日本人36例を含む）中387例（97.2%）に有害事象が認められ、主な有害事象は、貧血181例（45.5%）、悪心112例（28.1%）、疲労111例（27.9%）であった。（2021年7月30日データカットオフ）

〈*BRCA* 遺伝子変異陽性の治癒切除不能な膵癌における白金系抗悪性腫瘍剤を含む化学療法後の維持療法〉

17.1.9 海外第III相試験（POLO試験）[24)]

生殖細胞系列の*BRCA* 遺伝子変異陽性（病的変異又は病的変異疑い）で、白金系抗悪性腫瘍剤を含む一次化学療法が16週間以上継続された後、疾患進行が認められていない遠隔転移を有する膵腺癌患者154例（本剤群92例、プラセボ群62例）を対象として、本剤（錠剤）300mg1日2回投与の維持療法における有効性及び安全性をプラセボと比較する無作為化二重盲検プラセボ対照多施設共同第III相試験を実施した。主要評価項目である盲検下での独立中央評価による無増悪生存期間において、本剤はプラセボと比較して統計学的に有意な延長を示した（ハザード比0.53、95%信頼区間0.35～0.82、p=0.0038［両側］、中央値：本剤群7.4カ月、プラセボ群3.8カ月）。（2019年1月15日データカットオフ）



Number of patients at risk

本剤群	92	69	50	41	34	24	18	17	14	10	10	8	8	7	5	3	3	3	3	2	1	1	1	0
プラセボ群	62	39	23	10	6	6	4	4	4	2	2	2	2	1	1	0								

図　POLO試験：無増悪生存期間のKaplan-Meier曲線（最大解析対象集団、盲検下での独立中央評価）

本剤が投与された91例中87例（95.6%）に有害事象が認められ、主な有害事象は、疲労41例（45.1%）、悪心41例（45.1%）であった。（2019年1月15日データカットオフ）

〈ミスマッチ修復機能正常（pMMR）の進行・再発の子宮体癌におけるデュルバルマブ（遺伝子組換え）を含む化学療法後の維持療法〉

****17.1.10 国際共同第III相試験（DUO-E試験）[25)]**

化学療法歴のない[注15)]進行・再発[注16)]の子宮体癌患者[注17)]718例（①本剤/デュルバルマブ/化学療法群[注18)]239例、②デュルバルマブ/化学療法群[注18)]238例、③化学療法群[注18)]241例、うち、日本人はそれぞれ①26例、②30例、③32例）を対象として、上記①及び②の有効性及び安全性を、③と比較する無作為化二重盲検プラセボ対照多施設共同第III相試験を実施した。

主要評価項目である治験担当医師判定による無増悪生存期間において、本剤/デュルバルマブ/化学療法群及びデュルバルマブ/化学療法群は化学療法群に対して統計学的に有意な延長を示した（①化学療法群に対する本剤/デュルバルマブ/化学療法群のハザード比0.55、95%信頼区間0.43～0.69、p<0.0001［両側］、中央値：本剤/デュルバルマブ/化学療法群15.1カ月、化学療法群9.6カ月、②化学療法群に対するデュルバルマブ/化学療法群のハザード比0.71、95%信頼区間0.57～0.89、p=0.003［両側］、中央値：デュルバルマブ/化学療法群10.2カ月、化学療法群9.6カ月）。（2023年4月12日データカットオフ）

pMMRの患者集団及びミスマッチ修復機能欠損（dMMR）の患者集団における無増悪生存期間はそれぞれ下表のとおりであった。

注15）術前又は術後の補助療法として抗悪性腫瘍剤が投与された場合には、抗悪性腫瘍剤の最終投与日から再発までの期間が12カ月間以上の患者が対象とされた。

注16）以下のいずれかに該当する患者が対象とされた。

- International Federation of Gynecology and Obstetrics（FIGO）分類（2009年版）III期のうち、手術又は生検後にRECIST ver.1.1に基づく測定可能病変が認められた患者
- FIGO分類（2009年版）IV期の患者（手術又は生検後の残存病変の有無は問わない）
- 手術を含む治療により根治する可能性が低い再発の患者

注17）組織型は問わず、病理組織学的に上皮性子宮体癌と診断された患者が対象とされた（癌肉腫は組入れ可能とされ、子宮肉腫は組入れ不可とされた）。

注18）用法・用量は以下のとおりとされた。

投与群	化学療法併用期	維持療法期
本剤/デュルバルマブ/化学療法群	CBDCA及びPTX†1,2との併用で、デュルバルマブ1120mgをQ3Wで静脈内投与†3	・デュルバルマブ1500mgをQ4Wで静脈内投与 ・本剤300mgをBID経口投与
デュルバルマブ/化学療法群	CBDCA及びPTX†1,2との併用で、デュルバルマブ1120mgをQ3Wで静脈内投与†3	・デュルバルマブ1500mgをQ4Wで静脈内投与 ・本剤のプラセボをBID経口投与
化学療法群	CBDCA及びPTX†1,2との併用で、デュルバルマブのプラセボをQ3Wで静脈内投与†3	・デュルバルマブのプラセボをQ4Wで静脈内投与 ・本剤のプラセボをBID経口投与

BID：1日2回、CBDCA：カルボプラチン、PTX：パクリタキセル、Q3W：3週間間隔、Q4W：4週間間隔、†1：CBDCA AUC5又は6mg・min/mL相当量及びPTX 175mg/m^{2}をQ3Wで静脈内投与、†2：CBDCA/PTX投与による過敏症反応が発現した場合等には、①CBDCA及び②PTXをそれぞれ①シスプラチン及び②パクリタキセル（アルブミン懸濁型）又はドセタキセル水和物に変更することが可能とされた、†3：最大6回投与

表　pMMRの患者集団における無増悪生存期間（治験担当医師判定、RECIST ver.1.1、2023年4月12日データカットオフ）

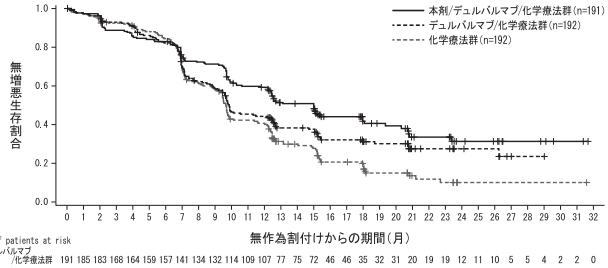
	本剤/デュルバルマブ/化学療法群	デュルバルマブ/化学療法群	化学療法群
例数	191	192	192
中央値［95%信頼区間］（カ月）	15.0［12.4, 18.0］	9.9［9.4, 12.5］	9.7［9.2, 10.1］
ハザード比［95%信頼区間］*1, *3	0.57［0.44, 0.73］	0.77［0.60, 0.97］	該当なし
ハザード比［95%信頼区間］*2, *3	0.76［0.59, 0.99］	該当なし	該当なし

*1：化学療法群との比較、*2：デュルバルマブ/化学療法群との比較、*3：非層別Cox比例ハザードモデルにより算出

表　dMMRの患者集団における無増悪生存期間（治験担当医師判定、RECIST ver.1.1、2023年4月12日データカットオフ）

	本剤/デュルバルマブ/化学療法群	デュルバルマブ/化学療法群	化学療法群
例数	48	46	49
中央値［95%信頼区間］（カ月）	31.8［12.4, 未達］	未達［未達, 未達］	7.0［6.7, 14.8］
ハザード比［95%信頼区間］*1, *3	0.41［0.21, 0.75］	0.42［0.22, 0.80］	該当なし
ハザード比［95%信頼区間］*2, *3	0.97［0.49, 1.98］	該当なし	該当なし

*1：化学療法群との比較、*2：デュルバルマブ/化学療法群との比較、*3：非層別Cox比例ハザードモデルにより算出



Number of patients at risk

本剤/デュルバルマブ/化学療法群	191	185	183	168	164	159	157	141	134	132	114	109	107	77	75	72	46	46	35	32	31	20	19	19	12	11	10	5	5	4	2	2	0
デュルバルマブ/化学療法群	192	186	182	174	169	159	152	128	113	107	83	81	79	53	53	50	36	36	31	27	27	17	15	15	8	7	7	3	2	2	0	0	0
化学療法群	192	184	178	172	170	163	156	126	113	108	77	76	73	44	40	37	25	25	21	13	13	8	7	6	1	1	1	1	1	1	1	1	0

図　DUO-E試験：無増悪生存期間のKaplan-Meier曲線（pMMRの患者集団、治験担当医師判定）

本剤が投与された192例（日本人20例を含む）中184例（95.8%）に有害事象が認められ、主な有害事象は、悪心79例（41.1%）、貧血70例（36.5%）、疲労43例（22.4%）及び嘔吐39例（20.3%）であった。（2023年4月12日データカットオフ）

18. 薬効薬理

18.1 作用機序

18.1.1 PARP阻害活性

オラパリブは、ヒトPARP-1及びPARP-2に対して阻害作用を示した（各IC_{50}値：5及び1nmol/L）[26)]。

18.1.2 腫瘍増殖抑制作用

オラパリブは、ヒト卵巣癌由来細胞株（59M、OVCAR-3、IGROV-1等）及びヒト乳癌由来細胞株（MDA-MB-436、HCC1395、SUM1315MO2等）の増殖を抑制し[27)]、ヒト乳癌患者由来HBCx-10腫瘍組織片を皮下移植したマウスにおいて、腫瘍の増殖を抑制した[28)]。

19. 有効成分に関する理化学的知見

一般的名称

オラパリブ（Olaparib）（JAN）

化学名

4-[(3-{[4-(Cyclopropylcarbonyl)piperazin-1-yl]carbonyl}-4-fluorophenyl)methyl]phthalazin-1(2*H*)-one

分子式

$C_{24}H_{23}FN_4O_3$

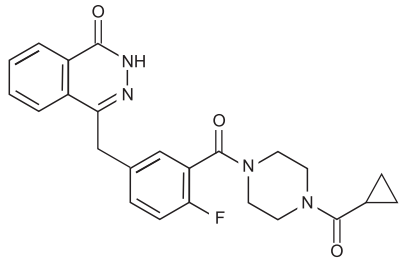
分子量

434.46

性状

本品は白色～微黄色の粉末である。

化学構造式



20. 取扱い上の注意

防湿のためPTP包装のまま保存すること。

21. 承認条件

医薬品リスク管理計画を策定の上、適切に実施すること。

22. 包装

〈リムパーザ錠100mg〉

56錠[8錠(PTP)×7]

〈リムパーザ錠150mg〉

56錠[8錠(PTP)×7]

***23. 主要文献

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3)Ruth Plummer R, et al. Cancer Chemother Pharmacol. 2015;76(4):723-729.
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5)社内資料(代謝に関与する代謝酵素[*in vitro* 試験], 2010)(2018年1月19日承認、CTD2.6.4.5.3)
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11)社内資料(CYPに対する誘導作用[*in vitro* 試験], 2015)(2018年1月19日承認、CTD2.7.2.3.3.2.2、2.7.2.2.3.1)
12)社内資料(UGTに対する阻害作用[*in vitro* 試験], 2019)(2020年12月25日承認、CTD2.6.4.7.1、2.6.5.15.1)
13)社内資料(内分泌療法剤の相互作用, 2015)(2018年1月19日承認、CTD2.7.2.2.2.10、2.7.6.2.6.2.3)
14)社内資料(P-糖蛋白質の関与, 2007)(2018年1月19日承認、CTD2.7.2.4.2.4.1)
15)社内資料(トランスポーターに対する阻害作用, 2014)(2018年1月19日承認、CTD2.7.2.3.3.2.2)
16)Pujade-Lauraine E, et al. Lancet Oncol. 2017;18:1274-1284.
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18)Moore K, et al. N Engl J Med. 2018;379:2495-2505.
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28)社内資料(HBCx-10腫瘍移植モデルにおけるオラパリブのPK、PD及び有効性の評価[*in vivo* 試験], 2016)(2018年1月19日承認、CTD2.6.2.2.5)

24. 文献請求先・製品情報お問い合わせ先

アストラゼネカ株式会社　メディカルインフォメーションセンター
〒530-0011　大阪市北区大深町3番1号
TEL 0120-189-115
https://www.astrazeneca.co.jp

26. 製造販売業者等

26.1 製造販売元

アストラゼネカ株式会社
大阪市北区大深町3番1号

26.2 プロモーション提携

ＭＳＤ株式会社
東京都千代田区九段北1-13-12

Ⓡ:アストラゼネカグループの登録商標です。
Ⓒ AstraZeneca 2018

AstraZeneca

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20XX年X月作成（第１版）

日本標準商品分類番号
874291

貯法：室温保存、凍結を避ける
有効期間：製造日時より120時間

承認番号	XXXXXXXXX
販売開始	20XX年XX月

放射性医薬品・抗悪性腫瘍剤
放射性医薬品基準 ルテチウムビピボチドテトラキセタン(177Lu)注射液

プルヴィクト®静注
PLUVICTO® Injection

劇薬、処方箋医薬品
（注意－医師等の処方箋により使用すること）

NOVARTIS

1. 警告
本剤は、緊急時に十分対応できる医療施設において、がん化学療法及び放射線治療に十分な知識・経験を持つ医師のもとで、本剤の投与が適切と判断される症例についてのみ投与すること。また、治療開始に先立ち、患者又はその家族に本剤の有効性及び危険性を十分説明し、同意を得てから投与すること。

2. 禁忌（次の患者には投与しないこと）
本剤の成分に対し過敏症の既往歴のある患者

3. 組成・性状

3.1 組成

販売名	プルヴィクト静注
有効成分	1バイアル（7.5～12.5mL）中 ルテチウムビピボチドテトラキセタン（177Lu） 7.4GBq（検定日時）
添加剤	1バイアル（7.5～12.5mL）中 酢酸　2.25～3.75mg 酢酸ナトリウム　3.08～5.13mg ゲンチジン酸　2.93～4.88mg アスコルビン酸ナトリウム　375.0～625.0mg ジエチレントリアミン五酢酸　0.75～1.25mg

3.2 製剤の性状

販売名	プルヴィクト静注
性状	無色～微黄色澄明の液
pH	4.5～7.0
浸透圧	528mOsm/L

4. 効能又は効果
PSMA陽性の遠隔転移を有する去勢抵抗性前立腺癌

5. 効能又は効果に関連する注意
5.1 承認された診断用医薬品を用いた検査により、PSMA陽性病変を有することが確認された患者に投与すること。なお、承認された診断用医薬品の情報については、以下のウェブサイトから入手可能である：
https://www.pmda.go.jp/review-services/drug-reviews/about-reviews/p-drugs/0035.html
5.2 アビラテロン、エンザルタミド、アパルタミド又はダロルタミドによる治療歴のない患者における有効性及び安全性は確立していない。
5.3 臨床試験に組み入れられた患者の治療歴等について、「17. 臨床成績」の項の内容を熟知し、本剤の有効性及び安全性を十分に理解した上で、タキサン系抗悪性腫瘍剤の適応となる患者においては、タキサン系抗悪性腫瘍剤による治療の実施についても慎重に検討し、適応患者の選択を行うこと。［17.1.1-17.1.3参照］
5.4 本剤の術後補助療法における有効性及び安全性は確立していない。

6. 用法及び用量
通常、成人にはルテチウムビピボチドテトラキセタン(177Lu)として1回7.4GBqを6週間間隔で最大6回静脈内投与する。なお、患者の状態により適宜減量する。

7. 用法及び用量に関連する注意
7.1 他の抗悪性腫瘍剤との併用について、有効性及び安全性は確立していない。
7.2 副作用が発現した場合には、以下の基準を参考に、本剤を休薬、減量又は中止すること。なお、副作用による休薬が4週間を超えた場合は、本剤の投与中止を考慮すること。副作用により本剤を減量した場合には、再増量しないこと。［8.1、8.2、11.1.1、11.1.2参照］

減量の目安

減量レベル	1回用量
通常投与量	7.4GBq
1段階減量	5.9GBq
2段階減量	投与中止

副作用発現時の休薬・減量・投与中止の目安

副作用	程度(注)	処置
骨髄抑制（貧血、血小板減少症、白血球減少症、好中球減少症、汎血球減少症）	Grade2	Grade1又はベースラインに回復するまで休薬し、同量で再開する。
	Grade3以上	Grade1又はベースラインに回復するまで休薬し、減量して再開する。
腎機能障害	・Grade2以上の血清クレアチニン増加 又は ・CLcr　＜　30mL/min（Cockcroft-Gault式により計算）	Grade1又はベースラインに回復するまで休薬し、同量で再開する。
	・ベースラインから40%以上の血清クレアチニン増加 かつ ・ベースラインから40%を超えるCLcr減少（Cockcroft-Gault式により計算）	ベースラインに回復するまで休薬し、減量して再開する。
	Grade3以上の再発	投与を中止する。
口内乾燥	Grade3	減量して再開する。
胃腸障害	Grade3以上	Grade2又はベースラインに回復するまで休薬し、減量して再開する。
AST上昇又はALT上昇	AST又はALTがULNの20倍超	投与を中止する。

注）GradeはNCI-CTCAE ver5.0に準じる。
ULN：基準値上限

7.3 外科的又は内科的去勢術と併用しない場合の有効性及び安全性は確立していない。

8. 重要な基本的注意

8.1 骨髄抑制があらわれることがあるので、本剤投与開始前及び投与中は定期的に血液検査を行い、患者の状態を十分に観察すること。［7.2、11.1.1参照］

8.2 腎機能障害があらわれることがあるので、本剤投与開始前及び投与中は定期的に腎機能検査を行い、患者の状態を十分に観察すること。また、本剤投与前後は十分な水分補給及び排尿を行うよう指導すること。［7.2、11.1.2参照］

9. 特定の背景を有する患者に関する注意

9.2 腎機能障害患者

9.2.1 重度の腎機能障害患者又は末期腎不全患者

投与の可否を慎重に判断すること。重度の腎機能障害患者（クレアチニンクリアランス（CLcr）15～29mL/分）又は末期腎不全患者を対象とした臨床試験は実施していない。［16.6.1参照］

9.4 生殖能を有する者

9.4.1 男性には、本剤投与中及び最終投与後14週間においてバリア法（コンドーム）を用いて避妊する必要性について説明すること。［9.4.2参照］

9.4.2 放射線に起因する生殖細胞への影響等があらわれる可能性があることを考慮すること。本剤の推奨累積投与量44.4GBqは、精巣への放射線吸収量として不妊を引き起こす可能性のある範囲に該当する。［9.4.1参照］

9.7 小児等

小児等を対象とした臨床試験は実施していない。

11. 副作用

次の副作用があらわれることがあるので、観察を十分に行い、異常が認められた場合には投与を中止するなど適切な処置を行うこと。

11.1 重大な副作用

11.1.1 骨髄抑制

貧血（22.4%）、血小板減少症（13.5%）、白血球減少症（12.3%）、リンパ球減少症（9.2%）、汎血球減少症（1.0%）、骨髄機能不全（0.1%）等の骨髄抑制があらわれることがある。［7.2、8.1参照］

11.1.2 腎機能障害（3.6%）

急性腎障害、腎不全、血中クレアチニン増加、血中尿素増加等の腎機能障害があらわれることがある。［7.2、8.2参照］

11.2 その他の副作用

	5%以上	5%未満
感染症及び寄生虫症	－	口腔真菌感染
神経系障害	味覚不全	頭痛、浮動性めまい
眼障害	－	ドライアイ
耳及び迷路障害	－	回転性めまい
胃腸障害	口内乾燥（41.1%）、悪心（26.6%）、嘔吐（10.2%）、下痢、便秘	腹痛、口内炎、食道障害
皮膚及び皮下組織障害	－	皮膚乾燥
腎及び尿路障害	－	尿路感染
一般・全身障害及び投与部位の状態	疲労（35.3%）、食欲減退（12.9%）	体重減少、末梢性浮腫、発熱

14. 適用上の注意

14.1 薬剤投与前の注意

14.1.1 投与前に遮蔽したスクリーン下で目視による確認を行い、微粒子又は変色が認められる場合は、バイアルを廃棄すること。

14.1.2 他の薬剤と混合しないこと。

14.2 薬剤投与時の注意

14.2.1 膀胱部の被曝を軽減させるため、本剤投与前後にできるだけ患者に水分を摂取させ、排尿させること。

15. その他の注意

15.1 臨床使用に基づく情報

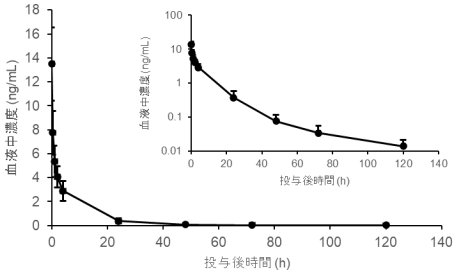
放射線曝露により、二次発癌や遺伝子異常のリスクが増加する可能性がある。

16. 薬物動態

16.1 血中濃度

16.1.1 単回投与

日本人去勢抵抗性前立腺癌患者（3例）に本剤7.4GBqを単回静脈内投与したときの血液中濃度推移及び薬物動態パラメータは以下のとおりであった[1)]。



日本人患者に本剤7.4GBqを単回静脈内投与したときの
血液中濃度推移（平均値±標準偏差又は平均値+標準偏差）

日本人患者に本剤7.4GBqを単回静脈内投与したときの
薬物動態パラメータ

n	Cmax (ng/mL)	AUCinf (h·ng/mL)	CL (L/h)	T1/2 (h)
3	13.3 (24.8)	57.9 (30.6)	1.71 (15.5)	28.9 (1.65)

幾何平均値（幾何CV%）

16.3 分布

16.3.1 吸収線量

日本人去勢抵抗性前立腺癌患者（3例）に本剤7.4GBqを単回又は6回静脈内投与したときの各臓器の吸収線量推定値は以下のとおりであった[1)]。

	本剤7.4GBqを単回静脈内投与(Gy)		本剤7.4GBqを6回(累積放射能として44.4GBq)静脈内投与(Gy)	
臓器	平均値	標準偏差	平均値	標準偏差
副腎	0.15	0.029	0.92	0.18
脳	0.11	0.055	0.68	0.33
食道	0.10	0.023	0.61	0.14
眼	0.090	0.020	0.54	0.12
胆嚢壁	0.13	0.031	0.77	0.18
左結腸	3.5	1.3	21	7.8
小腸	0.38	0.12	2.3	0.75
胃壁	0.10	0.024	0.62	0.14
右結腸	1.9	0.70	11	4.2
直腸	3.3	1.2	20	7.4
心臓壁	0.45	0.19	2.7	1.1
腎臓	2.6	0.44	15	2.6
涙腺	15	7.4	90	45
肝臓	0.74	0.093	4.4	0.56
肺	0.30	0.025	1.8	0.15
膵臓	0.12	0.027	0.69	0.16
前立腺	0.12	0.024	0.72	0.15
唾液腺	5.8	0.19	35	1.2
赤色骨髄	0.25	0.053	1.5	0.32
骨形成原細胞	0.19	0.037	1.1	0.22
脾臓	0.54	0.12	3.2	0.71
精巣	0.092	0.020	0.55	0.12

	本剤7.4GBqを単回静脈内投与(Gy)		本剤7.4GBqを6回(累積放射能として44.4GBq)静脈内投与(Gy)	
胸腺	0.096	0.020	0.58	0.13
甲状腺	0.37	0.049	2.2	0.29
膀胱壁	2.5	0.091	15	0.55
全身	0.18	0.037	1.1	0.22

16.3.2 血漿蛋白結合

非標識及び非放射性ルテチウムビピボチドテトラキセタン（^{175}Lu）のヒト血漿中での蛋白結合率は約60%～70%であった[2]（*in vitro*）。

16.4 代謝

放射性ルテチウムビピボチドテトラキセタン（^{177}Lu）は肝臓及び腎臓で代謝されない[3]（*in vitro*）。

16.5 排泄

本剤は主に腎臓を介して排泄される。去勢抵抗性前立腺癌患者30例に本剤を投与した結果、最初の48時間までに本剤の投与量の約50%が尿中に排泄されることが示された。また、本剤の投与量の約1～5%が糞中に排泄された[4]（外国人データ）。

16.6 特定の背景を有する患者

16.6.1 腎機能障害患者

母集団薬物動態解析を用いて、本剤の薬物動態に対する軽度から中等度の腎機能障害の影響を評価した結果、本剤の曝露量が増加する傾向が認められた[5]（外国人データ）。［9.2.1参照］

17. 臨床成績

17.1 有効性及び安全性に関する試験

17.1.1 国内第Ⅱ相試験（A11201 試験）

PSMA陽性[注1)]の遠隔転移を有する去勢抵抗性前立腺癌（mCRPC）患者のうち、①1剤以上の新規アンドロゲン受容体シグナル阻害薬（ARSI）及び1[注2)]又は2剤のタキサン系抗悪性腫瘍剤による治療歴のある患者12例、②1剤のARSIによる治療歴があり、タキサン系抗悪性腫瘍剤による治療歴のない[注3)]患者18例を対象に、①では本剤（7.4GBqを6週間間隔で最大6回静脈内投与）とBSC/BSoC[注4)]との併用投与の有効性、安全性等を、②では本剤の有効性、安全性等を検討することを目的とした非盲検非対照試験を実施した。

主要評価項目である治験担当医師判定による奏効率[注5)]［90%信頼区間］（%）はそれぞれ、①25.0［7.2, 52.7］、②33.3［15.6, 55.4］であった。

注1）ガリウム（^{68}Ga）ゼゼトチドを用いたPET/CT検査で、中央判定によりPSMA陽性と診断された患者

注2）2剤目のタキサン系抗悪性腫瘍剤による治療が適応にならないと治験担当医師に判断された場合に、組入れ可能とされた。

注3）2剤目のARSIによる治療が適切と治験担当医師に判断された患者が対象とされた。

注4）アンドロゲン除去療法（ADT）、ARSIの使用は可とされ、他の治験薬、細胞傷害性抗悪性腫瘍剤、免疫療法、他の放射性医薬品、半身放射線療法、PARP阻害剤及びAKT阻害剤の使用は不可とされた。

注5）前立腺癌ワーキンググループ3（PCWG3）基準に基づく奏効率

本剤の副作用は30例中20例（66.7%）に認められた。主な副作用は便秘及び血小板数減少各6例（20.0%）、貧血5例（16.7%）、口内乾燥及び倦怠感各4例（13.3%）、悪心、食欲減退及び味覚不全各3例（10.0%）であった（2023年12月8日データカットオフ）[1)]。［5.3参照］

17.1.2 海外第Ⅲ相試験（A12301/VISION 試験）

1剤以上のARSI及び1[注1)]又は2剤のタキサン系抗悪性腫瘍剤による治療歴のあるPSMA陽性[注2)]のmCRPC患者831例を対象に、本剤（7.4GBqを6週間間隔で最大6回静脈内投与）とBSC/BSoC[注3)]との併用投与の有効性及び安全性をBSC/BSoCと比較することを目的とした無作為化非盲検比較試験を実施した。

主要評価項目であるPCWG3基準に基づく盲検下独立中央判定による画像診断上の無増悪生存期間（rPFS）及び全生存期間（OS）は、BSC/BSoC群と比較して本剤+BSC/BSoC群で統計学的に有意な延長を示した（2021年1月27日データカットオフ）。

注1）2剤目のタキサン系抗悪性腫瘍剤による治療が適応にならないと治験担当医師に判断された場合に、組入れ可能とされた。

注2）ガリウム（^{68}Ga）ゼゼトチドを用いたPET/CT検査で、中央判定によりPSMA陽性と診断された患者

注3）ADT、ARSIの使用は可とされ、他の治験薬、細胞傷害性抗悪性腫瘍剤、免疫療法、他の放射性医薬品及び半身放射線療法の使用は不可とされた。

VISION試験：主要評価項目の成績

	本剤+BSC/BSoC群	BSC/BSoC群
画像診断に基づく無増悪生存期間（rPFS）*1,2	N = 385	N = 196
イベント数(%)	254（66.0）	93（47.4）
中央値（月）［99.2%信頼区間］*3	8.7［7.9, 10.8］	3.4［2.4, 4.0］
ハザード比［99.2%信頼区間］*4	0.40［0.29, 0.57］	
P値*5	<0.001	
全生存期間（OS）*6	N = 551	N = 280
イベント数（%）	343（62.3）	187（66.8）
中央値（月）［95%信頼区間］*3	15.3［14.2, 16.9］	11.3［9.8, 13.5］
ハザード比［95%信頼区間］*4	0.62［0.52, 0.74］	
P値*7	<0.001	

*1 PCWG3基準に基づく盲検下独立中央判定

*2 BSC/BSoC群で同意撤回による脱落割合が高かったことから、治験実施医療機関への教育等を行った後に無作為化された患者がPFS-FASとして解析対象集団とされた。

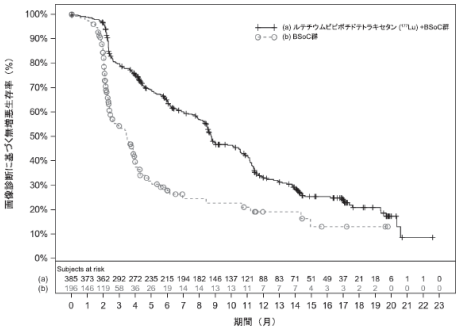
*3 Kaplan-Meier法

*4 層別Cox比例ハザードモデル

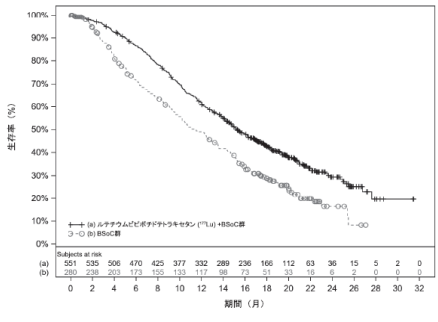
*5 層別log-rank検定、有意水準（片側）0.004

*6 本試験に登録され、無作為化された患者がFASとして解析対象集団とされた。

*7 層別log-rank検定、有意水準（片側）0.025



VISION試験：rPFSのKaplan-Meier曲線（盲検下独立中央判定）



VISION試験：OSのKaplan-Meier曲線

本剤の副作用は529例中451例（85.3%）に認められた。主な副作用は口内乾燥190例（35.9%）、疲労166例（31.4%）、悪心148例（28.0%）であった（2023年12月14日データカットオフ）[6)]。［5.3参照］

17.1.3 海外第Ⅲ相試験（B12302/PSMAfore 試験）

1剤のARSIによる治療歴があり、タキサン系抗悪性腫瘍剤による治療歴のない[注1)] PSMA陽性[注2)]のmCRPC患者469例を対象に、BSC[注3)]の併用下で、本剤（7.4GBqを6週間間隔で最大6回静脈内投与）と治験担当医師により選択された2剤目のARSIの有効性及び安全性

を検討することを目的とした無作為化非盲検比較試験を実施した。
主要評価項目であるPCWG3基準に基づく盲検下独立中央判定によるrPFSは、ARSI群と比較して本剤群で統計学的に有意な延長を示した（2022年10月2日データカットオフ）。

注1）タキサン系抗悪性腫瘍剤による治療を延期することが適切と治験担当医師に判断された場合に、組入れ可能とされた。

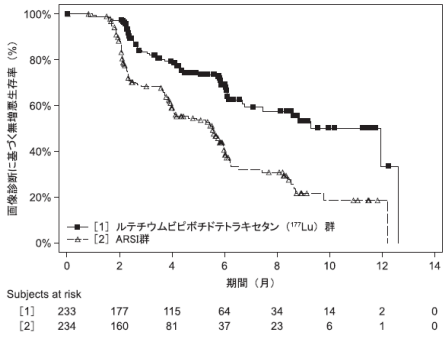
注2）ガリウム（^{68}Ga）ゴゼトチドを用いたPET/CT検査で、中央判定によりPSMA陽性と診断された患者。

注3）ADTの使用は可とされ、他の治験薬、生物学的製剤、免疫療法、細胞傷害性抗悪性腫瘍剤、他の放射性医薬品、PARP阻害剤及び半身放射線療法の使用は不可とされた。また、本剤群ではARSIの使用は不可とされた。

PSMAfore試験：主要評価項目の成績

画像診断に基づく無増悪生存期間（rPFS） *1	本剤群 N = 233	ARSI群 N = 234
イベント数(%)	60（25.8）	106（45.3）
中央値（月）［95%信頼区間］ *2	9.30［6.77, -］	5.55［4.04, 5.95］
ハザード比［95%信頼区間］ *3	0.41［0.29, 0.56］	
P値*4	<0.0001	

-：推定不能
*1 PCWG3基準に従った盲検下独立中央判定（データカットオフ 2022年10月2日）
*2 Kaplan-Meier法
*3 層別Cox比例ハザードモデル
*4 層別log-rank検定、有意水準（片側）0.025



PSMAfore試験：rPFSのKaplan-Meier曲線（盲検下独立中央判定）

本剤の副作用は227例中199例（87.7%）に認められた。主な副作用は口内乾燥126例（55.5%）、悪心59例（26.0%）、無力症55例（24.2%）、疲労42例（18.5%）、貧血33例（14.5%）、食欲減退32例（14.1%）であった（2024年2月27日データカットオフ）[7]。
［5.3参照］

18. 薬効薬理

18.1 作用機序

ルテチウムビピボチドテトラキセタン(^{177}Lu)は、PSMAのリガンドであるビピボチドテトラキセタンと^{177}Lu（ルテチウムの放射性同位体）の錯体である。本剤は前立腺癌で高発現するPSMAに結合し、^{177}Luから放出されるベータ線が細胞を傷害することにより、腫瘍増殖抑制作用を示すと考えられている。

19. 有効成分に関する理化学的知見

一般的名称

ルテチウムビピボチドテトラキセタン（^{177}Lu）

Lutetium（^{177}Lu）vipivotide tetraxetan（INN）

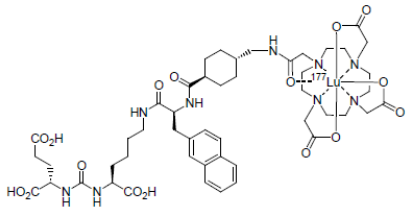
化学名

2-[4-[2-[[4-[[(2S)-1-[[(5S)-5-carboxy-5-[[(1S)-1,3-dicarboxy propyl]carbamoylamino]pentyl]amino]-3-naphthalen-2-yl-1-oxopropan-2-yl]carbamoyl]cyclohexyl]methylamino]-2-oxoethyl]-4,7,10-tris(carboxylatomethyl)-1,4,7,10-tetrazacyclododec-1-yl]acetate; lutetium-177(3+)

分子式

$C_{49}H_{68}{}^{177}LuN_9O_{16}$

化学構造式



核物理学的特性（^{177}Luとして）

- 物理的半減期：6.647日
- 主なβ線エネルギー：0.498MeV（78.6%）、0.385MeV（9.1%）、0.176MeV（12.2%）
- 主なγ線エネルギー：0.208MeV（11.0%）、0.113MeV（6.4%）
- 減衰表：

経過時間	残存放射能
0（hour）	1.000
1（hour）	0.996
2（hours）	0.991
5（hours）	0.979
10（hours）	0.958
24（1 day）	0.901
48（2 days）	0.812
72（3 days）	0.731
120（5 days）	0.594
168（7 days）	0.482
336（14 days）	0.232
720（30 days）	0.044
1080（45 days）	0.009

20. 取扱い上の注意

本剤は、医療法その他の放射線防護に関する法令、関連する告示及び通知等を遵守し、適正に使用すること。

22. 包装

1バイアル

23. 主要文献

1）社内資料：国内第Ⅱ相試験（A11201試験）（CTD2.7.2-2.3.2.2、CTD2.7.2-1.2.2.2、CTD2.7.6-4.2.1）
2）社内資料：ヒト蛋白結合（CTD2.7.2-2.1.1）
3）社内資料：*In vitro*代謝（CTD2.7.2-2.1.3）
4）Kratochwil C, et al.: J Nucl Med. 2016; 57(8): 1170-1176
5）社内資料：母集団薬物動態解析（CTD2.7.2-3.4.6）
6）社内資料：海外第Ⅲ相試験（A12301試験）（CTD2.7.6-4.1.1）
7）社内資料：海外第Ⅲ相試験（B12302試験）（CTD2.7.6-4.1.2）

24. 文献請求先及び問い合わせ先

ノバルティスファーマ株式会社　ノバルティスダイレクト
〒105-6333　東京都港区虎ノ門1-23-1
NOVARTIS DIRECT
0120-003-293
受付時間：月～金 9：00～17：30
（祝日及び当社休日を除く）
www.novartis.co.jp

26. 製造販売業者等

26.1 製造販売（輸入）

ノバルティスファーマ株式会社
東京都港区虎ノ門1-23-1

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略号一覧

略号	略していない表現（英）	略していない表現（日）
ADT	androgen deprivation therapy	アンドロゲン遮断療法
ALT	alanine aminotransferase	アラニンアミノトランスフェラーゼ
ARSI	novel androgen receptor signaling inhibitor	新規アンドロゲン受容体シグナル阻害薬
AST	aspartate aminotransferase	アスパラギン酸アミノトランスフェラーゼ
BSC/BSoC	best supportive care/standard of care	最良の支持療法／標準治療
mCRPC	metastatic castration-resistant prostate cancer	転移性去勢抵抗性前立腺癌
ORR	overall response rate	奏効率
OS	overall survival	全生存期間
PET	positron emission tomography	陽電子放出断層撮影
PSMA	prostate-specific membrane antigen	前立腺特異的膜抗原
rPFS	radiographic progression-free survival	画像診断による無増悪生存期間

1 効能又は効果の案及びその設定根拠

1.1 効能又は効果の案

前立腺特異的膜抗原（PSMA）陽性の遠隔転移を有する去勢抵抗性前立腺癌

1.2 効能又は効果の案の設定根拠

[^{177}Lu]Lu-PSMA-617（以下，本剤）の効能又は効果は，PSMA 陽性が確認されたタキサン既治療の転移性去勢抵抗性前立腺癌（mCRPC）患者を対象に本剤と BSC/BSoC の併用投与（以下，本剤+BSC/BSoC）の有効性及び安全性を BSC/BSoC 単独投与と比較し評価する非盲検ランダム化第 III 相試験（VISION 試験），PSMA 陽性が確認されたタキサン未治療の mCRPC 患者を対象に本剤の有効性及び安全性を ARSI の変更と比較し評価する非盲検ランダム化第 III 相試験（PSMAfore 試験），及びこれら外国第 III 相試験の結果を外挿することを目的とした国内第 II 相試験（A11201 試験）の成績より，PSMA 陽性の進行性 mCRPC 患者に本剤を投与したときのベネフィットはリスクを上回ると確認できたことから，効能又は効果を「前立腺特異的膜抗原（PSMA）陽性の遠隔転移を有する去勢抵抗性前立腺癌」と設定した。

有効性

VISION 試験

タキサン既治療 mCRPC 患者を対象とした VISION 試験で，本剤と BSC/BSoC を併用投与したときの有効性が認められた。主要評価項目（alternate primary endpoints）である rPFS 及び OS はいずれも，BSC/BSoC 群と比較して本剤+BSC/BSoC 群で有意に延長した。また，rPFS 及び OS の感度分析，補足的解析，及び部分集団解析から，rPFS 主要解析及び OS 最終解析と一貫性のある結果が得られた[2.5-4.6 項]。

PSMAfore 試験

タキサン未治療 mCRPC 患者を対象とした PSMAfore 試験で，本剤を投与したときの有効性が認められた。主要評価項目の rPFS は ARSI 群と比較して本剤群で有意に延長した。また，感度分析，補足的解析，及び部分集団解析から，rPFS 主要解析と一貫性のある結果が得られた[2.5-4.6 項]。

A11201 試験

国内試験 A11201 試験で，日本のタキサン既治療 mCRPC 患者に本剤と BSC/BSoC を併用投与した結果，また日本のタキサン未治療 mCRPC 患者に本剤を投与した結果，いずれも実施医療機関の判定に基づく ORR の 90% CI 下限は事前に設定した閾値を上回ったことから，主要目的が達成され，日本人でも腫瘍縮小効果が確認された。A11201 試験の結果は VISION 試験，PSMAfore 試

験と概ね大きな違いは示されず，日本人でも VISION 試験，PSMAfore 試験と同様の有効性が期待できる[2.5-4.6 項]。

安全性

VISION 試験

VISION 試験の有害事象の発現割合及び Grade 3 以上の有害事象の発現割合は，本剤 + BSC/BSoC 群で BSC/BSoC 群に比べ高かった（群間差 10%以上）。重篤な有害事象及び Grade 3 以上の重篤な有害事象の発現割合も同様であった（群間差 5%以上）。死亡に至った有害事象の発現割合は群間で同程度であった。本剤 + BSC/BSoC 群でより高頻度に認められた事象は，疲労，口内乾燥，胃腸障害（悪心，下痢，嘔吐），骨髄抑制（貧血，血小板減少症，リンパ球減少症，白血球減少症），尿路感染であった。全体として，有害事象は概ね一過性で，加療や減量又は休薬により投与継続が可能であり，管理可能であった。長期追跡調査期の有害事象のデータから，本剤の投与による遅発性の有害事象の発現や新たな安全性の懸念を示す所見は認められなかった[2.5-5.9 項]。

PSMAfore 試験

PSMAfore 試験の結果，本剤投与の忍容性及び安全性は良好であり，タキサン系薬剤既治療の mCRPC 患者で確認された良好な安全性プロファイルと一致していた。有害事象，投与中止に至った有害事象，及び死亡に至った有害事象の発現割合は群間で同程度であった。Grade 3 以上の有害事象，重篤な有害事象，Grade 3 以上の重篤な有害事象，休薬に至った有害事象の発現割合は，本剤群で ARSI 群に比べ低かった（群間差 5%以上）。本剤群でより高頻度に認められた事象は，口内乾燥，胃腸障害（悪心，便秘，下痢，嘔吐），貧血であった。Grade 3 以上の事象は貧血が多かった。長期追跡調査期の有害事象のデータから，本剤の投与による遅発性の有害事象の発現や新たな安全性の懸念を示す所見は認められなかった[2.5-5.9 項]。

A11201 試験

A11201 試験の結果，安全性プロファイルは良好で，日本人に特有の新たな安全性上の懸念は認められなかった。

VISION 試験，PSMAfore 試験，及び A11201 試験のいずれも主要目的を達成し，有効性が認められ，安全性プロファイルは良好であったことから，効能又は効果を上記のように設定した。

審査の過程で，医薬品医療機器総合機構との協議を踏まえ，効能又は効果を以下のとおり設定することとした。

PSMA 陽性の遠隔転移を有する去勢抵抗性前立腺癌

2 効能又は効果に関連する注意の案及びその設定根拠

2.1 効能又は効果に関連する注意の案

5.1 承認された診断用医薬品を用いた検査により、PSMA 陽性病変を有することが確認された患者に投与すること。

5.2 「17.臨床成績」の項の内容を熟知し、本剤の有効性及び安全性を十分に理解した上で、適応患者の選択を行うこと。［17.1.1-17.1.3 参照］

5.3 タキサン系薬剤未治療（術前術後化学療法を除く）の患者においては、患者の全身状態、経過等により、タキサン系薬剤による治療も考慮し、適切に治療選択を行うこと。

2.2 効能又は効果に関連する注意の案の設定根拠

本剤の作用機序及び臨床試験成績から，期待される効果を得るためには PSMA 陽性を適切な検査により確認することが重要であると考えた。このことから，効能又は効果に関連する注意として，「承認された診断用医薬品を用いた検査により、PSMA 陽性病変を有することが確認された患者に投与すること。」を設定した。ノバルティスファーマ株式会社は，PSMA 標的療法が有益と考えられる PSMA 陽性 mCRPC 患者の選択で使用する「ロカメッツキット」を本剤と同時に承認申請している。現在，本邦ではその他の PSMA PET 検査も開発されており，テリックスファーマジャパン株式会社がロカメッツキットと同様な有効成分を持つ前立腺癌画像診断薬[^{68}Ga]Ga-PSMA-11（以下，^{68}Ga-PSMA-11）を国内で開発している。その他に，^{68}Ga-PSMA-11 検査の診断精度をマルチパラメトリック MRI と比較する臨床研究も行われている。また，^{18}F-PSMA-1007 や[^{18}F]FSU-880 等の ^{18}F 製剤の PSMA PET 診断も国内で臨床研究が進められている。National Comprehensive Cancer Network（NCCN）ガイドライン version 4 2024 では，本剤の患者選択に ^{68}Ga-PSMA-11 のほか，米国で既承認の F-18 piflufolastat PSMA 及び F-18 flotufolastat PSMA の使用も認められている。さらに，本剤を含める PSMA 標的療法の外国試験では，PSMA 陽性病変の特定に ^{68}Ga-PSMA-11 や F-18 piflufolastat PSMA を用いている。

「17. 臨床成績」の項に，VISION 試験，PSMAfore 試験及び A11201 試験の臨床成績を記述しており，その内容を熟知した上で適切な患者選択をすることが重要であることから，「「17.臨床成績」の項の内容を熟知し、本剤の有効性及び安全性を十分に理解した上で、適応患者の選択を行うこと。」と設定した。さらに，タキサン系薬剤未治療の患者においては，タキサン系薬剤を含め，最適な治療が選択されることがより重要であると考えた。このことから，「17. 臨床成績」の項に加え，本項でも「タキサン系薬剤未治療（術前術後化学療法を除く）の患者においては、患者の全身状態、経過等により、タキサン系薬剤による治療も考慮し、適切に治療選択を行うこと。」と設定した。

審査の過程で，医薬品医療機器総合機構との協議を踏まえ，効能又は効果に関連する注意を以下のとおり設定することとした。

5.1 承認された診断用医薬品を用いた検査により、PSMA 陽性病変を有することが確認された患者に投与すること。なお、承認された診断用医薬品の情報については、以下のウェブサイトから入手可能である：

https://www.pmda.go.jp/review-services/drug-reviews/about-reviews/p-drugs/0035.html

5.2 アビラテロン、エンザルタミド、アパルタミド又はダロルタミドによる治療歴のない患者における有効性及び安全性は確立していない。

5.3 臨床試験に組み入れられた患者の治療歴等について、「17.臨床成績」の項の内容を熟知し、本剤の有効性及び安全性を十分に理解した上で、タキサン系抗悪性腫瘍剤の適応となる患者においては、タキサン系抗悪性腫瘍剤による治療の実施についても慎重に検討し、適応患者の選択を行うこと。［17.1.1-17.1.3 参照］

5.4 本剤の術後補助療法における有効性及び安全性は確立していない。

3 用法及び用量の案及びその設定根拠

3.1 用法及び用量の案

通常、成人にはルテチウムビピボチドテトラキセタン(^{177}Lu)として 1 回 7.4 GBq (7,400 MBq) (200 mCi) を 6 週間間隔で 6 回静脈内投与する。

3.2 用法及び用量の案の設定根拠

外国第 III 相試験及び国内第 II 相試験で用いた用法・用量は同一であり，いずれの試験でも本剤は 7.4 GBq（±10%）を 6 週（±1 週）に 1 回，最大 6 サイクル静脈内投与した。これは臨床使用経験に関する公表文献に基づいて設定した[2.5-4.2 項]。

本剤の添付文書の用法・用量は，VISION 試験，PSMAfore 試験，及び A11201 試験のいずれも主要目的を達成し，有効性が認められ，安全性プロファイルは良好であったことから（1.2 項），上記のように設定した。

審査の過程で，医薬品医療機器総合機構との協議を踏まえ，用法及び用量を以下のとおり設定することとした。

通常、成人にはルテチウムビピボチドテトラキセタン(^{177}Lu)として 1 回 7.4GBq を 6 週間間隔で最大 6 回静脈内投与する。なお、患者の状態により適宜減量する。

4 用法及び用量に関連する注意の案及びその設定根拠

4.1 用法及び用量に関連する注意の案

7.1 本剤の投与開始前及び投与中は以下の臨床検査を実施し、7.2 の基準を参考に投与量を調節すること。［7.2、8.1、8.2、11.1.1、11.1.2 参照］

- 血液学的検査（ヘモグロビン、白血球数、好中球絶対数、血小板数）
- 腎機能検査（血清クレアチニン、クレアチニンクリアランス値［CLcr］）
- 肝機能検査（AST、ALT、ALP、血清アルブミン、総ビリルビン）

7.2 副作用が発現した場合には、以下の基準を参考に、本剤の投与を中断、減量又は中止すること。なお、副作用による中断が 4 週間を超えた場合は、本剤の投与中止を考慮すること。本剤を 1 回のみ 20%減量（5.9GBq（160mCi））することができ、再増量は行わないこと。更なる減量が必要となる副作用が発現した場合は、本剤の投与を中止すること。［7.1、8.1、8.2、11.1.1、11.1.2 参照］

副作用	程度注)	処置
口内乾燥	Grade3	本剤の用量を 20%減量する。
胃腸毒性	Grade3 以上	Grade2 又はベースラインに回復するまで投与を中断する。 本剤の用量を 20%減量（5.9GBq（160mCi））する。
骨髄抑制（貧血、血小板減少症、白血球減少症、好中球減少症、汎血球減少症）	Grade2	Grade1 又はベースラインに回復するまで投与を中断する。 適切な処置を行うこと。増殖因子の使用は許容するが、Grade1 又はベースラインに改善した場合は中止すること。造血成分（鉄、B12 及び葉酸）値を確認し、補充することが推奨される。必要に応じて、輸血を行うことができる。
	Grade3 以上	Grade1 又はベースラインに回復するまで投与を中断する。 本剤の用量を 20%減量（5.9GBq（160mCi））する。
腎機能障害	・Grade2 以上の血清クレアチニン増加	改善するまで投与を中断する。

	・CLcr ＜30 mL/min （Cockcroft-Gault 式により計算）	
	・ベースラインから 40%以上の血清クレアチニン増加 かつ ・ベースラインから 40%を超えて CLcr 減少（Cockcroft-Gault 式により計算）	改善又はベースラインに回復するまで投与を中断する。 本剤の用量を 20%減量（5.9GBq（160mCi））する。
	Grade3 以上の再発	本剤の投与を中止する。
脊髄圧迫	すべて	脊髄圧迫が適切に治療され、神経学的後遺症が安定し、ECOG Performance Status が安定するまで投与を中断する。
体重支持骨の骨折	すべて	骨折が適切に安定/治療され、ECOG Performance Status が安定するまで投与を中断する。
AST 上昇又は ALT 上昇	肝転移がなく AST 又は ALT が ULN の 20 倍超	本剤の投与を中止する。

注）Grade は NCI-CTCAE ver5.0 準じる。
ULN：基準値上限

4.2 用法及び用量に関連する注意の案の設定根拠

各臨床試験では，治験薬と関連ありと判断された有害事象が認められた場合，必要に応じて治験薬の減量，休薬，又は中止を行った。これらの処置により有害事象を管理することが可能であった。骨髄抑制，腎機能障害，AST 上昇，又は ALT 上昇等の副作用の適切な管理のため，本剤の投与開始前及び投与中の上記臨床検査の実施を設定した。また，副作用が発現した場合に適切に対処するために，上記中断・減量・中止基準を設定した。

審査の過程で，医薬品医療機器総合機構との協議を踏まえ，用法及び用量に関連する注意を以下のとおり設定することとした。

7.1 他の抗悪性腫瘍剤との併用について、有効性及び安全性は確立していない。
7.2 副作用が発現した場合には、以下の基準を参考に、本剤を休薬、減量又は中止すること。なお、副作用による休薬が 4 週間を超えた場合は、本剤の投与中止を考慮すること。副作用により本剤を減量した場合には、再増量しないこと。［8.1、8.2、11.1.1、11.1.2 参照］

減量の目安

減量レベル	1 回用量
通常投与量	7.4GBq
1 段階減量	5.9GBq
2 段階減量	投与中止

副作用発現時の休薬・減量・投与中止の目安

副作用	程度[注)]	処置
骨髄抑制（貧血、血小板減少症、白血球減少症、好中球減少症、汎血球減少症）	Grade2	Grade1 又はベースラインに回復するまで休薬し、同量で再開する。
	Grade3 以上	Grade1 又はベースラインに回復するまで休薬し、減量して再開する。
腎機能障害	・Grade2 以上の血清クレアチニン増加 又は ・ CLcr ＜ 30mL/min （Cockcroft-Gault 式により計算）	Grade1 又はベースラインに回復するまで休薬し、同量で再開する。
	・ベースラインから 40%以上の血清クレアチニン増加 かつ ・ベースラインから 40%を超える CLcr 減少（Cockcroft-Gault 式により計算）	ベースラインに回復するまで休薬し、減量して再開する。
	Grade3 以上の再発	投与を中止する。
口内乾燥	Grade3	減量して再開する。
胃腸障害	Grade3 以上	Grade2 又はベースラインに回復するまで休薬し、減量して再開する。
AST 上昇又は ALT 上昇	AST 又は ALT が ULN の 20 倍超	投与を中止する。

注）Grade は NCI-CTCAE ver5.0 に準じる。

ULN：基準値上限

7.3 外科的又は内科的去勢術と併用しない場合の有効性及び安全性は確立していない。

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1. 警告欄

1. 警告

本剤は、緊急時に十分対応できる医療施設において、がん化学療法及び放射線治療に十分な知識・経験を持つ医師のもとで、本剤の投与が適切と判断される症例についてのみ投与すること。また、治療開始に先立ち、患者又はその家族に本剤の有効性及び危険性を十分説明し、同意を得てから投与すること。

1. 警告の設定根拠

本剤は放射性医薬品かつ抗悪性腫瘍剤であるため，放射性医薬品の取扱いに関する適切な基準を満たし，かつ，緊急時に十分対応できる医療施設において，がん化学療法及び放射線治療への十分な知識・経験を持つ医師のもとで使用される必要がある。

本剤の有効性及び安全性は，臨床試験で設定した基準に該当する患者で確認されていることから，電子添文の「17. 臨床成績」の項を熟知し，本剤の有効性及び安全性を十分に理解した上で適切に患者を選択することが必要である。

また，本剤は患者又はその家族から，本剤の有効性及び危険性について十分理解が得られた後に投与する必要がある。

2. 禁忌欄

2. 禁忌（次の患者には投与しないこと）

本剤の成分に対し過敏症の既往歴のある患者

2. 禁忌の設定根拠

本剤の成分に対し過敏症の既往歴のある患者に本剤を投与した場合，重篤な過敏症症状が発現する可能性が考えられることから，一般的な注意として記載した。

8. 重要な基本的注意欄

8. 重要な基本的注意

8.1 骨髄抑制があらわれることがあるので、本剤投与開始前及び投与中は定期的に血液検査を行い、患者の状態を十分に観察すること。［7.2、11.1.1 参照］

8.2 腎機能障害があらわれることがあるので、本剤投与開始前及び投与中は定期的に腎機能検査を行い、患者の状態を十分に観察すること。また、本剤投与前後は十分な水分補給及び排尿を行うよう指導すること。［7.2、11.1.2 参照］

8. 重要な基本的注意の設定根拠

8.1 海外第 III 相試験（A12301/VISION 試験）において，ベストスタンダードオブケア（BSC/BSoC）群と比較して本剤＋BSC/BSoC 群で，また海外第 III 相試験（B12302/PSMAfore 試験）において，新規アンドロゲン受容体シグナル阻害薬（ARSI）群と比較して本剤群で，骨髄抑制の発現頻度が高い傾向が認められていることから設定した。
8.2 VISION 試験において，BSC/BSoC 群と比較して本剤＋BSC/BSoC 群で，腎機能障害の発現頻度が高い傾向が認められていること，本剤は主に腎排泄され，近位尿細管が PSMA の発現部位であることにより腎被曝が生じると考えられることから設定した。

9. 特定の背景を有する患者に関する注意欄

9.2 腎機能障害患者欄

9.2 腎機能障害患者

9.2.1 重度の腎機能障害患者又は末期腎不全患者
投与の可否を慎重に判断すること。重度の腎機能障害患者（クレアチニンクリアランス（CLcr）15～29mL/分）又は末期腎不全患者を対象とした臨床試験は実施していない。［16.6.1 参照］

9.2 腎機能障害患者の設定根拠

臨床試験において，重度の腎機能障害患者（クレアチニンクリアランス（CLcr）15～29 mL/分）又は末期腎不全患者には投与経験がないため設定した。

9.4 生殖能を有する者欄

9.4 生殖能を有する者

9.4.1 男性には、本剤投与中及び最終投与後 14 週間においてバリア法（コンドーム）を用いて避妊する必要性について説明すること。［9.4.2 参照］
9.4.2 放射線に起因する生殖細胞への影響等があらわれる可能性があることを考慮すること。本剤の推奨累積投与量 44.4GBq は、精巣への放射線吸収量として不妊を引き起こす可能性のある範囲に該当する。［9.4.1 参照］

9.4 生殖能を有する者の設定根拠

9.4.1 男性に対する避妊期間は，本剤は放射性医薬品であることから遺伝的に損傷した精子の移行を考慮し，7 日間（実効半減期の 5 倍＝5×1.4 日間）＋90 日間（完全な精子形成周期）から 14 週間とした。なお，実効半減期（Te）は，物理学的半減期（Tp）（6.647 日）及び生物学的半減期（Tb）（41.6 時間）から算出した［33 時間（～1.4 日）］*。

*：1/Te = (1/Tp) + (1/Tb)

9.4.2 本剤による放射線被曝を考慮すると，放射線に起因する生殖細胞への影響等があらわれる可能性がある。本剤の推奨累積投与量44.4 GBqでは，永続的な男性不妊の閾値（3.5～6.0 Gy）を超える可能性があることから設定した。

9.7 小児等欄

9.7 小児等

小児等を対象とした臨床試験は実施していない。

9.7 小児等の設定根拠

小児等に対する有効性及び安全性が確立していないことから記載した。

11. 副作用欄

11. 副作用

次の副作用があらわれることがあるので、観察を十分に行い、異常が認められた場合には投与を中止するなど適切な処置を行うこと。

11.1 重大な副作用

11.1.1 骨髄抑制

貧血（22.4%）、血小板減少症（13.5%）、白血球減少症（12.3%）、リンパ球減少症（9.2%）、汎血球減少症（1.0%）、骨髄機能不全（0.1%）等の骨髄抑制があらわれることがある。［7.2、8.1参照］

11.1.2 腎機能障害（3.6%）

急性腎障害、腎不全、血中クレアチニン増加、血中尿素増加等の腎機能障害があらわれることがある。［7.2、8.2参照］

11.2 その他の副作用

	5%以上	5%未満
感染症及び寄生虫症	－	口腔真菌感染
神経系障害	味覚不全	頭痛、浮動性めまい
眼障害	－	ドライアイ
耳及び迷路障害	－	回転性めまい
胃腸障害	口内乾燥（41.1%）、悪心（26.6%）、嘔吐（10.2%）、下痢、便秘	腹痛、口内炎、食道障害
皮膚及び皮下組織障害	－	皮膚乾燥
腎及び尿路障害	－	尿路感染
一般・全身障害及び投与部位の状態	疲労（35.3%）、食欲減退（12.9%）	体重減少、末梢性浮腫、発熱

11. 副作用の設定根拠

冒頭は添付文書新記載要領の Q&A に基づき記載した。

本項に記載した副作用は，本剤の企業中核データシート（CCDS）に基づき設定した。発現頻度は，VISION 試験，PSMAfore 試験，及び国内第 II 相試験（A11201 試験）の本剤群における併合解析結果に基づき記載した。

11.1.1 VISION 試験及び PSMAfore 試験において，本剤群で，骨髄抑制の発現頻度が高い傾向が認められていることから設定した。また，汎血球減少症及び骨髄機能不全により死亡に至った症例が報告されている。

11.1.2 VISION 試験において，BSC/BSoC 群と比較して本剤 + BSC/BSoC 群で，腎機能障害の発現頻度が高い傾向が認められていることから設定した。

14. 適用上の注意欄

14. 適用上の注意

14.1 薬剤投与前の注意

14.1.1 投与前に遮蔽したスクリーン下で目視による確認を行い、微粒子又は変色が認められる場合は、バイアルを廃棄すること。

14.1.2 他の薬剤と混合しないこと。

14.2 薬剤投与時の注意

14.2.1 膀胱部の被曝を軽減させるため、本剤投与前後にできるだけ患者に水分を摂取させ、排尿させること。

14. 適用上の注意の設定根拠

14.1 本剤の臨床試験及び CCDS に基づき設定した。

14.2.1 本剤は腎排泄されることから，排尿により膀胱部への被曝を軽減させることができるため設定した。

15. その他の注意欄

15.1 臨床使用に基づく情報欄

15.1 臨床使用に基づく情報

放射線曝露により、二次発癌や遺伝子異常のリスクが増加する可能性がある。

15.1 臨床使用に基づく情報の設定根拠

本剤は放射性医薬品であるため，二次発癌や遺伝子異常のリスクが増加する可能性があることから設定した。

1 International Nonproprietary Names for Pharmaceutical Substances (INN)

r-INN

lutetium (^{177}Lu) vipivotide tetraxetan

（WHO Drug Information, Vol. 35, No. 1, 2021, Recommended INN List 85, P169）

2 放射性医薬品基準収載名

放射性医薬品基準 （以下，放薬基）第 1 通則 3 条では，「放薬基で「基準名」とは，第 4 医薬品各条に掲げる名称又はその別名をいい，法第 50 条の適用については，これを一般的名称とみなす。」とされている。

本剤の放薬基 （案）における基準名は，「ルテチウムビピボチドテトラキセタン (^{177}Lu) 注射液」を予定している。放薬基 （案）は，1.13 項に添付した。

放射性医薬品基準収載名 （予定）：ルテチウムビピボチドテトラキセタン (^{177}Lu) 注射液

International Nonproprietary Names for Pharmaceutical Substances (INN)

RECOMMENDED International Nonproprietary Names: List 85

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 (1–117) and Recommended (1–78) International Nonproprietary Names can be found in *Cumulative List No. 17, 2017* (available in CD-ROM only).

Dénominations communes internationales des Substances pharmaceutiques (DCI)

Dénominations communes internationales RECOMMANDÉES: Liste 85

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 (1–117) et recommandées (1–78) dans la *Liste récapitulative No. 17, 2017* (disponible sur CD-ROM seulement).

Denominaciones Comunes Internacionales para las Sustancias Farmacéuticas (DCI)

Denominaciones Comunes Internacionales RECOMENDADAS: Lista 85

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 (1–117) y Recomendadas (1–78) se encuentran reunidas en *Cumulative List No. 17, 2017* (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*

Please find the names from proposed **INN List 124 – COVID-19 (special edition)** that have reached the status of recommended INN in annex.
Veuillez trouver les noms de la **Liste 124 des DCI proposées – COVID-19 (édition spéciale)** ayant atteint le statut de DCI recommandées en annexe.
Por favor, abajo se encuentran los nombres de la **Lista 124 de DCI propuestas – COVID-19 (edición especial)** que han alcanzado el estatus de DCI recomendadas.

acapatamabum #

acapatamab	immunoglobulin scFv-scFv-scFc, anti-[*Homo sapiens* FOLH1 (folate hydrolase, prostate specific membrane antigen, PSMA)] and anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], monoclonal antibody single chain (scFv)2-scFc, bispecific; IG single chain scFv-scFv-scFc, anti FOLH1 and anti-CD3E (1-986) [scFv-VH-V-kappa anti-FOLH1 (1-243) [VH (*Homo sapiens* IGHV3-11*01 G49>C (44) (84.7%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -15-mer-tris(tetraglycyl-seryl) linker (122-136)-V-KAPPA (*Homo sapiens* IGKV1-16*01 (79.3%) -IGKJ2*01 Q120>C (236) (90.9%)) CDR-IMGT [6.3.9] (163-168.186-188.225-233) (137-243)] -6-mer seryl-tetraglycyl-seryl linker (244-249) -scFv-VH-V-lambda anti-CD3E (250-498) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87.0%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (275-282.300-309.348-363) (250-374) -15-mer-tris(tetraglycyl-seryl) linker (375-389) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (415-423.441-443.480-488) (390-498)] -4-mer- tetraglycyl linker (499-502) -scFc (h-CH2-CH3)-(h-CH2-CH3) (503-986) [*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (hinge 6-15 (503-512), CH2 R83>C (574), N84.4>G (579), V85>C (584) (513-622), CH3 E12 (638), M14 (640) (623-727), CHS (728-729)) (503-729) -30-mer hexakis(tetraglycyl-seryl) linker (730-759) -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (hinge 6-15 (760-769), CH2 R83>C (831), N84.4>G (836), V85>C (841) (770-879), CH3 E12 (895), M14 (897) (880-984), CHS (985-986)) (760-986)]], non-glycosylated, produced in Chinese hamster ovary (CHO) cells
acapatamab	immunoglobuline scFv-scFv-scFc, anti-[*Homo sapiens* FOLH1 (folate hydrolase, antigène membranaire spécifique de la prostate, PSMA)], et anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], anticorps monoclonal à chaîne unique (scFv)2-scFc, bispécifique;

	IG à chaîne unique scFv-scFv-scFc, anti FOLH1 et anti-CD3E (1-986) [scFv-VH-V-kappa anti-FOLH1 (1-243) [VH (*Homo sapiens* IGHV3-11*01 G49>C (84.7%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -15-mer-tris(tétraglycyl-séryl) linker (122-136)-V-KAPPA (*Homo sapiens* IGKV1-16*01 (79.3%) -IGKJ2*01 Q120>C (236) (90.9%)) CDR-IMGT [6.3.9] (163-168.186-188.225-233) (137-243)] -6-mer-séryl-tétraglycyl-séryl linker (244-249) -scFv-VH-V-lambda anti-CD3E (250-498) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87.0%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (275-282.300-309.348-363) (250-374) -15-mer-tris(tétraglycyl-séryl) linker (375-389) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (415-423.441-443.480-488) (390-498)] -4-mer-tétraglycyl linker (499-502) -scFc (h-CH2-CH3)-(h-CH2-CH3) (503-986) [*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (charnière 6-15 (503-512), CH2 R83>C (574), N84.4>G (579), V85>C (584) (513-622), CH3 E12 (638), M14 (640) (623-727), CHS (728-729)) (503-729) -30-mer-hexakis(tétraglycyl-séryl) linker (730-759) -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (charnière 6-15 (760-769), CH2 R83>C (831), N84.4>G (836), V85>C (841) (770-879), CH3 E12 (895), M14 (897) (880-984), CHS (985-986)) (760-986)]], non-glycosylé, produit dans des cellules ovariennes de hamster chinois (CHO)
acapatamab	inmunoglobulina scFv-scFv-scFc, anti-[*Homo sapiens* FOLH1 (folato hidrolasa, antígeno membranario específico de la prostata, PSMA)], y anti-[*Homo sapiens* CD3E (CD3 épsilon, Leu-4)], anticuerpo monoclonal con cadena única (scFv)2-scFc, biespecífica; IG con cadena única scFv-scFv-scFc, anti FOLH1 y anti-CD3E (1-986) [scFv-VH-V-kappa anti-FOLH1 (1-243) [VH (*Homo sapiens* IGHV3-11*01 G49>C (84.7%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -15-mer-tris(tetraglicil-seril) linker (122-136)-V-KAPPA (*Homo sapiens* IGKV1-16*01 (79.3%) -IGKJ2*01 Q120>C (236) (90.9%)) CDR-IMGT [6.3.9] (163-168.186-188.225-233) (137-243)] -6-mer-seril-tetraglicil-seril linker (244-249) -scFv-VH-V-lambda anti-CD3E (250-498) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87.0%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (275-282.300-309.348-363) (250-374) -15-mer-tris(tetraglicil-seril) linker (375-389) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (415-423.441-443.480-488) (390-498)] -4-mer- tetraglicil linker (499-502) -scFc (h-CH2-CH3)-(h-CH2-CH3) (503-986) [*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (bisagra 6-15 (503-512), CH2 R83>C (574), N84.4>G (579), V85>C (584) (513-622), CH3 E12 (638), M14 (640) (623-727), CHS (728-729)) (503-729) -30-mer-hexakis(tetraglicil-seril) linker (730-759) -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (bisagra 6-15 (760-769), CH2 R83>C (831), N84.4>G (836), V85>C (841) (770-879), CH3 E12 (895), M14 (897) (880-984), CHS (985-986)) (760-986)]], no glicosilado, producido en las células ováricas de hámster chino (CHO)

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVESGGG LVKPGESLRL SCAASGFTFS DYYMYWVRQA PGKCLEWVAI  50
ISDGGYYTYY SDIIKGRFTI SRDNAKNSLY LQMNSLKAED TAVYYCARGF 100
PLLRHGAMDY WGQGTLVTVS SGGGGSGGGG SGGGGSDIQM TQSPSSLSAS 150
VGDRVTITCK ASQNVDTNVA WYQQKPGQAP KSLIYSASYV YWDVPSRFSG 200
SASGTDFTLT ISSVQSEDFA TYYCQQYDQQ LITFGCGTKL EIKSGGGGSE 250
VQLVESGGGL VQPGGSLKLS CAASGFTFNK YAMNWVRQAP GKGLEWVARI 300
RSKYNNYATY YADSVKDRFT ISRDDSKNTA YLQMNNLKTE DTAVYYCVRH 350
GNFGNSYISY WAYWGQGTLV TVSSGGGGSG GGGSGGGGSQ TVVTQEPSLT 400
VSPGGTVTLT CGSSTGAVTS GNYPNWVQQK PGQAPRGLIG GTKFLAPGTP 450
ARFSGSLLGG KAALTLSGVQ PEDEAEYYCV LWYSNRWVFG GGTKLTVLGG 500
GGDKTHTCPP CPAPELLGGP SVFLFPPKPK DTLMISRTPE VTCVVVDVSH 550
EDPEVKFNWY VDGVEVHNAK TKPCEEQYGS TYRCVSVLTV LHQDWLNGKE 600
YKCKVSNKAL PAPIEKTISK AKGQPREPQV YTLPPSREEM TKNQVSLTCL 650
VKGFYPSDIA VEWESNGQPE NNYKTTPPVL DSDGSFFLYS KLTVDKSRWQ 700
QGNVFSCSVM HEALHNHYTQ KSLSLSPGKG GGGSGGGGSG GGGSGGGGSG 750
GGGSGGGGSD KTHTCPPCPA PELLGGPSVF LFPPKPKDTL MISRTPEVTC 800
VVVDVSHEDP EVKFNWYVDG VEVHNAKTKP CEEQYGSTYR CVSVLTVLHQ 850
DWLNGKEYKC KVSNKALPAP IEKTISKAKG QPREPQVYTL PPSREEMTKN 900
QVSLTCLVKG FYPSDIAVEW ESNGQPENNY KTTPPVLDSD GSFFLYSKLT 950
VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL SLSPGK               986
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Post-translational modifications

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

Intra-V (C23 C104)	22-96	159-224	271-347	411-479	
Intra-C (C23-C104)	543-603	649-707	800-860	906-964	
Intra-CH2 (C83-C85)	574-584	831-841			
Inter-VH-VL (C49-C120)	44-236				
Inter-h11 (h 11 - h 11)	508-765				
Inter-h14 (h 14 - h 14)	511-768				

No N-glycosylation sites / pas de sites de N-glycosylation / ningún posición de N-glicosilación
CH2 N84.4>G:
579, 836
Aglycosylated

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
CHS K2:
986

adrenomedullinum pegolum #

adrenomedullin pegol

human adrenomedullin, C-terminal L-tyrosil amide, pegylated at *O*^{4} of Y^{1} with [(3*S*)-3-amino-4-{[(2R)-1-amino-3-{[(3*RS*)-2,5-dioxo-1-{3-oxo-3-[α-methyl(polyoxyethylene)-ω-amino]propyl}pyrrolidin-3-yl]sulfanyl}-1-oxopropan-2-yl]amino}-4-oxobutyl]carbamoyl; *O*$^{4.1}$-{[(3*S*)-3-amino-4-{[(2*R*)-1-amino-3-{[(3*RS*)-1-{3-[α-methylpoly(oxyethylene)-ω-amino]-3-oxopropyl}-2,5-dioxopyrrolidin-3-yl]sulfanyl}-1-oxopropan-2-yl]amino}-4-oxobutyl]carbamoyl}adrenomedullin (human)

adrénomedulline pégol

adrénomédulline humaine, L-tyrosil amide C-terminal, pégylée en *O*^{4} de Y^{1} avec [(3*S*)-3-amino-4-{[(2R)-1-amino-3-{[(3*RS*)-2,5-dioxo-1-{3-oxo-3-[α-méthyl(polyoxyéthylène)-ω-amino]propyl}pyrrolidin-3-yl]sulfanyl}-1-oxopropan-2-yl]amino}-4-oxobutyl]carbamoyle; *O*$^{4.1}$-({(3*S*)-3-amino-4-[(2*R*)-1-amino-3-{[(3*RS*)-1-{3-[α-méthylpoly(oxyéthylène)-ω-amino]-3-oxopropyl}-2,5-dioxopyrrolidin-3-yl]sulfanyl}-1-oxopropan-2-yl]-4-oxobutyl}carbamoyl)adrénomédulline (humaine)

adrenomedulina pegol

adrenomedulina humana, C-terminal L-tirosil amida, pegilada en *O*^{4} de Y^{1} con [(3*S*)-3-amino-4-{[(2R)-1-amino-3-{[(3*RS*)-2,5-dioxo-1-{3-oxo-3-[α-metil(polioxietileno)-ω-amino]propil}pirrolidin-3-il]sulfanil}-1-oxopropan-2-il]amino}-4-oxobutil]carbamoilo; *O*$^{4.1}$-({(3*S*)-3-amino-4-[(2*R*)-1-amino-3-{[(3*RS*)-1-{3-[α-metilpoli(oxietileno)-ω-amino]-3-oxopropil}-2,5-dioxopirrolidin-3-il]sulfanil}-1-oxopropan-2-il]-4-oxobutil}carbamoil)adrenomedulina (humana)

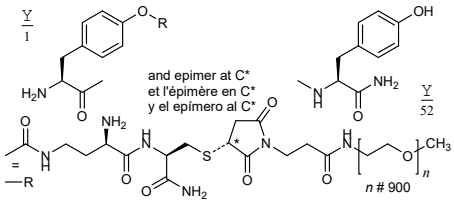
$C_{280}H_{430}N_{86}O_{83}S_4(C_2H_4O)_{\approx 900}$

Sequence / Séquence / Secuencia

YRQSMNNFQG LRSFGCRFGT CTVQKLAHQI YQFTDKDKDN VAPRSKISPQ 50
GY 52

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
36-86 43-89

Modified residues / Résidus modifiés / Restos modificados



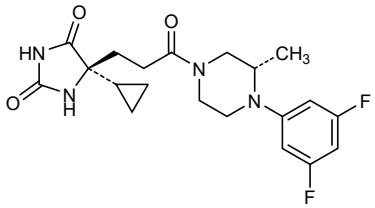
aldumastatum

aldumastat — (5*S*)-5-cyclopropyl-5-{3-[(3*S*)-4-(3,5-difluorophenyl)-3-methylpiperazin-1-yl]-3-oxopropyl}imidazolidine-2,4-dione

aldumastat — (5*S*)-5-cyclopropyl-5-{3-[(3*S*)-4-(3,5-difluorophényl)-3-méthylpipérazin-1-yl]-3-oxopropyl}imidazolidine-2,4-dione

aldumastat — (5*S*)-5-ciclopropil-5-{3-[(3*S*)-4-(3,5-difluorofenil)-3-metilpiperazin-1-il]-3-oxopropil}imidazolidina-2,4-diona

$C_{20}H_{24}F_2N_4O_3$



alnuctamabum #

alnuctamab — immunoglobulin G1-kappa/lambda with domain crossover, anti-[*Homo sapiens* TNFRSF17 (TNF receptor superfamily member 17, tumor necrosis factor receptor superfamily, member 17, B cell maturation antigen, BCMA, BCM, TNFRSF13A, CD269)] and anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], monoclonal antibody, bispecific, trivalent; gamma1-lambda heavy chain anti-TNFRSF17 and anti-CD3E (VH-CH1-V-lambda-CH1-h-CH2-CH3) (1-671) [VH anti-TNFRSF17 (*Homo sapiens* IGHV3-23*01 (94.9%) -(IGHD) -IGHJ5*01 (93.3%)) CDR-IMGT [8.8.9] (26-33.51-58.97-105) (1-116) -*Homo sapiens* IGHG1*01, G1m17 (CH1 K26>E (146), K119>E (212), K120 (213) (117-214), hinge 1-6 (215-220)) (117-220) -10-mer bis(tetraglycyl-seryl) linker (221-230) -V-LAMBDA anti-CD3E (*Mus musculus* IGLV1*01 (81.2%) -IGLJ1*01 (100%)/*Homo sapiens* IGLV7-46*01 (80.0%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (256-264.282-284.321-329) (231-339)) -2-mer diseryl linker (340-341) -*Homo sapiens* IGHG1*01 G1m17,1, G1v14 CH2 A1.3, A1.2, G1v32 CH3 W22 (CH1 K120 (438) (342-439), hinge 1-15 (440-454), CH2 L1.3>A (458), L1.2>A (459), P114>G (553) (455-564), CH3 S10>C (578), D12 (580), L14 (582), T22>W (590) (565-669), CHS (670-671)) (342-671)],

	(219-216')-disulfide with kappa light chain anti-TNFRSF17 (1'-216') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (90.6%) -IGKJ1*01 (91.7%)) CDR-IMGT [7.3.10] (27-33.51-53.90-99) (1'-109') -*Homo sapiens* IGKC*01 (98.1%) E12>R (125), Q13>K (126), Km3 A45.1 (155), V101 (193) (110'-216')]; (444-232''')-disulfide with VH-C-kappa light chain anti-CD3E, (1'''-232''') [VH (*Homo sapiens* IGHV3-23*03 (87.0%) -(IGHD) -IGHJ6*01 (90.9%)) CDR-IMGT [8.10.16] (26-33.51-60.99-114) (1'''-125''') -*Homo sapiens* IGKC*01 (99.1%) T1.3>S (127), Km3 A45.1 (171), V101 (209) (126'''-232''')]; gamma1 heavy chain anti-TNFRSF17 (1''-446'') [VH (*Homo sapiens* IGHV3-23*01 (94.9%) -(IGHD) -IGHJ5*01 (93.3%)) CDR-IMGT [8.8.9] (26-33.51-58.97-105) (1''-116'') -*Homo sapiens* IGHG1*01 G1m17,1, G1v14 CH2 A1.3, A1.2, G1v33 CH3 S22, A24, V86 (CH1 K26>E (146), K119>E (212), K120 (213) (117''-214''), hinge 1-15 (215''-229''), CH2 L1.3>A (233), L1.2>A (234), P114>G (328) (230''-339''), CH3 Y5>C (348), D12 (355), L14 (357), T22>S (365), L24>A (367), Y86>V (406) (340''-444''), CHS (445''-446'')) (117''-446'')], (219''-216'''')-disulfide with kappa light chain anti-TNFRSF17 (1''''-216'''') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (90.6%) -IGKJ1*01 (91.7%)) CDR-IMGT [7.3.10] (27-33.51-53.90-99) (1''''-109'''') -*Homo sapiens* IGKC*01 (98.1%) E12>R (125), Q13>K (126), Km3 A45.1 (155), V101 (193) (110''''-216'''')]; dimer (450-225'':453-228'':578-348'')-trisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa
alnuctamab	immunoglobuline G1-kappa/lambda avec domaines échangés, anti-[*Homo sapiens* TNFRSF17 (membre 17 de la superfamille des récepteurs du TNF, membre 17 de la superfamille des récepteurs du facteur de nécrose tumorale, antigène de maturation de cellule B, BCMA, BCM, TNFRSF13A, CD269)] et anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], anticorps monoclonal, bispécifique, trivalent; chaîne lourde gamma1 anti-TNFRSF17 et anti-CD3E (VH-CH1-V-lambda-CH1-h-CH2-CH3) (1-671) [VH anti-TNFRSF17 (*Homo sapiens* IGHV3-23*01 (94.9%) -(IGHD) -IGHJ4*01 (93.3%)) CDR-IMGT [8.8.9] (26-33.51-58.97-105) (1-116) -*Homo sapiens* IGHG1*01 G1m17 (CH1 K26>E (146), K119>E (212), K120 (213) (117-214), charnière 1-6 (215-220)) (117-220) -10-mer bis(tétraglycyl-séryl) linker (221-230) -V-LAMBDA anti-CD3E (*Mus musculus* IGLV1*01 (81.2%) -IGLJ1*01 (100%)/*Homo sapiens* (IGLV7-46*01 (80.0%) -IGLJ3*02 (100%) CDR-IMGT [9.3.9] (256-264.282-284.321-329) (231-339)) -2-merdiséryl linker (340-341) -*Homo sapiens* IGHG1*01 G1m17,1,G1v14 CH2 A1.3, A1.2, G1v32 CH3 W22 (CH1 K120 (438) (342-439), charnière 1-15 (440-454), CH2 L1.3>A (458), L1.2>A (459), P114>G (553) (455-564), CH3 S10>C (578), D12 (580), L14 (582), T22>W (590) (565-669), CHS (670-671)) (342-671)], (219-216')-disulfure avec la chaîne légère kappa anti-TNFRSF17 (1'-216') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (90.6%) -IGKJ1*01 (91.7%)) CDR-IMGT [7.3.10] (27-33.51-53.90-99) (1'-109') -*Homo sapiens* IGKC*01 (98.1%) E12>R (125), Q13>K (126), Km3 A45.1 (155), V101 (193) (110'-216')]; (444-232')-disulfure avec la chaîne légère VH-C-kappa anti-CD3E (1'''-232''') [VH (*Homo sapiens* IGHV3-23*03 (87.0%) -IGHJ6*01 (90.9%)) CDR-IMGT [8.10.16] (26-33.51-60.99-114) (1'''-125''') -*Homo sapiens* IGKC*01 (99.1%) T1.3>S (127), Km3 A45.1 (171), V101 (209) (126'''-232''')];

	chaîne lourde gamma1 anti-TNFRSF17 (1''-446'') [VH (*Homo sapiens* IGHV3-23*01 (94.9%) -(IGHD) -IGHJ4*01 (93.3%)) CDR-IMGT [8.8.9] (26-33.51-58.97-105) (1''-116'') -*Homo sapiens* IGHG1*01 G1m17,1, G1v14 CH2 A1.3, A1.2, G1v33 CH3 S22, A24, V86 (CH1 K26>E (146), K119>E (212), K120 (213) (117''-214''), charnière 1-15 (215''-229''), CH2 L1.3>A (233), L1.2>A (234), P114>G (328) (230''-339''), CH3 Y5>C (348), D12 (355), L14 (357), T22>S (365), L24>A (367), Y86>V (406) (340''-444''), CHS (445''-446'')) (117''-446'')], (219''-216'''')-disulfure avec la chaîne légère kappa anti-TNFRSF17 (1''''-216'''') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (90.6%) -IGKJ1*01 (91.7%)) CDR-IMGT [7.3.10] (27-33.51-53.90-99) (1''''-109'''') -*Homo sapiens* IGKC*01 (98.1%) E12>R (125), Q13>K (126), Km3 A45.1 (155), V101 (193) (110''''-216'''')]; dimère (450-225'':453-228'':578-348'')-trisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa
alnuctamab	inmunoglobulina G1-kappa/lambda con dominios cruzados, anti-[*Homo sapiens* TNFRSF17 (miembro 17 de la superfamilia de los receptores del TNF, miembro 17 de la superfamilia de los receptores del factor de necrosis tumoral, antígeno de maduración de célula B, BCMA, BCM, TNFRSF13A, CD269)] y anti-[*Homo sapiens* CD3E (CD3 épsilon, Leu-4)], anticuerpo monoclonal, biespecífico, trivalente; cadena pesada gamma1 anti-TNFRSF17 y anti-CD3E (VH-CH1-V-lambda-CH1-h-CH2-CH3) (1-671) [VH anti-TNFRSF17 (*Homo sapiens* IGHV3-23*01 (94.9%) -(IGHD) -IGHJ4*01 (93.3%)) CDR-IMGT [8.8.9] (26-33.51-58.97-105) (1-116) -*Homo sapiens* IGHG1*01 G1m17 (CH1 K26>E (146), K119>E (212), K120 (213) (117-214), bisagra 1-6 (215-220)) (117-220) -10-mer bis(tetraglicil-seril) linker (221-230) -V-LAMBDA anti-CD3E (*Mus musculus* IGLV1*01 (81.2%) -IGLJ1*01 (100%)/*Homo sapiens* (IGLV7-46*01 (80.0%) -IGLJ3*02 (100%) CDR-IMGT [9.3.9] (256-264.282-284.321-329) (231-339)) -2-merdiseril linker (340-341) -*Homo sapiens* IGHG1*01 G1m17,1,G1v14 CH2 A1.3, A1.2, G1v32 CH3 W22 (CH1 K120 (438) (342-439), bisagra 1-15 (440-454), CH2 L1.3>A (458), L1.2>A (459), P114>G (553) (455-564), CH3 S10>C (578), D12 (580), L14 (582), T22>W (590) (565-669), CHS (670-671)) (342-671)], (219-216')-disulfuro con la cadena ligera kappa anti-TNFRSF17 (1'-216') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (90.6%) -IGKJ1*01 (91.7%)) CDR-IMGT [7.3.10] (27-33.51-53.90-99) (1'-109') -*Homo sapiens* IGKC*01 (98.1%) E12>R (125), Q13>K (126), Km3 A45.1 (155), V101 (193) (110'-216')]; (444-232')-disulfuro con la cadena ligera VH-C-kappa anti-CD3E (1'''-232''') [VH (*Homo sapiens* IGHV3-23*03 (87.0%) -IGHJ6*01 (90.9%)) CDR-IMGT [8.10.16] (26-33.51-60.99-114) (1'''-125''') -*Homo sapiens* IGKC*01 (99.1%) T1.3>S (127), Km3 A45.1 (171), V101 (209) (126'''-232''')]; cadena pesada gamma1 anti-TNFRSF17 (1''-446'') [VH (*Homo sapiens* IGHV3-23*01 (94.9%) -(IGHD) -IGHJ4*01 (93.3%)) CDR-IMGT [8.8.9] (26-33.51-58.97-105) (1''-116'') -*Homo sapiens* IGHG1*01 G1m17,1, G1v14 CH2 A1.3, A1.2, G1v33 CH3 S22, A24, V86 (CH1 K26>E (146), K119>E (212), K120 (213) (117''-214''), bisagra 1-15 (215''-229''), CH2 L1.3>A (233), L1.2>A (234), P114>G (328) (230''-339''), CH3 Y5>C (348), D12 (355), L14 (357), T22>S (365), L24>A (367), Y86>V (406) (340''-444''), CHS (445''-446'')) (117''-446'')], (219''-216'''')-disulfuro con la cadena ligera kappa anti-TNFRSF17 (1''''-216'''') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (90.6%) -IGKJ1*01 (91.7%)) CDR-IMGT [7.3.10] (27-33.51-53.90-99) (1''''-109'''') -*Homo sapiens* IGKC*01 (98.1%) E12>R (125), Q13>K (126), Km3 A45.1 (155), V101 (193) (110''''-216'''')]; dímero (450-225'':453-228'':578-348'')-trisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada (1-671 anti-TNFRSF17 and anti-CD3)

```
EVQLLESGGG LVQPGGSLRL SCAASGFTFS DNAMGWVRQA PGKGLEWVSA  50
ISGPGSSTYY ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKVL 100
GWFDYWGQGT LVTVSSASTK GPSVFPLAPS SKSTSGGTAA LGCLVEDYFP 150
EPVTVSWNSG ALTSGVHTFP AVLQSSGLYS LSSVVTVPSS SLGTQTYICN 200
VNHKPSNTKV DEKVEPKSCD GGGGSGGGGS QAVVTQEPSL TVSPGGTVTL 250
TCGSSTGAVT TSNYANWVQE KPGQAFRGLI GGTNKRAPGT PARFSGSLLG 300
GKAALTLSGA QPEDEAEYYC ALWYSNLWVF GGGTKLTVLS SASTKGPSVF 350
PLAPSSKSTS GGTAALGCLV KDYFPEPVTV SWNSGALTSG VHTFPAVLQS 400
SGLYSLSSVV TVPSSSLGTQ TYICNVNHKP SNTKVDKKVE PKSCDKTHTC 450
PPCPAPEAAG GPSVFLFPPK PKDTLMISRT PEVTCVVVDV SHEDPEVKFN 500
WYVDGVEVHN AKTKPREEQY NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK 550
ALGAPIEKTI SKAKGQPREP QVYTLPPCRD ELTKNQVSLW CLVKGFYPSD 600
IAVEWESNGQ PENNYKTTPP VLDSDGSFFL YSKLTVDKSR WQQGNVFSCS 650
VMHEALHNHY TQKSLSLSPG K                                 671
```

Heavy chain / Chaîne lourde / Cadena pesada (1"-446" anti-TNFRSF17)

```
EVQLLESGGG LVQPGGSLRL SCAASGFTFS DNAMGWVRQA PGKGLEWVSA  50
ISGPGSSTYY ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKVL 100
GWFDYWGQGT LVTVSSASTK GPSVFPLAPS SKSTSGGTAA LGCLVEDYFP 150
EPVTVSWNSG ALTSGVHTFP AVLQSSGLYS LSSVVTVPSS SLGTQTYICN 200
VNHKPSNTKV DEKVEPKSCD KTHTCPPCPA PEAAGGPSVF LFPPKPKDTL 250
MISRTPEVTC VVVDVSHEDP EVKFNWYVDG VEVHNAKTKP REEQYNSTYR 300
VVSVLTVLHQ DWLNGKEYKC KVSNKALGAP IEKTISKAKG QPREPQVCTL 350
PPSRDELTKN QVSLSCAVKG FYPSDIAVEW ESNGQPENNY KTTPPVLDSD 400
GSFFLVSKLT VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL SLSPGK     446
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Light chain / Chaîne légère / Cadena ligera (1'-216' and 1'"-216"" anti-TNFRSF17)

```
EIVLTQSPGT LSLSPGERAT LSCRASQSVS DEYLSWYQQK PGQAPRLLIH  50
SASTRATGIP DRFSGSGSGT DFTLAISRLE PEDFAVYYCQ QYGYPPDFTF 100
GQGTKVEIKR TVAAPSVFIF PPSDRKLKSG TASVVCLLNN FYPREAKVQW 150
KVDNALQSGN SQESVTEQDS KDSTYSLSST LTLSKADYEK HKVYACEVTH 200
QGLSSPVTKS FNRGEC                                      216
```

Light chain / Chaîne légère / Cadena ligera (1'"-232"" anti-CD3E)

```
EVQLLESGGG LVQPGGSLRL SCAASGFTFS TYAMNWVRQA PGKGLEWVSR  50
IRSKYNNYAT YYADSVKGRF TISRDDSKNT LYLQMNSLRA EDTAVYYCVR 100
HGNFGNSYVS WFAYWGQGTL VTVSSASVAA PSVFIFPPSD EQLKSGTASV 150
VCLLNNFYPR EAKVQWKVDN ALQSGNSQES VTEQDSKDST YSLSSTLTLS 200
KADYEKHKVY ACEVTHQGLS SPVTKSFNRG EC                    232
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 143-199 252-320 368-424 485-545 591-649
22"-96" 143"-199" 260"-320" 366"-424"
Intra-L (C23-C104) 23'-89' 136'-196'
22'"-98"" 152'"-212'"
23'"-89'"" 136'"-196'""
Inter-H-L (h 5-CL 126) 219-216' 444-232'" 219"-216""
Inter-H-H (h 11, h 14) 450-225" 453-228"
Inter-H-H engineered 578-348"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
521, 296"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
671, 446"

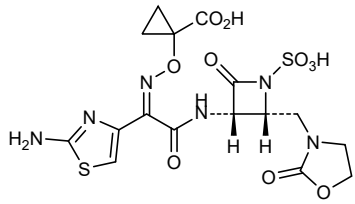
ancremonamum

ancremonam — 1-({(*Z*)-[1-(2-amino-1,3-thiazol-4-yl)-2-oxo-2-({(3*S*,4*R*)-2-oxo-4-[(2-oxo-1,3-oxazolidin-3-yl)methyl]-1-sulfoazetidin-3-yl}amino)ethylidene]amino}oxy) cyclopropane-1-carboxylic acid

ancrémonam — acide1-({(*Z*)-[1-(2-amino-1,3-thiazol-4-yl)-2-oxo-2-({(3*S*,4*R*)-2-oxo-4-[(2-oxo-1,3-oxazolidin-3-yl)méthyl]-1-sulfoazétidin-3-yl}amino)éthylidène]amino}oxy) cyclopropane-1-carboxylique

ancremonam — ácido1-({(*Z*)-[1-(2-amino-1,3-tiazol-4-il)-2-oxo-2-({(3*S*,4*R*)-2-oxo-4-[(2-oxo-1,3-oxazolidin-3-il)metil]-1-sulfoazetidin-3-il}amino)etilideno]amino}oxi) ciclopropano-1-carboxílico

$C_{16}H_{18}N_6O_{10}S_2$



apitegromabum #

apitegromab	immunoglobulin G4-lambda, anti-[*Homo sapiens* pro-MSTN (pro-growth differentiation factor 8, pro-GDF8, pro-myostatin, pro-GDF-8)], *Homo sapiens* monoclonal antibody; gamma4 heavy chain *Homo sapiens* (1-452) [VH (*Homo sapiens* IGHV3-30*03 (100%) -(IGHD) - IGHJ6*01 (94.4%)) CDR-IMGT [8.8.19] (26-33.51-58.97-115) (1-126)-*Homo sapiens* IGHG4*01, G4v5 h P10 (CH1 (127-224), hinge 1-12 S10>P (234) (225-236), CH2 (237-346), CH3 (347-451), CHS K>del (452)) (127-452)], (140-214')-disulfide with lambda light chain *Homo sapiens* (1'-215') [V-LAMBDA (*Homo sapiens* IGLV1-44*01 (98%) -IGLJ2*01 (100%)) CDR-IMGT [8.3.10] (26-33.51-53.90-99) (1'-109') -*Homo sapiens* IGLC2*01 (100%) (110'-215')]; dimer (232-232":235-235")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa
apitégromab	immunoglobuline G4-lambda, anti-[*Homo sapiens* pro-MSTN (pro-facteur de croissance et de différenciation 8, pro-GDF8, pro-myostatine, pro-GDF-8)], anticorps monoclonal *Homo sapiens*; chaîne lourde gamma4 *Homo sapiens* (1-452) [VH (*Homo sapiens* IGHV3-30*03 (100%) -(IGHD) - IGHJ6*01 (94.4%)) CDR-IMGT [8.8.19] (26-33.51-58.97-115) (1-126)-*Homo sapiens* IGHG4*01, G4v5 h P10 (CH1 (127-224), charnière 1-12 S10>P (234) (225-236), CH2 (237-346), CH3 (347-451), CHS K>del (452)) (127-452)], (140-214')-disulfure avec la chaîne légère lambda *Homo sapiens* (1'-215') [V-LAMBDA (*Homo sapiens* IGLV1-44*01 (98%) -IGLJ2*01 (100%)) CDR-IMGT [8.3.10] (26-33.51-53.90-99) (1'-109') -*Homo sapiens* IGLC2*01 (100%) (110'-215')]; dimère (232-232":235-235")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa
apitegromab	inmunoglobulina G4-lambda, anti-[*Homo sapiens* pro-MSTN (pro-factor de crecimiento y de diferenciación 8, pro-GDF8, pro-miostatina, pro-GDF-8)], anticuerpo monoclonal *Homo sapiens*;

cadena pesada gamma4 *Homo sapiens* (1-452) [VH (*Homo sapiens* IGHV3-30*03 (100%) -(IGHD) - IGHJ6*01 (94.4%)) CDR-IMGT [8.8.19] (26-33.51-58.97-115) (1-126)-*Homo sapiens* IGHG4*01, G4v5 h P10 (CH1 (127-224), bisagra 1-12 S10>P (234) (225-236), CH2 (237-346), CH3 (347-451), CHS K>del (452)) (127-452)], (140-214')-disulfuro con la cadena ligera lambda *Homo sapiens* (1'-215') [V-LAMBDA (*Homo sapiens* IGLV1-44*01 (98%) -IGLJ2*01 (100%)) CDR-IMGT [8.3.10] (26-33.51-53.90-99) (1'-109') - *Homo sapiens* IGLC2*01 (100%) (110'-215')]; dímero (232-232":235-235")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVESGGG VVQPGRSLRL SCAASGFTFS SYGMHWVRQA PGKGLEWVAV  50
ISYDGSNKYY ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARDL 100
LVRFLEWSHY YGMDVWGQGT TVTVSSASTK GPSVFPLAPC SRSTSESTAA 150
LGCLVKDYFP EPVTVSWNSG ALTSGVHTFP AVLQSSGLYS LSSVVTVPSS 200
SLGTKTYTCN VDHKPSNTKV DKRVESKYGP PCPPCPAPEF LGGPSVFLFP 250
PKPKDTLMIS RTPEVTCVVV DVSQEDPEVQ FNWYVDGVEV HNAKTKPREE 300
QFNSTYRVVS VLTVLHQDWL NGKEYKCKVS NKGLPSSIEK TISKAKGQPR 350
EPQVYTLPPS QEEMTKNQVS LTCLVKGFYP SDIAVEWESN GQPENNYKTT 400
PPVLDSDGSF FLYSRLTVDK SRWQEGNVFS CSVMHEALHN HYTQKSLSLS 450
LG                                                      452
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Light chain / Chaîne légère / Cadena ligera

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QSVLTQPPSA SGTPGQRVTI SCSGSSSNIG SNTVHWYQQL PGTAPKLLIY  50
SDNQRPSGVP DRFSGSKSGT SASLAISGLQ SEDEADYYCA AWDDSLNGVF 100
GGGTKLTVLG QPKAAPSVTL FPPSSEELQA NKATLVCLIS DFYPGAVTVA 150
WKADSSPVKA GVETTTPSKQ SNNKYAASSY LSLTPEQWKS HRSYSCQVTH 200
EGSTVEKTVA PTECS                                        215
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 153-209 267-327 373-431
22"-96" 153"-209" 267"-327" 373"-431"
Intra-L (C23-C104) 22'-89' 137'-196'
22'"-89'" 137'"-196'"
Inter-H-L (h 10-CL 126) 140-214' 140"-214'"
Inter-H-H (h 8, h 11) 232-232" 235-235"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"
L VL Q1:
1', 1'"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
303, 303"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

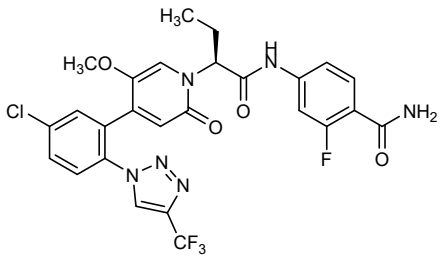
asundexianum

asundexian — (4*S*)-2^4-chloro-4-ethyl-7^3-fluoro-3^5-methoxy-3^2,5-dioxo-1^4-(trifluoromethyl)-3^2*H*-6-aza-3(4,1)-pyridina-1(1)-[1,2,3]triazola-2(1,2),7(1)-dibenzenaheptaphane-7^4-carboxamide

asundexian — (4*S*)-2^4-chloro-4-éthyl-7^3-fluoro-3^5-méthoxy-3^2,5-dioxo-1^4-(trifluorométhyl)-3^2*H*-6-aza-3(4,1)-pyridina-1(1)-[1,2,3]triazola-2(1,2),7(1)-dibenzénaheptaphane-7^4-carboxamide

asundexián — (4*S*)-2^4-cloro-4-etil-7^3-fluoro-3^5-metoxi-3^2,5-dioxo-1^4-(trifluorometil)-3^2*H*-6-aza-3(4,1)-piridina-1(1)-[1,2,3]triazola-2(1,2),7(1)-dibencenaheptafano-7^4-carboxamida

$C_{26}H_{21}ClF_4N_6O_4$



atidarsagenum autotemcelum #

atidarsagene autotemcel

Autologous CD34+ hematopoietic stem and progenitor cells transduced *ex vivo* with a replication-incompetent lentiviral vector encoding human arylsulfatase A (ARSA). Autologous CD34+ hematopoietic stem and progenitor cells (HSPC), obtained from bone marrow (BM) or mobilised peripheral blood (mPB), transduced *ex vivo* with a replication-incompetent pseudotyped HIV-1 based lentiviral vector encoding the human arylsulfatase A (ARSA) transgene under the control of a human phosphoglycerate kinase (PGK) promoter. The vector is pseudotyped with the vesicular stomatitis virus (VSV) envelope glycoprotein. The vector genome also contains a mutated Woodchuck hepatitis virus post-transcriptional regulatory element (WPRE), a fragment of the HIV-1 *gag,* the HIV-1 Rev response element (RRE), the HIV-1 central polypurine tract (cPPT) and a fragment of *nef*. The CD34+ cell population corresponds to an heterogenous population of stem and progenitor cells, some expressing the CD90 and/or CD133 markers.

atidarsagène autotemcel

Des cellules souches et progénitrices hématopoïétiques CD34+ autologues ont été transduites *ex vivo* avec un vecteur lentiviral incompétent à la réplication codant pour l'arylsulfatase A humaine (ARSA).
Des cellules souches et progénitrices hématopoïétiques CD34+ autologues (HSPC), obtenues à partir de moelle osseuse (BM) ou de sang périphérique mobilisé (mPB), ont été transduites *ex vivo* avec un vecteur lentiviral, à base de VIH-1 pseudotypé et incompétent à la réplication, codant pour le transgène de l'arylsulfatase A humaine (ARSA), sous le contrôle d'un promoteur de la phosphoglycérate kinase (PGK) humaine. Le vecteur est pseudotypé avec la glycoprotéine d'enveloppe du virus de la stomatite vésiculeuse (VSV). Le génome du vecteur contient également l'élément régulateur post-transcriptionnel Woodchuck (WPRE) du virus de l'hépatite, un fragment du *gag* du VIH-1, l'élément de réponse post-transcriptionnel (RRE) du VIH-1 et le tractus central de polypurine du VIH-1 (cPPT), ainsi qu'un fragment de *nef*. La population de cellules CD34+ correspond à une population hétérogène de cellules souches et progénitrices, certaines exprimant les marqueurs CD90 et/ou CD133.

atidarsagén autotemcel	Células troncales y progenitoras hematopoyéticas CD34+ autólogas transducidas *ex vivo* con un vector lentiviral incompetente en replicación que codifica para la arilsulfatasa A humana (ARSA). Las células troncales y progenitoras hematopoyéticas CD34+ autólogas, obtenidas de médula ósea o movilizadas de sangre periférica, se transducen *ex vivo* con un vector lentiviral basado en VIH-1 seudotipado y incompetente en replicación, que codifica el transgen de la arilsulfatasa A humana (ARSA) bajo el control de un promotor de la fosfoglicerato quinasa humana (PGK). El vector está seudotipado con la glicoproteína de la envuelta del virus de la estomatitis vesicular (VSV). El genoma del vector también contiene el elemento regulador post-transcipcional del virus de la hepatitis de la marmota (WPRE), un fragmento de *gag* del VIH-1, un elemento de respuesta post-transcripcional (RRE) del VIH-1 y un tramo central de poli-purinas (cPPT) de VIH-1, así como un fragmento de *nef*. La población de células CD34+corresponde en una población de celulas troncales y progenitoras, algunas expressando los marcadores CD90 y/o CD133.
avipendekinum pegolum #	
avipendekin pegol	human L-methionyl-interleukin 15, produced in *Escherichia coli*, pegylated at N^2 of Met^1 and N^6 of Lys residues with 4-[α-methylpoly(oxyethylene)-ω-oxy]butanoyl groups; L-methionyl-interleukin 15 (human, non-glycosylated), produced in *Escherichia coli*, substituted on an average of one site among N^2 of Met^1 and/or N^6 of lysyl residues with 4-[α-methylpoly(oxyethylene)-ω-oxy]butanoyl groups (~40 kDa each)
avipendékine pégol	L-méthionyl-interleukine 15 humaine, produite par *Escherichia coli*, pégylée en N^2 de Met^1 et N^6 des résidus Lys avec des groupes 4-[α-méthylpoly(oxyéthylène)-ω-oxy]butanoyle; L-méthionyl-interleukine 15 (humaine, non-glycosylée), produite dans *Escherichia coli*, substituée sur une moyenne d'un site parmi le N^2 du Met^1 et/ou N^6 des résidus lysyl par des groupes 4-[α-méthylpoly(oxyéthylène)-ω-oxy]butanoyle (~40 kDa chacun)
avipendekina pegol	L-metionil-interleukina 15 humana, producida en *Escherichia coli*, pegilada en N^2 de Met^1 y N^6 de residuos Lis con grupos 4-[α-metilpoli(oxietileno)-ω-oxi]butanoilo; L-metionil-interleukina 15 (humana, no glicosilada), producida en *Escherichia coli*, sustituida pro término medio de un sitio entre el N^2 del Met^1 y/o el N^6 de los residuos lisil por grupos 4-[α-metilpoli(oxietileno)-ω-oxi]butanoilo (~40 kDa cada uno)

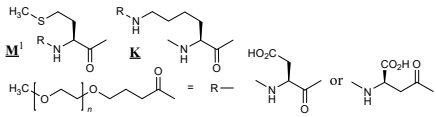
$C_{563}H_{898}N_{144}O_{185}S_8[C_5H_8O_2(C_2H_4O)_n]_x$ n ≈ 900, x ≈ 1

Sequence / Séquence / Secuencia

MNWVNVISDL **KK**IEDLIQSM HIDATLYTES DVHPSC**K**VTA M**K**CFLLELQV 50
ISLESGDASI HDTVENLIIL ANNSLSSNGN VTESGC**K**ECE ELEE**K**NI**K**EF 100
LQSFVHIVQM FINTS 115

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
36-86, 43-89
Partial deamidation / Désamidation partielle / Desamidación parcial
N78 (Asn>Asp, isoaspartyl)

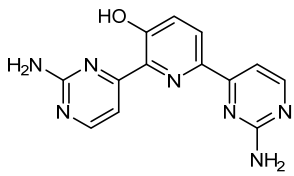
Modified residues / Résidus modifiés / Restos modificados
avipendekin : pegol ~ 1:1
M[1] (Met 1: ~32-40 %), **K** (Lys 11, 37, 42, 87: ~33-42 %; Lys 12, 95, 98: ~18-35 %)



avotaciclibum

avotaciclib	2,6-bis(2-aminopyrimidin-4-yl)pyridin-3-ol
avotaciclib	2,6-bis(2-aminopyrimidin-4-yl)pyridin-3-ol
avotaciclib	2,6-bis(2-aminopirimidin-4-il)piridin-3-ol

$C_{13}H_{11}N_7O$



azercabtagenum zapreleucelum #

azercabtagene zapreleucel

Adult allogeneic CD4+ and CD8+ enriched T cells transduced with an anti-CD19 chimeric antigen receptor (CAR) that is site-specific integrated into the cellular genome.
Adult allogeneic CD4+ and CD8+ enriched T cells, gene edited through the electroporation of homing endonuclease mRNA, which is translated into endonuclease protein that introduces a double-stranded DNA break in exon 1 of the endogenous T cell receptor alpha constant (TRAC) locus. Cells are subsequently transduced with a recombinant non-replicating adeno-associated virus type 6 (rAAV6) vector, encoding an anti-CD19 CAR transgene consisting of a murine CD19-specific scFv (clone FMC63), a CD8 hinge/transmembrane domain, a novel 6 (N6) co-stimulatory domain and CD3 zeta signaling domain, under the control of the synthetic promoter JeT and the SV40 poly(A) signal. CAR transgene integration is achieved via homology directed recombination at the endonuclease target site (exon 1 of TRAC). Depletion of CD3+ cells is performed on the

	transduced cells to remove cells with functional endogenous T cell receptor (TCR). The substance is a mixture of non-effector (naive, stem cell memory, central memory) (CCR7+) and effector memory and effector (CCR7-) CD4+ and CD8+ T cells with generally ≥99% T cell receptor knockout, and ≥40% anti-CD19 CAR knock-in. Activation of the cells is accompanied *in vitro* by release of IFNγ, IL-2, IL-6, and TNFα in an antigen-dependent manner.
azercabtagène zapréleucel	Lymphocytes T adultes allogéniques de type CD4+ et CD8+ transduits avec un récepteur d'antigène chimérique (CAR) anti-CD19 qui est intégré de manière spécifique au site. Lymphocytes T allogéniques enrichies en cellules de type CD4+ et CD8+, dont les gènes ont été édités par l'électroporation du mRNA de l'endonucléase de ciblage, qui est traduite en une protéine endonucléase qui introduit une rupture d'ADN double brin dans l'exon 1 du locus du récepteur alpha endogène aux cellules T (TRAC). Les cellules sont transduites ensuite avec un vecteur du virus recombinant adéno-associé, non réplicatif de type 6 (rAAV6), qui code pour un trangène anti-CD19 CAR, qui consiste en un scFv spécifique à CD19 (clone FMC63), un domaine CD8 transmembranaire/charnière, en un nouveau domaine de co-stimulation 6 (N6) et en un domaine de signalisation CD3 zêta, sous le contrôle du promoteur synthétique JeT et d'un signal poly(A) SV40. L'intégration du transgène CAR est obtenue via la recombinaison homologue dirigée au site de ciblage de l'endonucléase (l'exon 1 du TRAC). La déplétion des cellules CD3+ est effectuée sur les cellules transduites pour éliminer les cellules avec des récepteurs T (TCR) endogènes. La substance est un mélange de lymphocytes T non-effecteurs (naïfs, cellules souches mémoire, mémoire centrale) (CCR7+) et lymphocytes T mémoire effecteurs et effecteurs (CCR7-) CD4+ et CD8+ avec en général ≥99% de récepteurs des lymphocytes T knock-out et ≥40% de CAR anti-CD19 knock-in. L'activation des cellules est accompagnée *in vitro* par le relâchement d'IFNγ, IL-2, IL-6, et TNFα d'une manière antigène-dépendante.
azercabtagén zapreleucel	Linfocitos T adultos, alogénicos, enriquecidos en CD4+ y CD8+, transducidos con un receptor de antígenos quimérico (CAR) anti-CD19 que se integra en el genoma celular de forma específica de sitio. Linfocitos T adultos, alogénicos, enriquecidos en CD4+ y CD8+, con genes editados mediante la electroporación del ARNm de una endonucleasa de homing, que se traduce a una proteína endonucleasa que introduce una rotura en el ADN de doble cadena en el exón 1 del locus de la región constante del receptor alfa de células T endógenas (TRAC). Las células son posteriormente transducidas con un vector recombinante, no replicativo, de virus adeno-asociado tipo 6 (rAAV6) que codifica para un transgén de CAR anti-CD19 que consiste en un scFv murino nti-CD19 (clon FMC63), un dominio bisagra/transmenbrana

	CD8, un nuevo dominio de co-estimulación 6 (N6) y el dominio de señalización CD3 zeta, bajo el control del promotor sintético JeT y la señal poly(A) del SV40. La integración del transgén CAR se consigue mediante recombinación homóloga dirigida en el sitio diana de la endonucleasa (exón 1 de TRAC). Se realiza la depleción de células CD3+ en las células transducidas para eliminar las células con un receptor de células T (TCR) endógeno funcional. La sustancia es una mezcla de linfocitos T no efectores (ingenuos, células troncales memoria, memoria central) (CCR7+) y linfocitos T memoria efectores y efectores (CCR7-) CD4+ y CD8+ con en general ≥99% de receptores de linfocitos T (TCR) knock-out y ≥40% de CAR anti-CD19 knock-in. La activación de las células está acompañada *in vitro* por la liberación de IFNγ, IL-2, IL-6, y TNFα de una manera antígeno-dependiente.
bapotulimabum #	
bapotulimab	immunoglobulin G2-kappa, anti-[*Homo sapiens* ILDR2 (immunoglobulin like domain containing receptor 2, C1orf32)], *Homo sapiens* monoclonal antibody; gamma2 heavy chain *Homo sapiens* (1-445) [VH (*Homo sapiens* IGHV1-69*10 (100%) -(IGHD) -IGHJ5*01 (81.2%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG2*01, G2m.. CH2 V45.1 (CH1 (121-218), hinge 1-12 (219-230), CH2 V45.1 (281) (231-339), CH3 (340-444), CHS K>del (445)) (121-445)], (134-219')-disulfide with kappa light chain *Homo sapiens* (1'-219') [V-KAPPA (*Homo sapiens* IGKV2-28*01 (99%) -IGKJ4*01 (83.3%)) CDR-IMGT [11.3.9] (27-37.55-57.94-102) (1'-112') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (158), V101 (196) (113'-219')]; dimer (222-222":223-223":226-226":229-229")-tetrakisdisulfide, produced in a Chinese hamster ovary (CHO)-derived cell line, glycoform alfa
bapotulimab	immunoglobuline G2-kappa, anti-[*Homo sapiens* ILDR2 (récepteur 2 contenant un domaine immunoglobuline-like, C1orf32)], anticorps monoclonal *Homo sapiens*; chaîne lourde gamma2 *Homo sapiens* (1-445) [VH (*Homo sapiens* IGHV1-69*10 (100%) -(IGHD) -IGHJ5*01 (81.2%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG2*01, G2m.. CH2 V45.1 (CH1 (121-218), charnière 1-12 (219-230), CH2 V45.1 (281) (231-339), CH3 (340-444), CHS K>del (445)) (121-445)], (134-219')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-219') [V-KAPPA (*Homo sapiens* IGKV2-28*01 (99%) -IGKJ4*01 (83.3%)) CDR-IMGT [11.3.9] (27-37.55-57.94-102) (1'-112') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (158), V101 (196) (113'-219')]; dimère (222-222":223-223":226-226":229-229")-tétrakisdisulfure, produite dans une lignée cellulaire dérivée des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

bapotulimab

inmunoglobulina G2-kappa, anti-[*Homo sapiens* ILDR2 (receptor 2 que contiene un dominio inmunoglobulina-like, C1orf32)], anticuerpo monoclonal *Homo sapiens*;
cadena pesada gamma2 *Homo sapiens* (1-445) [VH (*Homo sapiens* IGHV1-69*10 (100%) -(IGHD) -IGHJ5*01 (81.2%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG2*01, G2m.. CH2 V45.1 (CH1 (121-218), bisagra 1-12 (219-230), CH2 V45.1 (281) (231-339), CH3 (340-444), CHS K>del (445)) (121-445)], (134-219')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-219') [V-KAPPA (*Homo sapiens* IGKV2-28*01 (99%) -IGKJ4*01 (83.3%)) CDR-IMGT [11.3.9] (27-37.55-57.94-102) (1'-112') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (158), V101 (196) (113'-219')];
dímero (222-222":223-223":226-226":229-229")-tetrakisdisulfuro, producido en una línea celular derivada de las células ováricas de hamster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG  50
IIPILGIANY AQKFQGRVTI TADKSTSTAY MELSSLRSED TAVYYCARGR 100
LPYGDFWDSW GQGTLVTVSS ASTKGPSVFP LAPCSRSTSE STAALGCLVK 150
DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSNFGTQT 200
YTCNVDHKPS NTKVDKTVER KCCVECPPCP APPVAGPSVF LFPPKPKDTL 250
MISRTPEVTC VVVDVSHEDP EVQFNWYVDG VEVHNAKTKP REEQFNSTFR 300
VVSVLTVVHQ DWLNGKEYKC KVSNKGLPAP IEKTISKTKG QPREPQVYTL 350
PPSREEMTKN QVSLTCLVKG FYPSDIAVEW ESNGQPENNY KTTPPMLDSD 400
GSFFLYSKLT VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL SLSPG      445
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Light chain / Chaîne légère / Cadena ligera

```
DIVMTQSPLS LPVTPGEPAS ISCRSSQSLL YSNGYNYLDW YLQKPGQSPQ  50
LLIYLGSNRA SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCMQALQTP 100
LTFGGGTKLE IRRTVAAPSV FIFPPSDEQL KSGTASVVCL LNNFYPREAK 150
VQWKVDNALQ SGNSQESVTE QDSKDSTYSL SSTLTLSKAD YEKHKVYACE 200
VTHQGLSSPV TKSFNRGEC                                   219
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 147-203 260-320 366-424
22"-96" 147"-203" 260"-320" 366"-424"
Intra-L (C23-C104) 23'-93' 139'-199'
23'"-93'" 139'"-199'"
Inter-H-L (CH1 10-CL 126)* 134-219' 134"-219'"
Inter-H-H (h 4, h 5, h 8, h 11)* 222-222" 223-223" 226-226" 229-229"
*A-isoform, predominant

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"

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

barecetamabum #
barecetamab

immunoglobulin G1-lambda, anti-[*Homo sapiens* ERBB3 (receptor tyrosine-protein kinase erbB-3, HER3)], *Homo sapiens* monoclonal antibody;
gamma1 heavy chain *Homo sapiens* (1-451) [VH (*Homo sapiens* IGHV3-23*01 (90.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -*Homo sapiens* IGHG1*01, nG1m1, G1m17 (CH1 K120 (218) (122-219), hinge 1-15 (220-234), CH2 (235-344), CH3 E12 (360), M14 (362) (345-449), CHS (450-451)) (122-451)], (224-215')-disulfide with lambda light chain *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV1-47*02 (92.9%) -IGLJ2*01 (100%)) CDR-IMGT [8.3.11] (26-33.51-53.90-100) (1'-110') -*Homo sapiens* IGLC3*03 (100%) (111'-216')];
dimer (230-230":233-233")-bisdisulfide, produced in Chinese hamster ovary (CHO)-K1 cell line, glycoform alfa

barécétamab

immunoglobuline G1-lambda, anti-[*Homo sapiens* ERBB3 (récepteur à activité tyrosine kinase erbB-3, HER3)], *Homo sapiens* anticorps monoclonal;
chaîne lourde gamma1 *Homo sapiens* (1-451) [VH (*Homo sapiens* IGHV3-23*01 (90.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -*Homo sapiens* IGHG1*01, nG1m1, G1m17 (CH1 K120 (218) (122-219), charnière 1-15 (220-234), CH2 (235-344), CH3 E12 (360), M14 (362) (345-449), CHS (450-451)) (122-451)], (225-215')-disulfure avec la chaîne légère lambda *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV1-47*02 (92.9%) -IGLJ2*01 (100%)) CDR-IMGT [8.3.11] (26-33.51-53.90-100) (1'-110') -*Homo sapiens* IGLC3*03 (100%) (111'-216')]; dimère (230-230":233-233")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-K1, glycoforme alfa

barecetamab

inmunoglobulina G1-lambda, anti-[*Homo sapiens* ERBB3 (receptor de la actividad tirosina kinasa erbB-3, HER3)], *Homo sapiens* anticuerpo monoclonal;
cadena pesada gamma1 *Homo sapiens* (1-451) [VH (*Homo sapiens* IGHV3-23*01 (90.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -*Homo sapiens* IGHG1*01, nG1m1, G1m17 (CH1 K120 (218) (122-219), bisagra 1-15 (220-234), CH2 (235-344), CH3 E12 (360), M14 (362) (345-449), CHS (450-451)) (122-451)], (225-215')-disulfuro con la cadena ligera lambda *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV1-47*02 (92.9%) -IGLJ2*01 (100%)) CDR-IMGT [8.3.11] (26-33.51-53.90-100) (1'-110') -*Homo sapiens* IGLC3*03 (100%) (111'-216')]; dímero (230-230":233-233")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-K1, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLLESGGG LVQPGGSLRL SCAASGFTFS DYDMSWVRQA PGKGLEWVST  50
IDLDSGSIYY ADSVQGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKDL 100
HMGPEGPFDY WGQGTLVTVS SASTKGPSVF PLAPSSKSTS GGTAALGCLV 150
KDYFPEPVTV SWNSGALTSG VHTFPAVLQS SGLYSLSSVV TVPSSSLGTQ 200
TYICNVNHKP SNTKVDKKVE 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

```
QSVLTQPPSA SGTPGQRVTI SCSGSSSNIG SNSVSWYQQL PGTAPKLLIY  50
SDNHRPSGVP DRFSGSKSGT SASLAISGLR SEDEADYYCQ GWDTSLSGHV 100
FGGGTKLTVL GQPKAAPSVT LFPPSSEELQ ANKATLVCLI SDFYPGAVTV 150
AWKADSSPVK AGVETTTPSK QSNNKYAASS YLSLTPEQWK SHKSYSCQVT 200
HEGSTVEKTV APTECS                                       216
```

Post-translational modifications
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) 22'-89' 138'-197'
22'"-89'" 138'"-197'"
Inter-H-L (h 5-CL 126) 224-215' 224"-215'"
Inter-H-H (h 11, h 14) 230-230" 233-233"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
L VL Q1:
1', 1'"

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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
451, 451"

batiraxceptum #

batiraxcept

human tyrosine-protein kinase receptor UFO (AXL oncogene) fragment (8-202, 1-195 in the current sequence), variant ($G^{14}>S^{7}$, $A^{54}>V^{47}$, $D^{69}>G^{62}$, $V^{74}>A^{67}$, $G^{109}>R^{102}$), fused via peptidyl linker (^{196}GGGGS^{200}) to a human immunoglobulin G1 Fc fragment (201-426, C-terminal Lys residue deleted), dimer, glycosylated, produced in Chinese hamster ovary (CHO) cells;
[$G^{14}>S(7)$, $A^{54}>V(47)$, $D^{69}>G(62)$, $V^{74}>A(67)$, $G^{109}>R(102)$] human AXL receptor tyrosine kinase (AXL oncogene, tyrosine-protein kinase receptor UFO) (8-202)-peptide (1-195), fused via a G_4S linker (196-200) to a human immunoglobulin G1 C-terminal K>del Fc fragment (201-426), dimer (206-206':209-209')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

batiraxcept

récepteur de la tyrosine kinase-protéine UFO (oncogène AXL), fragment (8-202, 1-195 dans la séquence présente), variant ($G^{14}>S^{7}$, $A^{54}>V^{47}$, $D^{69}>G^{62}$, $V^{74}>A^{67}$, $G^{109}>R^{102}$), fusionné via un peptide liant (^{196}GGGGS^{200}) à un fragment Fc de l'immunoglobuline humaine G1 (201-426, résidu Lys C-terminal supprimé), dimère, glycosylé, produit par des cellules ovariennes de hamsters chinois (CHO);
[$G^{14}>S(7)$, $A^{54}>V(47)$, $D^{69}>G(62)$, $V^{74}>A(67)$, $G^{109}>R(102)$] tyrosine kinase du récepteur AXL humaine (oncogène AXL, récepteur de la tyrosine kinase-protéine UFO) (8-202)-peptide (1-195), fusionné via un peptide liant G_4S (196-200) au fragment Fc C-terminal K>del de l'immunoglobuline G1 humaine (201-426), dimère (206-206':209-209')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

batiraxcept

receptor de la proteína tirosina kinasa humana UFO (oncogén AXL) fragmento (8-202, 1-195 en la secuencia actual), variante ($G^{14}>S^{7}$, $A^{54}>V^{47}$, $D^{69}>G^{62}$, $V^{74}>A^{67}$, $G^{109}>R^{102}$), fusionado a través de un conector peptidil (^{196}GGGGS^{200}) a una inmunoglobulina humana G1 Fc fragmento (201-426, residuo Lis C-terminal eliminado), dímero, glicosilado, producido en células ováricas de hámster Chino (CHO);
[$G^{14}>S(7)$, $A^{54}>V(47)$, $D^{69}>G(62)$, $V^{74}>A(67)$, $G^{109}>R(102)$] AXL receptor tirosina kinasa humana (oncogén AXL, receptor de la proteína tirosina-kinasa UFO) (8-202)-péptido (1-195), fusionado a través de un péptido G_4S (196-200) con un fragmento Fc C-terminal K>del de la inmunoglobulina G1 humana (201-426), dímero (206-206':209-209')-bisdisulfuro, producido en células ováricas de hámster Chino (CHO), glicosilada alfa

Sequence / Séquence / Secuencia

```
EESPFVSNPG NITGARGLTG TLRCQLQVQG EPPEVHWLRD GQILELVDST   50
QTQVPLGEDE QGDWIVASQL RITSLQLSDT GQYQCLVFLG HQTFVSQPGY  100
VRLEGLPYFL EEPEDRTVAA NTPFNLSCQA QGPPEPVDLL WLQDAVPLAT  150
APGHGPQRSL HVPGLNKTSS FSCEAHNAKG VTTSRTATIT VLPQQGGGGS  200
DKTHTCPPCP APELLGGPSV FLFPPKPKDT LMISRTPEVT CVVVDVSHED  250
PEVKFNWYVD GVEVHNAKTK PREEQYNSTY RVVSVLTVLH QDWLNGKEYK  300
CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSREEMTK NQVSLTCLVK  350
GFYPSDIAVE WESNGQPENN YKTTPPVLDS DGSFFLYSKL TVDKSRWQQG  400
NVFSCSVMHE ALHNHYTQKS LSLSPG                            426
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

intra-AXL	24-85	128-173	intra-Fc	241-301	347-405
	24'-85'	128'-173'		241'-301'	347'-405'
inter-Fc	206-206'	209-209'			

Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación
AXL: N11, N125, N166, N11', N125', N166';
Fc: N277, N277'

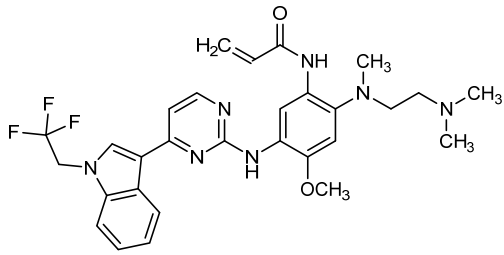
befotertinibum

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

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

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

$C_{29}H_{32}F_3N_7O_2$



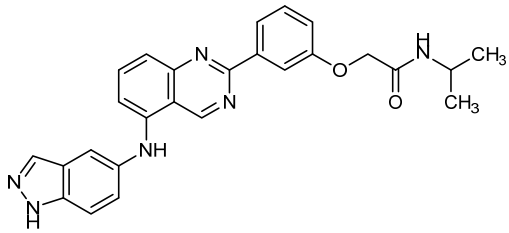
belumosudilum

belumosudil — 2-(3-{4-[(1*H*-indazol-5-yl)amino]quinazolin-2-yl}phenoxy)-*N*-(propan-2-yl)acetamide

bélumosudil — 2-(3-{4-[(1*H*-indazol-5-yl)amino]quinazolin-2-yl}phénoxy)-*N*-(propan-2-yl)acetamide

belumosudil — 2-(3-{4-[(1*H*-indazol-5-il)amino]quinazolin-2-il}fenoxi)-*N*-(propan-2-il)acetamida

$C_{26}H_{24}N_6O_2$



bentracimabum #

bentracimab — immunoglobulin Fab G1-lambda, anti-[*ticagrelor* and its active metabolite AR-C124910XX], *Homo sapiens* monoclonal antibody; VH-(CH1-hinge) gamma1 heavy chain *Homo sapiens* (1-234) [VH (*Homo sapiens* IGHV1-69*06 (85.7%) -(IGHD) -IGHJ1*01 (100%)) CDR-IMGT [8.7.14] (26-33.51-58.97-118) (1-129) -*Homo sapiens* IGHG1*03 (100%) G1m3 (CH1 R120 (226) (130-227), hinge 1-7 (228-234)) (130-234)], (232-215')-disulfide with lambda light chain *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV1-51*01 (94.6%) -IGLJ2*01 (81.8%)) CDR-IMGT [8.3.11] (26-33.51-53.90-100) (1'-110') -*Homo sapiens* IGLC2*01(100%) (111'-216')], non-glycosylated, produced in the bacteria *Escherichia coli* (*E. coli*)

bentracimab

immunoglobuline Fab G1-lambda, anti-[*ticagrelor* et son métabolite actif AR-C124910XX], anticorps monoclonal *Homo sapiens*;
VH-(CH1-charnière) chaîne lourde gamma1 *Homo sapiens* (1-234) [VH (*Homo sapiens* (1-234) [VH (*Homo sapiens* IGHV1-69*06 (85.7%) -(IGHD) -IGHJ1*01 (100%)) CDR-IMGT [8.7.14] (26-33.51-58.97-118) (1-129) -*Homo sapiens* IGHG1*03 (100%) G1m3 (CH1 R120 (226) (130-227), charnière 1-7 (228-234)) (130-234)], (232-215')-disulfure avec la chaîne légère lambda *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV1-51*01 (94.6%) -IGLJ2*01 (81.8%)) CDR-IMGT [8.3.11] (26-33.51-53.90-100) (1'-110') -*Homo sapiens* IGLC2*01(100%) (111'-216')], non-glycosylé, produit dans la bactérie *Escherichia coli* (*E. coli*)

bentracimab

inmunoglobulina Fab G1-lambda, anti-[*ticagrelor* y su metabolito activo AR-C124910XX], anticuerpo monoclonal *Homo sapiens*;
VH-(CH1-bisagra) cadena pesada gamma1 *Homo sapiens* (1-234) [VH (*Homo sapiens* (1-234) [VH (*Homo sapiens* IGHV1-69*06 (85.7%) -(IGHD) -IGHJ1*01 (100%)) CDR-IMGT [8.7.14] (26-33.51-58.97-118) (1-129) -*Homo sapiens* IGHG1*03 (100%) G1m3 (CH1 R120 (226) (130-227), bisagra 1-7 (228-234)) (130-234)], (232-215')-disulfuro con la cadena ligera lambda *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV1-51*01 (94.6%) -IGLJ2*01 (81.8%)) CDR-IMGT [8.3.11] (26-33.51-53.90-100) (1'-110') -*Homo sapiens* IGLC2*01(100%) (111'-216')], no glicosilado, producido en la bacteria *Escherichia coli* (*E. coli*)

Heavy chain / Chaîne lourde / Cadena pesada
```
QVQLQESGAE VKKPGSSVRV SCKASGGTFD SYSIHWVRQA PGQGLEWMGG  50
IIPAFGTLSS AQDFQARVTI SADKSTSTAY MELSGLRSED TAVYYCARGS 100
FDYYFWSASH PPNDALAIWG QGTLVTVSSA STKGPSVFPL APSSKSTSGG 150
TAALGCLVKD YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV 200
PSSSLGTQTY ICNVNHKPSN TKVDKRVEPK SCDK                  234
```

Light chain / Chaîne légère / Cadena ligera
```
QSVVTQPPSV SAAPGQKVTI SCSGSNSDIG NNYVSWYQQL PGTAPKLLIY  50
DNNKRPSGIP DRFSGSKSGT SATLAITGLQ AGDEADYYCG TWLYDRAVGL 100
FGGGTKVTVL GQPKAAPSVT LFPPSSEELQ ANKATLVCLI SDFYPGAVTV 150
AWKADSSPVK AGVETTTPSK QSNNKYAASS YLSLTPEQWK SHRSYSCQVT 200
HEGSTVEKTV APTECS                                      216
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 156-212
Intra-L (C23-C104) 22'-89' 138'-197'
Inter-H-L (h 5-CL 126) 232-215'

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
L VH Q1:
1
L VL Q1:
1'

No N-glycosylation site / pas de sites de N-glycosylation / ningùm posición de N-glycosilación
Agycosylated

bepirovirsenum

bepirovirsen

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

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

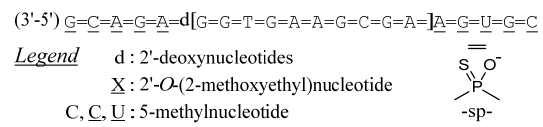
bépirovirsen

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

bepirovirsén

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

$C_{230}H_{309}N_{88}O_{115}P_{19}S_{19}$



beremagenum geperpavecum #

beremagene geperpavec

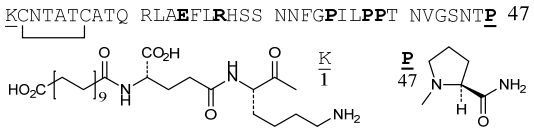
A replication-defective herpes simplex virus encoding human collagen type VII alpha 1 chain (COL7A1).

	A recombinant replication-defective, non-integrating herpes simplex virus-1 (HSV-1) (KOS strain) encoding two copies of human collagen type VII alpha 1 chain (COL7A1), inserted into the immediate early (IE) infected cell protein 4 (ICP4) gene regions after deletion of both copies of ICP4 genes, under the control of the human cytomegalovirus (hCMV) immediate early promoter and bovine growth hormone polyadenylation signal (bGHpA). The infected cell protein 22 (ICP22) gene is also deleted.
bérémagène géperpavec	Un virus herpès simplex à réplication défectueuse codant pour la chaîne du collagène humain de type VII alpha 1 (COL7A1). Un virus recombinant de l'herpès simplex-1 (HSV-1) (souche KOS), non intégrateur et à défaut de réplication, codant pour deux copies de la chaîne du collagène humain de type VII alpha 1 (COL7A1), insérées dans les régions du gène de la protéine d'infection cellulaire précoce 4 (ICP4) après délétion des deux copies des gènes ICP4, sous le contrôle du promoteur précoce immédiat du cytomégalovirus humain (hCMV) et du signal de polyadénylation de l'hormone de croissance bovine (bGHpA). Le gène de la protéine d'infection cellulaire précoce 22 (ICP22) est également supprimé.
beremagén geperpavec	Un virus herpes simplex deficiente para replicación que codifica para la cadena de colágeno humano de tipo VII alfa 1 (COL7A1). Un virus herpes simplex -1 (HSV-1) (cepa KOS) recombinante, no integrativo y deficiente en replicación, que codifica dos copias de la cadena de colágeno humano de tipo VII alfa 1 (COL7A1), insertadas en las regiones del gen de la proteína de infección celular inmediatamente temprana 4 (ICP4) tras la deleción de las dos copias de genes ICP4, bajo el control del promotor inmediatamente temprano del citomeglovirus humano (hCMV) y la señal de poliadenilación de la hormona de crecimiento bovina (bGHpA). El gen de la proteína de infección celular 22 (ICP22) está también delecionado.

cagrilintidum

cagrilintide	$N^{2.1}$-[*N*-(19-carboxynonadecanoyl)-L-γ-glutamyl]-[N^{14}>E, V^{17}>R, A^{25}>P, S^{28}>P, S^{29}>P, Y^{37}>P]-human amylin (islet amyloid polypeptide, IAPP, diabetes-associated peptide, DAP, insulinoma amyloid peptide, *INN: amlintide*), (35-40)-disulfide
cagrilintide	$N^{2.1}$-[*N*-(19-carboxynonadécanoyl)-L-γ-glutamyl]-[N^{14}>E, V^{17}>R, A^{25}>P, S^{28}>P, S^{29}>P, Y^{37}>P]-amyline humaine (polypeptide amyloïde des ilots, IAPP, peptide associé au diabète, DAP, polypeptide amyloïde de l'insulinome, *DCI: amlintide*), (35-40)-disulfure
cagrilintida	$N^{2.1}$-[*N*-(19-carboxinonadecanoil)-L-γ-glutamil]-[N^{14}>E, V^{17}>R, A^{25}>P, S^{28}>P, S^{29}>P, Y^{37}>P]-amilina humana (polipéptido amiloide de los islotes, IAPP, péptido asociado a la diabetes, DAP, polipéptido amiloide insulinoma, *DCI: amlintida*), (35-40)-disulfuro

$C_{194}H_{312}N_{54}O_{59}S_2$



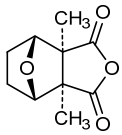
cantharidinum

cantharidin — (3a*R*,4*S*,7*R*,7a*S*)-3a,7a-dimethylhexahydro-4,7-epoxy-2-benzofuran-1,3-dione

cantharidine — (3a*R*,4*S*,7*R*,7a*S*)-3a,7a-diméthylhexahydro-4,7-époxy-2-benzofurane-1,3-dione

cantaridina — (3a*R*,4*S*,7*R*,7a*S*)-3a,7a-dimetilhexahidro-4,7-epoxi-2-benzofurano-1,3-diona

$C_{10}H_{12}O_4$



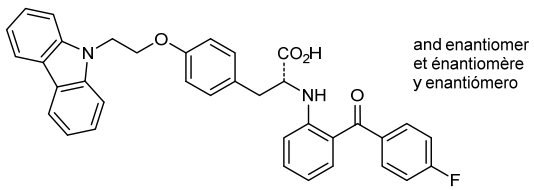
carfloglitazarum

carfloglitazar — *O*-[2-(9*H*-carbazol-9-yl)ethyl]-*N*-[2-(4-fluorobenzoyl)phenyl]-DL-tyrosine

carfloglitazar — *O*-[2-(9*H*-carbazol-9-yl)éthyl]-*N*-[2-(4-fluorobenzoyl)phényl]-DL-tyrosine

carfloglitazar — *O*-[2-(9*H*-carbazol-9-il)etil]-*N*-[2-(4-fluorobenzoil)fenil]-DL-tirosina

$C_{36}H_{29}FN_2O_4$



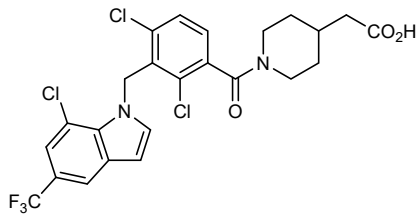
cedirogantum

cedirogant — [1-(2,4-dichloro-3-{[7-chloro-5-(trifluoromethyl)-1*H*-indol-1-yl]methyl}benzoyl)piperidin-4-yl]acetic acid

cédirogant — acide [1-(2,4-dichloro-3-{[7-chloro-5-(trifluorométhyl)-1*H*-indol-1-yl]méthyl}benzoyl)pipéridin-4-yl]acétique

cedirogant — ácido [1-(2,4-dicloro-3-{[7-cloro-5-(trifluorometil)-1*H*-indol-1-il]metil}benzoil)piperidin-4-il]acético

$C_{24}H_{20}Cl_3F_3N_2O_3$



cevaretigenum ritoparvovecum #

cevaretigene ritoparvovec

A non-replicating adeno-associated viral vector serotype 5 vector encoding human retinoid isomerohydrolase (RPE65).
A recombinant non-replicating adeno-associated viral vector serotype 5 (rAAV5), encoding codon-optimised human retinoid isomerohydrolase (retinal pigment epithelium-specific 65 kDa protein [RPE65]), under the control of the human RPE65 promoter and an SV40 poly(A) signal, flanked by AAV2 inverted terminal repeats (ITR).

cévarétigène ritoparvovec

Un vecteur adénoviral à réplication défectueuse de sérotype 5 et codant pour l'isomérohydrolase rétinoïde humaine (RPE65).
Un vecteur adénoviral recombinant à réplication défectueuse de sérotype 5 (rAAV5), codant pour une isomérohydrolase rétinoïde humaine, avec des codons optimisés (protéine de 65 kDa spécifique de l'épithélium pigmentaire rétinien [RPE65]), sous le contrôle du promoteur RPE65 humain et d'un signal SV40 poly(A), flanqué de répétitions terminales inversées (ITR) AAV2.

cevaretigén ritoparvovec

Un vector de virus adeno-asociado serotipo 5, no replicativo, que codifica para la isomerohidrolasa retinoide humana (RPE65).
Un vector de virus adeno-asociado recombinante serotipo 5, (rAAV5) no replicativo, que codifica para la isomerohidrolasa retinoide humana (proteína de 65 kDa específica del epitelio pigmentario retiniano [RPE65]) con los codones optimizados, bajo el control del promotor de RPE65 humano y una señal poly(A) de SV40, flanqueado por las repeticiones terminales invertidas (ITR) del AAV2.

cipaglucosidasum alfa #

cipaglucosidase alfa

human lysosomal α-glucosidase (acid alpha-glucosidase, acid maltase) fragment (57-952, 57-69 from the propeptide sequence), (1-896, 1-13 in the current sequence), produced in Chinese hamster ovary (CHO) cells, glycosylated;
human lysosomal α-glucosidase (acid alpha-glucosidase, GAA, acid maltase; EC 3.2.1.20) pre-pro-protein (57-952)-peptide (with 13 residues (57-69) of the propeptide (28-69)), produced in Chinese hamster ovary (CHO) cells, glycoform alfa

cipaglucosidase alfa

α-glucosidase lysosomale humaine (alpha-glucosidase acide, maltase acide) fragment (57-952, 57-69 de la séquence du propeptide), (1-896, 1-13 dans la séquence actuelle), produit dans des cellules ovariennes de hamster chinois (CHO), glycosylée;
α-glucosidase lysosomale humaine (alpha-glucosidase acide, GAA, maltase acide; EC 3.2.1.20) pré-pro-protéine (57-952)-peptide (avec 13 résidus (57-69) du propeptide (28-69)), produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

cipaglucosidasa alfa

α-glucosidasa humana lisosomal (ácido alfa-glucosidasa, ácido maltasa) fragmento (57-952, 57-69 de la secuencia propétido), (1-896, 1-13 en la secuencia actual), producido en células ováricas de hámster Chino (CHO), glisosiladas;
α-glucosidasa lisosomal humana (alfa glucosidasa ácida, GAA, maltasa ácida; EC 3.2.1.20) pre-pro-proteína (57-952)-péptido, (con 13 residuos (57-69) del propéptido (28-69)), producido en las células ováricas de hámster Chino (CHO), glicosilada alfa

Sequence / Séquence / Secuencia

```
QQGASRPGPR DAQAHPGRPR AVPTQCDVPP NSRFDCAPDK AITQEQCEAR   50
GCCYIPAKQG LQGAQMGQPW CFFPPSYPSY KLENLSSSEM GYTATLTRTT  100
PTFFPKDILT LRLDVMMETE NRLHFTIKDP ANRRYEVPLE TPHVHSRAPS  150
PLYSVEFSEE PFGVIVRRQL DGRVLLNTTV APLFFADQFL QLSTSLPSQY  200
ITGLAEHLSP LMLSTSWTRI TLWNRDLAPT PGANLYGSHP FYLALEDGGS  250
AHGVFLLNSN AMDVVLQPSP ALSWRSTGGI LDVYIFLGPE PKSVVQQYLD  300
VVGYPFMPPY WGLGFHLCRW GYSSTAITRQ VVENMTRAHF PLDVQWNDLD  350
YMDSRRDFTF NKDGFRDFPA MVQELHQGGR RYMMIVDPAI SSSGPAGSYR  400
PYDEGLRRGV FITNETGQPL IGKVWPGSTA FPDFTNPTAL AWWEDMVAEF  450
HDQVPFDGMW IDMNEPSNFI RGSEDGCPNN ELENPPYVPG VVGGTLQAAT  500
ICASSHQFLS THYNLHNLYG LTEAIASHRA LVKARGTRPF VISRSTFAGH  550
GRYAGHWTGD VWSSWEQLAS SVPEILQFNL LGVPLVGADV CGFLGNTSEE  600
LCVRWTQLGA FYPFMRNHNS LLSLPQEPYS FSEPAQQAMR KALTLRYALL  650
PHLYTLFHQA HVAGETVARP LFLEFPKDSS TWTVDHQLLW GEALLITPVL  700
QAGKAEVTGY FPLGTWYDLQ TVPVEALGSL PPPPAAPREP AIHSEGQWVT  750
LPAPLDTINV HLRAGYIIPL QGPGLTTTES RQQPMALAVA LTKGGEARGE  800
LFWDDGESLE VLERGAYTQV IFLARNNTIV NELVRVTSEG AGLQLQKVTV  850
LGVATAPQQV LSNGVPVSNF TYSPDTKVLD ICVSLLMGEQ FLVSWC      896
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
26-53, 36-52, 47-71, 477-502, 591-602

Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación
N84, N177, N334, N414, N596, N826, N869

cirtuvivintum

cirtuvivint

2-(4-methylpiperazin-1-yl)-*N*-[6-(1-methyl-1*H*-pyrazol-4-yl)isoquinolin-3-yl]pyridine-4-carboxamide

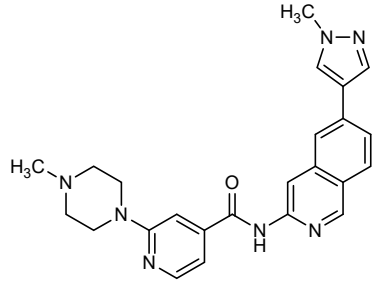
cirtuvivint

2-(4-méthylpipérazin-1-yl)-*N*-[6-(1-méthyl-1*H*-pyrazol-4-yl)isoquinoléin-3-yl]pyridine-4-carboxamide

cirtuvivint

2-(4-metilpiperazin-1-il)-*N*-[6-(1-metil-1*H*-pirazol-4-il)isoquinolein-3-il]piridina-4-carboxamida

$C_{24}H_{25}N_7O$



coprelotamabum #

coprelotamab	immunoglobulin G1-kappa, anti-[*Homo sapiens* ERBB2 (epidermal growth factor receptor 2, receptor tyrosine protein kinase erbB-2, EGFR2, HER2, HER-2, p185cerbB2, NEU, CD340)], humanized monoclonal antibody; gamma1 heavy chain humanized (1-450) [VH humanized (*Homo sapiens* IGHV3-66*01 (81.6%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (217) (121-218), hinge 1-15 (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS (449-450)) (121-450)], (223-214')-disulfide with kappa light chain humanized (1'-214') [V-KAPPA humanized (*Homo sapiens* IGKV1-39*01 (86.3%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dimer (229-229":232-232")-bisdisulfide, produced in Chinese hamster ovary (CHO)-DG44 cell line, glycoform alfa
coprélotamab	immunoglobuline G1-kappa, anti-[*Homo sapiens* ERBB2 (récepteur 2 du facteur de croissance épidermique, récepteur tyrosine-protéine kinase erbB-2, EGFR2, HER2, HER-2, p185c-erbB2, NEU, CD340)], anticorps monoclonal humanisé; chaîne lourde gamma1 humanisée (1-450) [VH humanisé (*Homo sapiens* IGHV3-66*01 (81.6%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (217) (121-218), charnière 1-15 (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS (449-450)) (121-450)], (223-214')-disulfure avec la chaîne légère kappa humanisée (1'-214') [V-KAPPA humanisé (*Homo sapiens* IGKV1-39*01 (86.3%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dimère (229-229":232-232")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-DG44, glycoforme alfa
coprelotamab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* ERBB2 (receptor 2 del factor de crecimiento epidérmico, receptor tirosina-proteína kinasa erbB-2, EGFR2, HER2, HER-2, p185c-erbB2, NEU, CD340)], anticuerpo monoclonal humanizado; cadena pesada gamma1 humanizada (1-450) [VH humanizado (*Homo sapiens* IGHV3-66*01 (81.6%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (217) (121-218), bisagra 1-15 (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS (449-450)) (121-450)], (223-214')-disulfuro con la cadena ligera kappa humanizada (1'-214') [V-KAPPA humanizado (*Homo sapiens* IGKV1-39*01 (86.3%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dímero (229-229":232-232")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-DG44, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGGSLRL SCAASGFNIK DTYIHWVRQA PGKGLEWVAR  50
IYPTNGYTRY ADSVKGRFTI SADTSKNTAY LQMNSLRAED TAVYYCSRWG 100
GDGFYAMDYW 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

```
DIQMTQSPSS LSASVGDRVT ITCRASQDVN TAVAWYQQKP GKAPKLLIYS  50
ASFLYSGVPS RFSGSRSGTD FTLTISSLQP EDFATYYCQQ HYTTPPTFGQ 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Post-translational modifications
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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
450, 450"

cotoretigenum toliparvovecum

cotoretigene toliparvovec

A replication-defective adeno-associated viral vector encoding codon-optimised human retinitis pigmentosa GTPase regulator (RPGR).
A recombinant replication-defective adeno-associated viral vector serotype 8 (rAAV8) encoding codon-optimised human retinitis pigmentosa GTPase regulator (RPGR), under the control of human rhodopsin kinase (RK) promoter and bovine growth hormone poly(A) sequence, flanked by AAV2 inverted terminal repeats (ITR).

cotoretigène toliparvovec

Un vecteur adénoviral défectueux en terme de réplication et codant pour le régulateur de la GTPase de la rétinite pigmentaire humaine avec des codons optimisés (RPGR).
Un vecteur adénoviral recombinant de sérotype 8 (rAAV8) à réplication défectueuse codant pour un régulateur de la GTPase de la rétinite pigmentaire humaine (RPGR) avec des codons optimisés, sous contrôle du promoteur de la kinase de la rhodopsine humaine et de la séquence poly(A) de l'hormone de croissance bovine, flanqué de répétitions terminales inversées (ITR) de l'AAV2.

cotoretigén toliparvovec

Un vector de virus adeno-asociado, deficiente de replicación, que codifica para el regulador de la GTPasa implicado en la retinosis pigmentaria humana (RPGR) con los codones optimizados.
Un vector de virus adeno-asociado recombinante de serotipo 8 (rAAV8), deficiente de replicación, que codifica para el regulador de la GTPasa implicado en la retinosis pigmentaria humana (RPGR) con los codones optimizados, bajo el control del promotor de la rodopsin quinasa (RK) humana y la secuencia poly(A) de la hormona de crecimiento bovina, flanqueado por las repeticiones terminales invertidas (ITR) del AAV2.

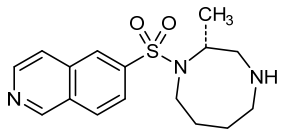
cotosudilum

cotosudil — 6-[(2*R*)-2-methyl-1,4-diazocane-1-sulfonyl]isoquinoline

cotosudil — 6-[(2*R*)-2-méthyl-1,4-diazocane-1-sulfonyl]isoquinoléine

cotosudil — 6-[(2*R*)-2-metil-1,4-diazocano-1-sulfonil]isoquinoleína

$C_{16}H_{21}N_3O_2S$



dafsolimabum #

dafsolimab — immunoglobulin G2B-kappa, anti-[CD3E (CD3 epsilon, Leu-4)], *Mus musculus* monoclonal antibody;
gamma2b heavy chain *Mus musculus* (1-456) [VH (*Mus musculus* IGHV1-4*01 (95.9%) -(IGHD) -IGHJ4*01 (94.1%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Mus musculus* IGHG2B*02 (100%) (CH1 (121-217), hinge 1-22 (218-239), CH2 (240-349), CH3 (350-454), CHS (455-456)) (121-456)], (135-213')-disulfide with kappa light chain *Mus musculus* (1'-213') [V-KAPPA (*Mus musculus* IGKV4-59*01 (100%) -IGKJ5*01 (100%)) CDR-IMGT [5.3.9] (27-31.49-51.88-96) (1'-106') -*Mus musculus* IGKC1*01 (100%) (107'-213')];
dimer (229-229":232-232":235-235":238-238")-tetrakisdisulfide, produced in SP2/0-derived mouse myeloma cells, glycoform alfa

dafsolimab — immunoglobuline G2B-kappa, anti-[CD3E (CD3 epsilon, Leu-4)], anticorps monoclonal *Mus musculus*;
chaîne lourde gamma2b *Mus musculus* ((1-456) [VH (*Mus musculus* IGHV1-4*01 (95.9%) -(IGHD) -IGHJ4*01 (94.1%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Mus musculus* IGHG2B*02 (100%) (CH1 (121-217), charnière 1-22 (218-239), CH2 (240-349), CH3 (350-454), CHS (455-456)) (121-456)], (135-213')-disulfure avec la chaîne légère kappa *Mus musculus* (1'-213') [V-KAPPA (*Mus musculus* IGKV4-59*01 (100%) -IGKJ5*01 (100%)) CDR-IMGT [5.3.9] (27-31.49-51.88-96) (1'-106') -*Mus musculus* IGKC1*01 (100%) (107'-213')];
dimère (229-229":232-232":235-235":238-238")-tétrakisdisulfure, produit par une ligne cellulaire dérivée de myélome murin SP2/0, glycoforme alfa

dafsolimab — inmunoglobulina G2B-kappa, anti-[CD3E (CD3 épsilon, Leu-4)], anticuerpo monoclonal *Mus musculus*;
cadena pesada gamma2b *Mus musculus* ((1-456) [VH (*Mus musculus* IGHV1-4*01 (95.9%) -(IGHD) -IGHJ4*01 (94.1%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Mus musculus* IGHG2B*02 (100%) (CH1 (121-217), bisagra 1-22 (218-239), CH2 (240-349), CH3 (350-454), CHS (455-456)) (121-456)], (135-213')-disulfuro con la cadena ligera kappa *Mus musculus* (1'-213') [V-KAPPA (*Mus musculus* IGKV4-59*01 (100%) -IGKJ5*01 (100%)) CDR-IMGT [5.3.9] (27-31.49-51.88-96) (1'-106') -*Mus musculus* IGKC1*01 (100%) (107'-213')];
dímero (229-229":232-232":235-235":238-238")-tetrakisdisulfuro, producido en una línea celular de mieloma murino SP2/0, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLQQSGAE LARPGASVKM SCKASGYTFT SYTMHWVKQR PGQGLEWIGY  50
INPSSGYTNY IQRFKDKATL TADKSSSTAY MQVSSLTSED SAVYYCARGS 100
RYDYYGMDYW GQGTSVTVSS AKTTPPSVYP LAPGCGDTTG SSVTLGCLVK 150
GYFPESVTVT WNSGSLSSSV HTFPALLQSG LYTMSSSVTV PSSTWPSQTV 200
TCSVAHPASS TTVDKKLEPS GPISTINPCP PCKECHKCPA PNLEGGPSVF 250
IFPPNIKDVL MISLTPKVTC VVVDVSEDDP DVQISWFVNN VEVHTAQTQT 300
HREDYNSTIR VVSTLPIQHQ DWMSGKEFKC KVNNKDLPSP IERTISKIKG 350
LVRAPQVYIL PPPAEQLSRK DVSLTCLVVG FNPGDISVEW TSNGHTEENY 400
KDTAPVLDSD GSYFIYSKLN MKTSKWEKTD SFSCNVRHEG LKNYYLKKTI 450
SRSPGK                                                  456
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Light chain / Chaîne légère / Cadena ligera

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QIVLTQSPAI MSASPGEKVT MTCSASSSVS YMHWYQQKSG TSPKRWIYDT  50
SKLASGVPAR FSGSGSGTSY SLTISSMEAE DAATYYCQQW SSNPLTFGAG 100
TKLELKRADA APTVSIFPPS SEQLTSGGAS VVCFLNNFYP KDINVKWKID 150
GSERQNGVLN SWTDQDSKDS TYSMSSTLTL TKDEYERHNS YTCEATHKTS 200
TSPIVKSFNR NEC                                         213
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Post-translational modifications

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

Intra-H (C23-C104) 22-96 147-202 270-330 376-434
22"-96" 147"-202" 270"-330' 376"-434"
Intra-L (C23-C104) 23'-87" 133'-193'
23'"-87"" 133'"-193'"
Inter-H-L (CH1 11-CL 126) 135-213' 135"-213'"
Inter-H-H (h 12, h 15, h 18, h 21) 229-229" 232-232" 235-235" 238-238"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"
L VL Q1:
1', 1'"

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

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
C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
456, 456"

dafsolimabum setaritoxum

dafsolimab setaritox — immunoglobulin G2B-kappa, anti-[CD3E (CD3 epsilon, Leu-4)], *Mus musculus* monoclonal antibody conjugated to aglycosylated ricin toxin A (RTA);
gamma2b heavy chain *Mus musculus* (1-456) [VH (*Mus musculus* IGHV1-4*01 (95.9%) -(IGHD) -IGHJ4*01 (94.1%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Mus musculus* IGHG2B*02 (100%) (CH1 (121-217), hinge 1-22 (218-239), CH2 (240-349), CH3 (350-454), CHS (455-456)) (121-456)], (135-213')-disulfide with kappa light chain *Mus musculus* (1'-213') [V-KAPPA (*Mus musculus* IGKV4-59*01 (100%) -IGKJ5*01 (100%)) CDR-IMGT [5.3.9] (27-31.49-51.88-96) (1'-106') -*Mus musculus* IGKC1*01 (100%) (107'-213')];
dimer (229-229":232-232":235-235":238-238")-tetrakisdisulfide, produced in SP2/0-derived mouse myeloma cells, glycoform alfa, substituted at N^6 of an average of 1.6 lysyl residues with 4-[(1*RS*)-1-{[L-methionyl-ricin toxin A-chain (Met-RTA, non-glycosylated, produced in *Escherichia coli*)-S^{260}-yl]sulfanyl}ethyl]benzoyl groups

dafsolimab sétaritox — immunoglobuline G2B-kappa, anti-[CD3E (CD3 epsilon, Leu-4)], anticorps monoclonal *Mus musculus* conjugué à la toxine A de la ricine aglycosylée (RTA);
chaîne lourde gamma2b *Mus musculus* -(1-456) [VH (*Mus musculus* IGHV1-4*01 (95.9%) -(IGHD) -IGHJ4*01 (94.1%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Mus musculus* IGHG2B*02 (100%) (CH1 (121-217), charnière 1-22 (218-239), CH2 (240-349), CH3 (350-454), CHS (455-456)) (121-456)], (135-213')-disulfure avec la chaîne légère kappa *Mus musculus* (1'-213') [V-KAPPA (*Mus musculus* IGKV4-59*01 (100%) -IGKJ5*01 (100%)) CDR-IMGT [5.3.9] (27-31.49-51.88-96) (1'-106') -*Mus musculus* IGKC1*01 (100%) (107'-213')];
dimère (229-229":232-232":235-235":238-238")-tétrakisdisulfure, produit par une lignée cellulaire dérivée de myélome murin SP2/0, glycoforme alfa, substitué en N^6 sur un moyenne de 1.6 résidus lysyl par des groupes 4-[(1*RS*)-1-{[L-méthionyl-chaîne A de la toxine de ricine (Met-RTA, non-glycosylée, produite par *Escherichia coli*)-S^{260}-yl]sulfanyl}éthyl]benzoyle

dafsolimab setaritox

inmunoglobulina G2B-kappa, anti-[CD3E (CD3 épsilon, Leu-4)], anticuerpo monoclonal *Mus musculus* conjugado con la toxina A de la ricina aglicosilada (RTA);
cadena pesada gamma2b *Mus musculus* -(1-456) [VH (*Mus musculus* IGHV1-4*01 (95.9%) -(IGHD) -IGHJ4*01 (94.1%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Mus musculus* IGHG2B*02 (100%) (CH1 (121-217), bisagra 1-22 (218-239), CH2 (240-349), CH3 (350-454), CHS (455-456)) (121-456)], (135-213')-disulfuro con la cadena ligera kappa *Mus musculus* (1'-213') [V-KAPPA (*Mus musculus* IGKV4-59*01 (100%) -IGKJ5*01 (100%)) CDR-IMGT [5.3.9] (27-31.49-51.88-96) (1'-106') -*Mus musculus* IGKC1*01 (100%) (107'-213')];
dímero (229-229":232-232":235-235":238-238")-tetrakisdisulfuro, producido en una línea celular de mieloma murino SP2/0, forma glicosilada alfa, sustituída en N^6 de un promedio de 1,6 residuos de lisilo con grupos de 4-[(1*RS*)-1-{[L-metionil-cadena A de toxina de ricina (Met-RTA, no glicosilada, producida por *Escherichia coli*)-S^{260}-il]sulfanil}etil]benzoilo

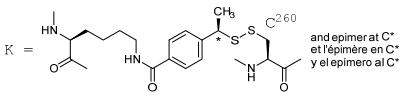
Heavy chain / Chaîne lourde / Cadena pesada
```
QVQLQQSGAE LARPGASVKM SCKASGYTFT SYTMHWVKQR PGQGLEWIGY  50
INPSSGYTNY IQRFKDKATL TADKSSSTAY MQVSSLTSED SAVYYCARGS 100
RYDYYGMDYW GQGTSVTVSS AKTTPPSVYP LAPGCGDTTG SSVTLGCLVK 150
GYFPESVTVT WNSGSLSSSV HTFPALLQSG LYTMSSSVTV PSSTWPSQTV 200
TCSVAHPASS TTVDKKLEPS GPISTINPCP PCKECHKCPA PNLEGGPSVF 250
IFPPNIKDVL MISLTPKVTC VVVDVSEDDP DVQISWFVNN VEVHTAQTQT 300
HREDYNSTIR VVSTLPIQHQ DWMSGKEFKC KVNNKDLPSP IERTISKIKG 350
LVRAPQVYIL PPPAEQLSRK DVSLTCLVVG FNPGDISVEW TSNGHTEENY 400
KDTAPVLDSD GSYFIYSKLN MKTSKWEKTD SFSCNVRHEG LKNYYLKKTI 450
SRSPGK                                                  456
```

Light chain / Chaîne légère / Cadena ligera
```
QIVLTQSPAI MSASPGEKVT MTCSASSSVS YMHWYQQKSG TSPKRWIYDT  50
SKLASGVPAR FSGSGSGTSY SLTISSMEAE DAATYYCQQW SSNPLTFGAG 100
TKLELKRADA APTVSIFPPS SEQLTSGGAS VVCFLNNFYP KDINVKWKID 150
GSERQNGVLN SWTDQDSKDS TYSMSSTLTL TKDEYERHNS YTCEATHKTS 200
TSPIVKSFNR NEC                                         213
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Met-Ricin A chain / Met-chaîne A de la Ricine / Met-cadena A de la Ricina
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MIFPKQYPII NFTTAGATVQ SYTNFIRAVR GRLTTGADVR HDIPVLPNRV 50
GLPINQRFIL VELSNHAELS VTLALDVTNA YVVGYRAGNS AYFFHPDNQE 100
DAEAITHLFT DVQNRYTFAF GGNYDRLEQL AGNLRENIEL GNGPLEEAIS 150
ALYYYSTGGT QLPTLARSFI ICIQMISEAA RFQYIEGEMR TRIRYNRRSA 200
PDPSVITLEN SWGRLSTAIQ ESNQGAFASP IQLQRRNGSK FSVYDVSILI 250
PIIALMVYRC APPPSSQF                                    268
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 147-202 270-330 376-434
22"-96" 147"-202" 270"-330' 376'-434"
Intra-L (C23-C104) 23'-87' 133'-193'
23'"-87'" 133'"-193'"
Inter-H-L (CH1 11-CL 126) 135-213' 135"-213'"
Inter-H-H (h 12, h 15, h 18, h 21) 229-229" 232-232" 235-235" 238-238"
Met-RTA: C172 = Cys-SH,
C260 = Cys-S-S-CH(CH3)-p-C6H4-CO-[N6-Lys(H,L)]

Conjugation sites / Sites de conjugaison / Posiciones de coniugación
major: K74 K141' K206'
K74" K141'" K206'"
minor: K326 K329 K349 K442 K447 K18' K52' K168'
K326" K329" K349" K442" K447" K18'" K52'" K168'"



N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"
L VL Q1:
1', 1'"

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

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
456, 456"

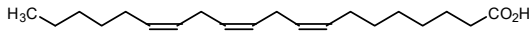
daleutonum

daleuton (8*Z*,11*Z*,14*Z*)-icosa-8,11,14-trienoic acid

daleuton acide (8*Z*,11*Z*,14*Z*)-icosa-8,11,14-triénoïque

daleutón ácido (8*Z*,11*Z*,14*Z*)-icosa-8,11,14-trienoico

$C_{20}H_{34}O_2$



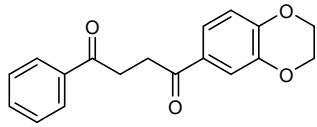
dalosirvatum

dalosirvat 1-(2,3-dihydro-1,4-benzodioxin-6-yl)-4-phenylbutane-1,4-dione

dalosirvat 1-(2,3-dihydro-1,4-benzodioxin-6-yl)-4-phénylbutane-1,4-dione

dalosirvat 1-(2,3-dihidro-1,4-benzodioxin-6-il)-4-fenilbutano-1,4-diona

$C_{18}H_{16}O_4$



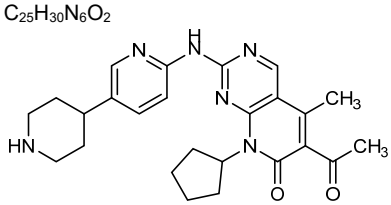
dalpiciclibum

dalpiciclib 6-acetyl-8-cyclopentyl-5-methyl-2-{[5-(piperidin-4-yl)pyridin-2-yl]amino}pyrido[2,3-*d*]pyrimidin-7(8*H*)-one

dalpiciclib 6-acétyl-8-cyclopentyl-5-méthyl-2-{[5-(pipéridin-4-yl)pyridin-2-yl]amino}pyrido[2,3-*d*]pyrimidin-7(8*H*)-one

dalpiciclib 6-acetil-8-ciclopentil-5-metil-2-{[5-(piperidin-4-il)piridin-2-il]amino}pirido[2,3-*d*]pirimidin-7(8*H*)-ona

$C_{25}H_{30}N_6O_2$

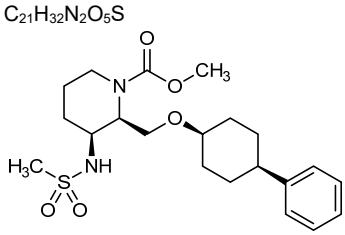


danavorextonum

danavorexton methyl (2*R*,3*S*)-3-(methanesulfonamido)-2-{[(*cis*-4-phenylcyclohexyl)oxy]methyl}piperidine-1-carboxylate

danavorexton (2*R*,3*S*)-3-(méthanesulfonamido)-2-{[(*cis*-4-phénylcyclohexyl)oxy]méthyl}pipéridine-1-carboxylate de méthyle

danavorextón (2*R*,3*S*)-2-{[(*cis*-4-fenilciclohexil)oxi]metil}-3-(metanosulfonamido)piperidina-1-carboxilato de metilo



dapiglutidum

dapiglutide — human glucagon like peptide-2 (GLP-2) analogue; $N^{6.16}$-[*N*-(17-carboxyheptadecanoyl)-L-γ-glutamyl]-[A^{2}>Aib (2-methylalanine), D^{3}>E, S^{7}>T, D^{8}>S, M^{10}>L, N^{11}>A, N^{16}>K, L^{17}>Q, N^{24}>A, T^{29}>H]human glucagon-like peptide 2 (GLP-2)

dapiglutide — analogue du peptide 2 semblable au glucagon (GLP-2) humain; $N^{6.16}$-[*N*-(17-carboxyheptadécanoyl)-L-γ-glutamyl]-[A^{2}>Aib (2-méthylalanine), D^{3}>E, S^{7}>T, D^{8}>S, M^{10}>L, N^{11}>A, N^{16}>K, L^{17}>Q, N^{24}>A, T^{29}>H]peptide 2 semblable au glucagon humain (GLP-2)

dapiglutida — análogo del péptido 2 semejante al glucagón (GLP-2) humano; $N^{6.16}$-[*N*-(17-carboxiheptadecanoil)-L-γ-glutamil]-[A^{2}>Aib (2-metilalanina), D^{3}>E, S^{7}>T, D^{8}>S, M^{10}>L, N^{11}>A, N^{16}>K, L^{17}>Q, N^{24}>A, T^{29}>H]]péptido 2 semejante al glucagón humano (GLP-2)

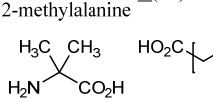
$C_{192}H_{302}N_{46}O_{57}$

Sequence / Séquence / Secuencia

HXEGSFTSEL ATILDKQAAR DFIAWLIQHK ITD 33

Modified residues / Résidus modifiés / Restos modificados

X (2) 2-methylalanine



K(16) N^{6}-[17-carboxyheptadecanoyl-γ-Glu]-Lys

daplusiranum

daplusiran — *all-P-ambo-O*-[(2*R*,3*S*)-2-(hydroxymethyl)oxolan-3-yl] hydrogen 5'-*O*-({[(2*R*,3*S*)-3-({[(*cis*-4-{(3*S*,8*S*)-17-[(2-acetamido-2-deoxy-β-D-galactopyranosyl)oxy]-3,8-bis[(2-{2-[(2-acetamido-2-deoxy-β-D-galactopyranosyl)oxy]ethoxy}ethyl)carbamoyl]-6,11-dioxo-15-oxa-2,7,12-triazaheptadecan-1-oyl}cyclohexyl)oxy]hydroxyphosphorothioyl}oxy)oxolan-2-yl]methoxy}hydroxyphosphorothioyl)-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-methyl-*P*-thio-3'-uridylate duplex with *all-P-ambo*-2'-*O*-methyl-*P*-thioadenylyl-(3'→5')-2'-deoxy-2'-fluoro-*P*-thioguanylyl-(3'→5')-2'-*O*-methyl-*P*-thioadenylyl-(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'-deoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-deoxy-2'-fluoroadenylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-deoxy-2'-fluoroadenylyl-(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'-fluorocytidylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-methyl-*P*-thioadenylyl-(3'→5')-2'-*O*-methylcytidine

daplusiran

tout-P-ambo-5'-*O*-({[(2*R*,3*S*)-3-({[(*cis*-4-{(3*S*,8*S*)-17-[(2-acétamido-2-désoxy-β-D-galactopyranosyl)oxy]-3,8-bis[(2-{2-[(2-acétamido-2-désoxy-β-D-galactopyranosyl)oxy]éthoxy}éthyl)carbamoyl]-6,11-dioxo-15-oxa-2,7,12-triazaheptadécan-1-oyl}cyclohexyl)oxy]hydroxyphosphorothioyl}oxy)oxolan-2-yl]méthoxy}hydroxyphosphorothioyl)-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthylcytidylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-désoxy-2'-fluorocytidylyl-(3'→5')-2'-désoxy-2'-fluorouridylyl-(3'→5')-2'-désoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthylcytidylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthylcytidylyl-(3'→5')-hydrogéno-2'-*O*-méthyl-*P*-thio-3'-uridylate de *O*-[(2*R*,3*S*)-2-(hydroxyméthyl)oxolan-3-yle]
duplex avec *tout-P-ambo*-2'-*O*-méthyl-*P*-thioadénylyl-(3'→5')-2'-désoxy-2'-fluoro-*P*-thioguanylyl-(3'→5')-2'-*O*-méthyl-*P*-thioadénylyl-(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'-désoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-désoxy-2'-fluoroadénylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-désoxy-2'-fluoroadénylyl-(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'-fluorocytidylyl-(3'→5')-2'-*O*-méthylcytidylyl-(3'→5')-2'-*O*-méthyl-*P*-thioadénylyl-(3'→5')-2'-*O*-méthylcytidine

daplusirán

todo-P-ambo-5'-*O*-({[(2*R*,3*S*)-3-({[(*cis*-4-{(3*S*,8*S*)-17-[(2-acetamido-2-desoxi-β-D-galactopiranosil)oxi]-3,8-bis[(2-{2-[(2-acetamido-2-desoxi-β-D-galactopiranosil)oxi]etoxi}etil)carbamoil]-6,11-dioxo-15-oxa-2,7,12-triazaheptadecan-1-oil}ciclohexil)oxi]hidroxifosforotioil}oxi)oxolan-2-il]metoxi}hidroxifosforotioil)-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metilcitidilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metilcitidilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metilcitidilil-(3'→5')-hidrógeno-2'-*O*-metil-*P*-tio-3'-uridilato de *O*-[(2*R*,3*S*)-2-(hidroximetil)oxolan-3-ilo]
duplex con *todo-P-ambo*-2'-*O*-metil-*P*-tioadenilil-(3'→5')-2'-desoxi-2'-fluoro-*P*-tioguanilil-(3'→5')-2'-*O*-metil-*P*-tioadenilil-(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'-desoxi-2'-fluorouridilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-desoxi-2'-fluoroadenilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-desoxi-2'-fluoroadenilil-(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'-fluorocitidilil-(3'→5')-2'-*O*-metilcitidilil-(3'→5')-2'-*O*-metil-*P*-tioadenilil-(3'→5')-2'-*O*-metilcitidina

$C_{492}H_{650}F_{12}N_{163}O_{310}P_{43}S_7$

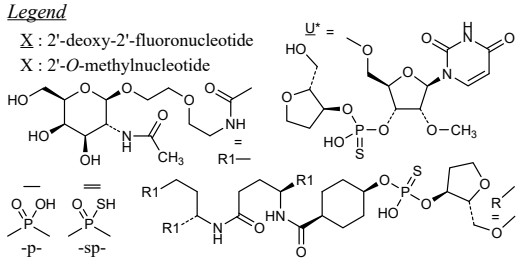
(3'-5') R=G-U-G-G-A-C-U-U-C-U-C-U-C-A-A-U-U-U-U-C-U*

(5'-3') C=A-C-C-U-G-A-A-G-A-G-A-G-U-U-A-A-A=A=G=A

Legend

X : 2'-deoxy-2'-fluoronucleotide

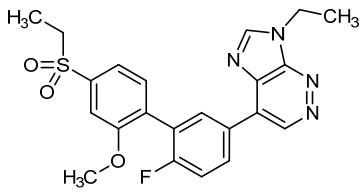
X : 2'-*O*-methylnucleotide



darigabatum

darigabat	4-[4'-(ethanesulfonyl)-6-fluoro-2'-methoxy[1,1'-biphenyl]-3-yl]-7-ethyl-7*H*-imidazo[4,5-*c*]pyridazine
darigabat	4-[4'-(éthanesulfonyl)-6-fluoro-2'-méthoxy[1,1'-biphényl]-3-yl]-7-éthyl-7*H*-imidazo[4,5-*c*]pyridazine
darigabat	4-[4'-(etanosulfonil)-6-fluoro-2'-metoxi[1,1'-bifenil]-3-il]-7-etil-7*H*-imidazo[4,5-*c*]piridazina

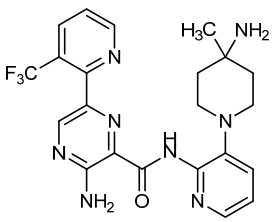
$C_{22}H_{21}FN_4O_3S$



darovasertibum

darovasertib	3-amino-*N*-[3-(4-amino-4-methylpiperidin-1-yl)pyridin-2-yl]-6-[3-(trifluoromethyl)pyridin-2-yl]pyrazine-2-carboxamide
darovasertib	3-amino-*N*-[3-(4-amino-4-méthylpipéridin-1-yl)pyridin-2-yl]-6-[3-(trifluorométhyl)pyridin-2-yl]pyrazine-2-carboxamide
darovasertib	3-amino-*N*-[3-(4-amino-4-metilpiperidin-1-il)piridin-2-il]-6-[3-(trifluorometil)piridin-2-il]pirazina-2-carboxamida

$C_{22}H_{23}F_3N_8O$



daxdilimabum #

daxdilimab	immunoglobulin G1-lambda, anti-[*Homo sapiens* LILRA4 (leukocyte immunoglobulin like receptor A4, ILT7, CD85g)], *Homo sapiens* monoclonal antibody; gamma1 heavy chain *Homo sapiens* (1-452) [VH (*Homo sapiens* IGHV1-18*01 (98.0%) -(IGHD) -IGHJ2*01 (92.9%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (219) (123-220), hinge 1-15 (221-235), CH2 (236-345), CH3 E12 (361), M14 (363) (346-450), CHS (451-452)) (123-452)], (225-215')-disulfide with lambda light chain *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV2-14*01 (98.0%) -IGLJ2*01 (90.9%)) CDR-IMGT [9.3.10] (26-34.52-54.91-100) (1'-110') -*Homo sapiens* IGLC2*01 (100%) (111'-216')]; dimer (231-231'':234-234'')-bisdisulfide, produced in a Chinese hamster ovary (CHO)-derived cell line, glycoform alfa
daxdilimab	immunoglobuline G1-lambda, anti-[*Homo sapiens* LILRA4 (récepteur A4 immunoglobuline-like des leucocytes, ILT7, CD85g)], anticorps monoclonal *Homo sapiens*; chaîne lourde gamma1 *Homo sapiens* (1-452) [VH (*Homo sapiens* IGHV1-18*01 (98.0%) -(IGHD) -IGHJ2*01 (92.9%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (219) (123-220), charnière 1-15 (221-235), CH2 (236-345), CH3 E12 (361), M14 (363) (346-450), CHS (451-452)) (123-452)], (225-215')-disulfure avec la chaîne légère lambda *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV2-14*01 (98.0%) -IGLJ2*01 (90.9%)) CDR-IMGT [9.3.10] (26-34.52-54.91-100) (1'-110') -*Homo sapiens* IGLC2*01 (100%) (111'-216')]; dimère (231-231'':234-234'')-bisdisulfure, produite dans une lignée cellulaire dérivée des cellules ovariennes de hamster chinois (CHO), glycoforme alfa
daxdilimab	inmunoglobulina G1-lambda, anti-[*Homo sapiens* LILRA4 (receptor A4 inmunoglobulina-like de los leucocitos, ILT7, CD85g)], anticuerpo monoclonal *Homo sapiens*; cadena pesada gamma1 *Homo sapiens* (1-452) [VH (*Homo sapiens* IGHV1-18*01 (98.0%) -(IGHD) -IGHJ2*01 (92.9%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (219) (123-220), bisagra 1-15 (221-235), CH2 (236-345), CH3 E12 (361), M14 (363) (346-450), CHS (451-452)) (123-452)], (225-215')-disulfuro con la cadena ligera lambda *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV2-14*01 (98.0%) -IGLJ2*01 (90.9%)) CDR-IMGT [9.3.10] (26-34.52-54.91-100) (1'-110') -*Homo sapiens* IGLC2*01 (100%) (111'-216')]; dímero (231-231'':234-234'')-bisdisulfuro, producido en una línea celular derivada de las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLQQSGAE VKKPGASVKV SCKASGYTFT SYGISWVRQA PGQGLEWMGW  50
ISAYNGNTNY AQKLQGRVTM TIDTSTSTAY MELRSLRSDD TAVYYCARNG 100
LWGWDSDAFD IWGRGTLVTV SSASTKGPSV FPLAPSSKST SGGTAALGCL 150
VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ SSGLYSLSSV VTVPSSSLGT 200
QTYICNVNHK PSNTKVDKRV EPKSCDKTHT CPPCPAPELL GGPSVFLFPP 250
KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NWYVDGVEVH NAKTKPREEQ 300
YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQPRE 350
PQVYTLPPSR EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP 400
PVLDSDGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP 450
GK                                                      452
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Light chain / Chaîne légère / Cadena ligera

```
QSALTQPASV SGSPGQSITI SCTGTSSDVG GYNYVSWYQQ HPGKAPKLMI  50
YDVSNRPSGV SNRFSGSKSG NTASLTISGL QAEDEADYYC SSYTSSSTVV 100
FGGGTKVTVL GQPKAAPSVT LFPPSSEELQ ANKATLVCLI SDFYPGAVTV 150
AWKADSSPVK AGVETTTPSK QSNNKYAASS YLSLTPEQWK SHRSYSCQVT 200
HEGSTVEKTV APTECS                                       216
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 149-205 266-326 372-430
22"-96" 149"-205" 266"-326" 372"-430"
Intra-L (C23-C104) 22'-90' 138'-197'
22'"-90'" 138'"-197'"
Inter-H-L (h 5-CL 126) 225-215' 225"-215'"
Inter-H-H (h 11, h 14) 231-231" 234-234"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"
L VL Q1:
1', 1'"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
302, 302"
Afucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires
complexes afucosylés / glicanos de tipo CHO biantenarios complejos afucosilados

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
452, 452"

dazodalibepum #

dazodalibep

engineered binding protein (1-85) anti-(human CD40 ligand) derived from the human tenascin third fibronectin type III domain (785-869), fused via the peptidyl linker ^{86}GGGGGGGGGGGGGGG^{100} to engineered binding protein (101-190) anti-(human CD40 ligand) derived from the human tenascin third fibronectin type III domain (780-869), fused via the peptidyl linker ^{191}GGGGGGGGGG^{200} to human albumin (201-785), variant (C^{34}>S^{234}), produced in *Escherichia coli*; [tenascin (785-869)-peptide (1-85) (containing a third fibronectin type III domain), engineered for binding to the CD40 ligand (CD40L)]-[G_{15} linker (86-100)]-[tenascin (780-869)-peptide (101-190) (containing a third fibronectin type III domain), engineered for binding to the CD40 ligand (CD40L)]-[G_{10} linker (91-100)]-[(C^{34}>S)-human serum albumin (HSA)] fusion protein, produced in *Escherichia coli*

dazodalibep

protéine de liaison mise au point (1-85) anti-(ligand de CD40 humain) dérivée du troisième domaine de la fibronectine de type III de la ténascine humaine, fusionnée via un peptide liant ^{86}GGGGGGGGGGGGGGG^{100} à la protéine de liaison mise au point (101-190) anti-(ligand de CD40 humain) dérivée du troisième domaine de la fibronectine de type III de la ténascine humaine, fusionnée via un peptide liant ^{191}GGGGGGGGGG^{200} à l'albumine humaine (201-785), variant (C^{34}>S^{234}), produite par *Escherichia coli*;
protéine de fusion de [ténascine (785-869)-peptide (1-85) (contenant un troisième domaine de fibronectine de type III), conçu pour se lier au ligand de CD40 (CD40L)]-[peptide G_{15} de liaison (86-100)]-[ténascine (780-869)-peptide (101-190) (contenant un troisième domaine de fibronectine de type III), conçu pour se lier au ligand de CD40 (CD40L)]-[peptide G_{10} de liaison (91-100)]-[(C^{34}>S)-albumine sérique humaine (ASH)], produite par *Escherichia coli*

dazodalibep

proteína de unión diseñada (1-85) anti-(ligando CD40 humano) derivada de un tercer dominio de fibronectina tipo III de tenascina humana (785-869), fusionada a través de un conector ^{86}GGGGGGGGGGGGGGG^{100} a la proteína de unión diseñada (101-190) anti-(ligando CD40 humano) derivado de un tercer dominio de fibronectina tipo III de tenascina humana (780-869), fusionado a través de un conector peptidil ^{191}GGGGGGGGGG^{200} a la albúmina humana (201-785), variante (C^{34}>S^{234}), producida en *Escherichia coli*;
proteína de fusión de [tenascina (785-869)-péptido (1-85) (que contiene un tercer dominio de fibronectina tipo III), diseñado para unirse al ligando de CD40 (CD40L)]-[péptido conector G_{15} (86-100)]-[tenascina (780-869)-péptido (101-190) (que contiene un tercer dominio de fibronectina tipo III), diseñado para unirse al ligando de CD40 (CD40L)]-[péptido conector G_{10} (91-100)]-[(C^{34}>S)-albúmina sérica humana (ASH)], producida por *Escherichia coli*

Sequence / Séquence / Secuencia

```
SQIEVKDVTD TTALITWSDD FGEYVWCELT YGIKDVPGDR TTIDLWYHHA   50
HYSIGNLKPD TEYEVSLICR SGDMSSNPAK ETFTTGGGGG GGGGGGGGGG  100
RLDAPSQIEV KDVTDTTALI TWSDDFGEYV WCELTYGIKD VPGDRTTIDL  150
WYHHAHYSIG NLKPDTEYEV SLICRSGDMS SNPAKETFTT GGGGGGGGGG  200
DAHKSEVAHR FKDLGEENFK ALVLIAFAQY LQQSPFEDHV KLVNEVTEFA  250
KTCVADESAE NCDKSLHTLF GDKLCTVATL RETYGEMADC CAKQEPERNE  300
CFLQHKDDNP NLPRLVRPEV DVMCTAFHDN EETFLKKYLY EIARRHPYFY  350
APELLFFAKR YKAAFTECCQ AADKAACLLP KLDELRDEGK ASSAKQRLKC  400
ASLQKFGERA FKAWAVARLS QRFPKAEFAE VSKLVTDLTK VHTECCHGDL  450
LECADDRADL AKYICENQDS ISSKLKECCE KPLLEKSHCI AEVENDEMPA  500
DLPSLAADFV ESKDVCKNYA EAKDVFLGMF LYEYARRHPD YSVVLLLRLA  550
KTYETTLEKC CAAADPHECY AKVFDEFKPL VEEPQNLIKQ NCELFEQLGE  600
YKFQNALLVR YTKKVPQVST PTLVEVSRNL GKVGSKCCKH PEAKRMPCAE  650
DYLSVVLNQL CVLHEKTPVS DRVTKCCTES LVNRRPCFSA LEVDETYVPK  700
EFNAETFTFH ADICTLSEKE RQIKKQTALV ELVKHKPKAT KEQLKAVMDD  750
FAAFVEKCCK ADDKETCFAE EGKKLVAASQ AALGL                  785
```

Mutations / Mutations / Mutaciones
$F^{18,123}$>S, $K^{19,124}$>D, $P^{20,125}$>D, $L^{21,126}$>F, $A^{22,127}$>G, $I^{24,129}$>Y, $D^{25,130}$>V, $G^{26,131}$>W, $I^{27,132}$>C, $T^{46,151}$>W, $E^{47,152}$>Y, $D^{48,153}$>H, $E^{49,154}$>H, $N^{50,155}$>A, $Q^{51,156}$>H, $S^{69,174}$>C, $R^{71,176}$>S, C^{234}>S

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
27-69, 132-174, 253-262, 275-290, 291-301, 324-368, 369-377, 400-445, 446-453, 465-478, 479-489, 516-560, 561-569, 592-637, 638-648, 661-676, 677-687, 714-758, 759-767

Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación
none / aucune / ninguna

depemokimabum #
depemokimab

immunoglobulin G1-kappa, anti-[*Homo sapiens* IL5 (interleukin 5, IL-5)], humanized monoclonal antibody;
gamma1 heavy chain humanized (1-449) [VH humanized (*Homo sapiens* IGHV2-70*19 (75.8%) -(IGHD) -IGHJ4*01 (85.7%)) CDR-IMGT [8.7.13] (26-33.51-57.96-108) (1-119) -*Homo sapiens* IGHG1*03 G1m3, nG1m1, G1v21 CH2 Y15.1, T16, E18 (CH1 R120 (216) (120-217), hinge 1-15 (218-232), CH2 M15.1>Y (254), S16>T (256), T18>E (258) (233-342), CH3 E12 (358), M14 (360) (343-447), CHS (448-449)) (120-449)], (222-220')-disulfide with kappa light chain humanized (1'-220') [V-KAPPA (*Homo sapiens* IGKV4-1*01 (91.1%) -IGKJ2*02 (90.9%)) CDR-IMGT [12.3.9] (27-38.56-58.95-103) (1'-113') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (159), V101 (197) (114'-220')]; dimer (228-228":231-231")-bisdisulfide, produced in Chinese hamster ovary (CHO)-K1 cell line lacking the glutamine synthetase (GS) gene, glycoform alfa

dépémokimab

immunoglobuline G1-kappa, anti-[*Homo sapiens* IL5 (interleukine 5, IL-5)], anticorps monoclonal humanisé;
chaîne lourde gamma1 humanisée (1-449) [VH humanisé (*Homo sapiens* IGHV2-70*19 (75.8%) -(IGHD) -IGHJ4*01 (85.7%)) CDR-IMGT [8.7.13] (26-33.51-57.96-108) (1-119) -*Homo sapiens* IGHG1*03 G1m3, nG1m1, G1v21 CH2 Y15.1, T16, E18 (CH1 R120 (216) (120-217), charnière 1-15 (218-232), CH2 M15.1>Y (254), S16>T (256), T18>E (258) (233-342), CH3 E12 (358), M14 (360) (343-447), CHS (448-449)) (120-449)], (222-220')-disulfure avec la chaîne légère kappa humanisée (1'-220') [V-KAPPA humanisé (*Homo sapiens* IGKV4-1*01 (91.1%) -IGKJ2*02 (90.9%)) CDR-IMGT [12.3.9] (27-38.56-58.95-103) (1'-113') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (159), V101 (197) (114'-220')];
dimère (228-228":231-231")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-K1 ne présentant pas le gène de la glutamine synthétase, glycoforme alfa

depemokimab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* IL5 (interleukina 5, IL-5)], anticuerpo monoclonal humanizado;
cadena pesada gamma1 humanizada (1-449) [VH humanizado (*Homo sapiens* IGHV2-70*19 (75.8%) -(IGHD) -IGHJ4*01 (85.7%)) CDR-IMGT [8.7.13] (26-33.51-57.96-108) (1-119) -*Homo sapiens* IGHG1*03 G1m3, nG1m1, G1v21 CH2 Y15.1, T16, E18 (CH1 R120 (216) (120-217), bisagra 1-15 (218-232), CH2 M15.1>Y (254), S16>T (256), T18>E (258) (233-342), CH3 E12 (358), M14 (360) (343-447), CHS (448-449)) (120-449)], (222-220')-disulfuro con la cadena ligera kappa humanizada (1'-220') [V-KAPPA humanizado (*Homo sapiens* IGKV4-1*01 (91.1%) -IGKJ2*02 (90.9%)) CDR-IMGT [12.3.9] (27-38.56-58.95-103) (1'-113') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (159), V101 (197) (114'-220')];
dímero (228-228":231-231")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-K1 en ausencia del gen glutamina sintetasa (GS), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVTLRESGPA LVKPTQTLTL TCTVSGFSLT GSSVHWVRQP PGKGLEWLGV  50
IWASGGTDYN SALMSRLSIS KDTSRNQVVL TMTNMDPVDT ATYYCARDPP 100
SGLLRLDYWG RGTLVTVSSA STKGPSVFPL APSSKSTSGG TAALGCLVKD 150
YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY 200
ICNVNHKPSN TKVDKRVEPK SCDKTHTCPP CPAPELLGGP SVFLFPPKPK 250
DTLYITREPE 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

```
DIVMTQSPDS LAVSLGERAT INCKSSQSLL NSGNQKNYLA WYQQKPGQPP  50
KLLIYGASTR ESGVPDRFSG SGSGTDFTLT ISSLQAEDVA VYYCQNVHSF 100
PFTFGGGTKL EIKRTVAAPS VFIFPPSDEQ LKSGTASVVC LLNNFYPREA 150
KVQWKVDNAL QSGNSQESVT EQDSKDSTYS LSSTLTLSKA DYEKHKVYAC 200
EVTHQGLSSP VTKSFNRGEC                                   220
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-95 146-202 263-323 369-427
22"-95" 146"-202" 263"-323" 369"-427"
Intra-L (C23-C104) 23'-94' 140'-200'
23'"-94'" 140'"-200'"
Inter-H-L (h 5-CL 126) 222-220' 222"-220'"
Inter-H-H (h 11, h 14) 228-228" 231-231"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
VH Q1:
1, 1"

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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
449, 449"

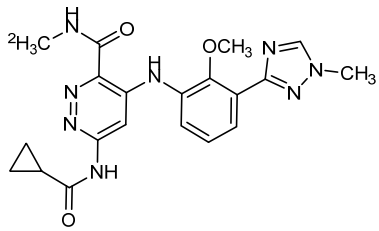
deucravacitinibum

deucravacitinib — 6-(cyclopropanecarboxamido)-4-[2-methoxy-3-(1-methyl-1*H*-1,2,4-triazol-3-yl)anilino]-*N*-($^2H_3$)methylpyridazine-3-carboxamide

deucravacitinib — 6-(ciclopropanocarboxamido)-4-[2-méthoxy-3-(1-méthyl-1*H*-1,2,4-triazol-3-yl)anilino]-*N*-($^2H_3$)méthylpyridazine-3-carboxamide

deucravacitinib — 6-(ciclopropanocarboxamido)-*N*-($^2H_3$)metil-4-[3-(1-metil-1*H*-1,2,4-triazol-3-il)-2-metoxianilino]piridazina-3-carboxamida

$C_{20}H_{19}{}^2H_3N_8O_3$



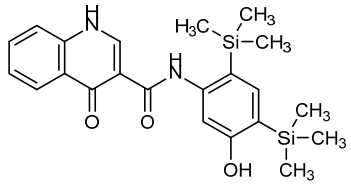
dirocaftorum

dirocaftor — *N*-[5-hydroxy-2,4-bis(trimethylsilyl)phenyl]-4-oxo-1,4-dihydroquinoline-3-carboxamide

dirocaftor — *N*-[5-hydroxy-2,4-bis(triméthylsilyl)phényl]-4-oxo-1,4-dihydroquinoléine-3-carboxamide

dirocaftor — *N*-[5-hidroxi-2,4-bis(trimetilsilil)fenil]-4-oxo-1,4-dihidroquinoleína-3-carboxamida

$C_{22}H_{28}N_2O_3Si_2$



divozilimabum #

divozilimab — immunoglobulin G1-kappa, anti-[*Homo sapiens* MS4A1 (membrane-spanning 4-domains subfamily A member 1, CD20)], monoclonal antibody;
gamma1 heavy chain (1-451) [VH (*Homo sapiens* IGHV1-46*01 (86.7%) -(IGHD) -IGHJ1*01 (86.7%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (218) (122-219), hinge 1-15 (220-234), CH2 (235-344), CH3 E12 (360), M14 (362) (345-449), CHS (450-451)) (122-451)], (224-213')-disulfide with kappa light chain (1'-213') [V-KAPPA (*Mus musculus* IGKV4-72*01 (85.3%) -IGKJ1*01 (90.9%)/*Homo sapiens* IGKV3D-11*02 (73.3%) -IGKJ4*01 (100%)) CDR-IMGT [5.3.9] (27-31.49-51.88-96) (1'-106') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (152), V101 (190) (107'-213')];
dimer (230-230'':233-233'')-bisdisulfide, produced in a Chinese hamster ovary (CHO)-S cell line, glycoform alfa

divozilimab

immunoglobuline G1-kappa, anti-[*Homo sapiens* MS4A1 (membre 1 de la sous-famille A à 4 domaines transmembranaires, CD20)], anticorps monoclonal;
chaîne lourde gamma1 (1-451) [VH (*Homo sapiens* IGHV1-46*01 (86.7%) -(IGHD) -IGHJ1*01 (86.7%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (218) (122-219), charnière 1-15 (220-234), CH2 (235-344), CH3 E12 (360), M14 (362) (345-449), CHS (450-451)) (122-451)], (224-213')-disulfure avec la chaîne légère kappa (1'-213') [V-KAPPA (*Mus musculus* IGKV4-72*01 (85.3%) -IGKJ1*01 (90.9%)/*Homo sapiens* IGKV3D-11*02 (73.3%) -IGKJ4*01 (100%)) CDR-IMGT [5.3.9] (27-31.49-51.88-96) (1'-106') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (152), V101 (190) (107'-213')]; dimère (230-230":233-233")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-S, glycoforme alfa

divozilimab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* MS4A1 (miembro 1 de la subfamilia A con 4 dominios transmembranarios, CD20)], anticuerpo monoclonal;
cadena pesada gamma1 (1-451) [VH (*Homo sapiens* IGHV1-46*01 (86.7%) -(IGHD) -IGHJ1*01 (86.7%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (218) (122-219), bisagra 1-15 (220-234), CH2 (235-344), CH3 E12 (360), M14 (362) (345-449), CHS (450-451)) (122-451)], (224-213')-disulfuro con la cadena ligera kappa (1'-213') [V-KAPPA (*Mus musculus* IGKV4-72*01 (85.3%) -IGKJ1*01 (90.9%)/*Homo sapiens* IGKV3D-11*02 (73.3%) -IGKJ4*01 (100%)) CDR-IMGT [5.3.9] (27-31.49-51.88-96) (1'-106') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (152), V101 (190) (107'-213')]; dímero (230-230":233-233")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-S, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVQPGAE VVKPGASVKV SCKASGYTFT SYNMHWVRQA PGRGLEWMGA  50
IYPGNGDTSY NQKFKGRVTM TRDKSTSTVY MELSSLRSED TAVYYCARST 100
YYGGDWYFNV 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
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Light chain / Chaîne légère / Cadena ligera

```
QIVLSQSPAI LSASPGERVT LTCRASSSVS YIHWFQQKPG KAPKPLIYAT  50
SNLASGVPSR FSGSGSGTDF SLTISRVEPE DFAVYYCQQW TSNPPTFGGG 100
TKVEIKRTVA APSVFIFPPS DEQLKSGTAS VVCLLNNFYP REAKVQWKVD 150
NALQSGNSQE SVTEQDSKDS TYSLSSTLTL SKADYEKHKV YACEVTHQGL 200
SSPVTKSFNR GEC                                          213
```

Post-translational modifications
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'-87' 133'-193'
23'"-87'" 133'"-193'"
Inter-H-L (h 5-CL 126) 224-213' 224"-213'"
Inter-H-H (h 11, h 14) 230-230" 233-233"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
L VL Q1:
1', 1'"

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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
451, 451"

ebronucimabum #

ebronucimab

immunoglobulin G1-lambda2, anti-[*Homo sapiens* PCSK9 (proprotein convertase subtilisin/kexin type 9, neural apoptosis-regulated convertase 1, NARC1, NARC-1, proprotein convertase 9, PC9)], *Homo sapiens* monoclonal antibody;
gamma1 heavy chain *Homo sapiens* (1-453) [VH (*Homo sapiens* IGHV3-21*01 (91.8%) -(IGHD) - IGHJ3*01 (100%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123)-*Homo sapiens* IGHG1*01 (100%), G1m17,1 (CH1 K120 (220) (124-221), hinge 1-15 (222-236), CH2 (237-346), CH3 D12 (362), L14 (364) (347-451), CHS (452-453)) (124-453)], (226-216')-disulfide with lambda2 light chain *Homo sapiens* (1'-217') [V-LAMBDA (*Homo sapiens* IGLV2-11*01 (81.6%) -IGLJ1*01 (90.9%)) CDR-IMGT [9.3.11] (26-34.52-54.91-101) (1'-111') -*Homo sapiens* IGLC2*01 (100%) (112'-217')];
dimer (232-232":235-235")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

ébronucimab

immunoglobuline G1-lambda2, anti-[*Homo sapiens* PCSK9 (proprotéine convertase subtilisine/kexine type 9, convertase 1 régulée par l'apoptose neuronale, NARC1, NARC-1, proprotéine convertase 9, PC9)], anticorps monoclonal *Homo sapiens*;
chaîne lourde gamma1 *Homo sapiens* (1-453) [VH (*Homo sapiens* IGHV3-21*01 (91.8%) -(IGHD) - IGHJ3*01 (100%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Homo sapiens* IGHG1*01 (100%), G1m17,1 (CH1 K120 (220) (124-221), charnière 1-15 (222-236), CH2 (237-346), CH3 D12 (362), L14 (364) (347-451), CHS (452-453)) (124-453)], (226-216')-disulfure avec la chaîne légère lambda2 *Homo sapiens* (1'-217') [V-LAMBDA (*Homo sapiens* IGLV2-11*01 (81.6%) -IGLJ1*01 (90.9%)) CDR-IMGT [9.3.11] (26-34.52-54.91-101) (1'-111') -*Homo sapiens* IGLC2*01 (100%) (112'-217')];
dimère (232-232":235-235")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

ebronucimab

inmunoglobulina G1-lambda2, anti-[*Homo sapiens* PCSK9 (proproteína convertasa subtilisina/kexina tipo 9, convertasa 1 regulada por la apoptosis neuronal, NARC1, NARC-1, proproteína convertasa 9, PC9)], anticuerpo monoclonal *Homo sapiens*;
cadena pesada gamma1 *Homo sapiens* (1-453) [VH (*Homo sapiens* IGHV3-21*01 (91.8%) -(IGHD) - IGHJ3*01 (100%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Homo sapiens* IGHG1*01 (100%), G1m17,1 (CH1 K120 (220) (124-221), bisagra 1-15 (222-236), CH2 (237-346), CH3 D12 (362), L14 (364) (347-451), CHS (452-453)) (124-453)], (226-216')-disulfuro con la cadena ligera lambda2 *Homo sapiens* (1'-217') [V-LAMBDA (*Homo sapiens* IGLV2-11*01 (81.6%) -IGLJ1*01 (90.9%)) CDR-IMGT [9.3.11] (26-34.52-54.91-101) (1'-111') -*Homo sapiens* IGLC2*01 (100%) (112'-217')];
dímero (232-232":235-235")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGRSLRL SCAASGFTFS SYSMNWVRQA PGKGLEWVSG  50
ISSSSSYISY ADSVQGRFTI SRDNGKNSLY LQMNSLRAED TALYFCAREY 100
DFWSAYYDAF DVWGQGTMVT VSSASTKGPS VFPLAPSSKS TSGGTAALGC 150
LVKDYFPEPV TVSWNSGALT SGVHTFPAVL QSSGLYSLSS VVTVPSSSLG 200
TQTYICNVNH KPSNTKVDKK VEPKSCDKTH TCPPCPAPEL LGGPSVFLFP 250
PKPKDTLMIS RTPEVTCVVV DVSHEDPEVK FNWYVDGVEV HNAKTKPREE 300
QYNSTYRVVS VLTVLHQDWL NGKEYKCKVS NKALPAPIEK TISKAKGQPR 350
EPQVYTLPPS RDELTKNQVS LTCLVKGFYP SDIAVEWESN GQPENNYKTT 400
PPVLDSDGSF FLYSKLTVDK SRWQQGNVFS CSVMHEALHN HYTQKSLSLS 450
PGK                                                     453
```

Light chain / Chaîne légère / Cadena ligera

```
QSELTQPRSV SGSPGQSVTI SCTGTSRNIG GGNDVHWYQQ HPGKAPKLLI  50
SGVIERSSGV PDRFSGSKSG NTASLTISGL QAEDEADYYC QSFDGSLSGS 100
VFGTGTDVTV LGQPKAAPSV TLFPPSSEEL QANKATLVCL ISDFYPGAVT 150
VAWKADSSPV KAGVETTTPS KQSNNKYAAS SYLSLTPEQW KSHRSYSCQV 200
THEGSTVEKT VAPTECS                                      217
```

Post-translational modifications
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) 22'-90' 139'-198'
22'"-90'" 139'"-198'"
Inter-H-L (h 5-CL 126) 226-216' 226"-216"
Inter-H-H (h 11, h 14) 232-232" 235-235"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
L VL Q1:
1', 1'"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
303, 303"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
453, 453"

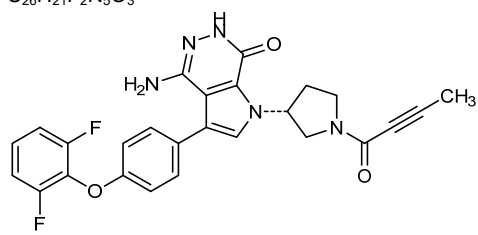
edralbrutinibum

edralbrutinib — 4-amino-1-[(3*R*)-1-(but-2-ynoyl)pyrrolidin-3-yl]-3-[4-(2,6-difluorophenoxy)phenyl]-1,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyridazin-7-one

édralbrutinib — 4-amino-1-[(3*R*)-1-(but-2-ynoyl)pyrrolidin-3-yl]-3-[4-(2,6-difluorophénoxy)phényl]-1,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyridazin-7-one

edralbrutinib — 4-amino-1-[(3*R*)-1-(but-2-inoil)pirrolidin-3-il]-3-[4-(2,6-difluorofenoxi)fenil]-1,6-dihidro-7*H*-pirrolo[2,3-*d*]piridazin-7-ona

$C_{26}H_{21}F_2N_5O_3$



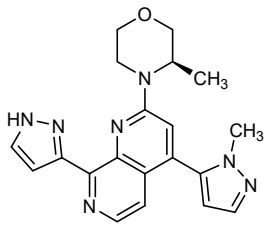
elimusertibum

elimusertib — 2-[(3*R*)-3-methylmorpholin-4-yl]-4-(1-methyl-1*H*-pyrazol-5-yl)-8-(1*H*-pyrazol-3-yl)-1,7-naphthyridine

élimusertib — 2-[(3*R*)-3-méthylmorpholin-4-yl]-4-(1-méthyl-1*H*-pyrazol-5-yl)-8-(1*H*-pyrazol-3-yl)-1,7-naphtyridine

elimusertib 2-[(3*R*)-3-metilmorfolin-4-il]-4-(1-metil-1*H*-pirazol-5-il)-8-(1*H*-pirazol-3-il)-1,7-naftiridina

$C_{20}H_{21}N_7O$



eluvixtamabum #

eluvixtamab immunoglobulin scFv-scFv, anti-[*Homo sapiens* CD33 (sialic acid binding Ig-like lectin 3, SIGLEC3, SIGLEC-3, gp67, p67)] and anti-[*Homo sapiens* CD3E (CD3 epsilon)], monoclonal antibody single chain, bispecific;
IG scFv-scFv single chain, anti-CD33 and anti-CD3E (1-511) [scFv-VH-V-kappa anti-CD33 (1-250) [VH (*Homo sapiens* IGHV1-18*01 (82.7%) -(IGHD) -IGHJ4*01 (93.3%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122)-15-mer tris(tetraglycyl-seryl) linker (123-137) -V-KAPPA (*Homo sapiens* IGKV4-1*01 (83.2%) -IGKJ5*01 (100%)) CDR-IMGT [12.3.9] (164-175.193-195.232-240) (138-250)] -6-mer seryl-tetraglycyl-seryl linker (251-256) -scFv-VH-V-lambda anti-CD3E (257-505) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD)-IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (282-289.307-316.355-370) (257-381) -15-mer tris(tetraglycyl-seryl) linker (382-396) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (422-430.448-450.487-495) (397-505)] -hexahistidine (506-511)], non-glycosylated, produced in Chinese hamster ovary (CHO) cells

éluvixtamab immunoglobuline scFv-scFv, anti-[*Homo sapiens* CD33 (lectine 3 de type Ig-like liant l'acide sialique, SIGLEC3, SIGLEC-3, gp67, p67)] et anti-[*Homo sapiens* CD3E (CD3 epsilon)], anticorps monoclonal à chaîne unique, bispécifique;
IG scFv-scFv à chaîne unique, anti-CD33 et anti-CD3E (1-511) [scFv-VH-V-kappa anti-CD33 (1-250) [VH (*Homo sapiens* IGHV1-18*01 (82.7%) -(IGHD) -IGHJ4*01 (93.3%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122)-15-mer tris(tétraglycyl-séryl) linker (123-137) -V-KAPPA (*Homo sapiens* IGKV4-1*01 (83.2%) -IGKJ5*01 (100%)) CDR-IMGT [12.3.9] (164-175.193-195.232-240) (138-250)] -6-mer séryl-tétraglycyl-séryl linker (251-256) -scFv-VH-V-lambda anti-CD3E (257-505) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD)-IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (282-289.307-316.355-370) (257-381) -15-mer tris(tétraglycyl-séryl) linker (382-396) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%) CDR-IMGT [9.3.9] (422-430.448-450.487-495) (397-505)] -hexahistidine (506-511)], non-glycosylé, produit dans des cellules ovariennes de hamster chinois (CHO)

eluvixtamab inmunoglobulina scFv-scFv, anti-[*Homo sapiens* CD33 (lectina 3 de tipo Ig-like aglutinando el ácido siálico, SIGLEC3, SIGLEC-3, gp67, p67)] y anti-[*Homo sapiens* CD3E (CD3 épsilon)], anticuerpo monoclonal con cadena única, biespecífico;

IG scFv-scFv con cadena única, anti-CD33 y anti-CD3E (1-511) [scFv-VH-V-kappa anti-CD33 (1-250) [VH (*Homo sapiens* IGHV1-18*01 (82.7%) -(IGHD) -IGHJ4*01 (93.3%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122)-15-mer tris(tetraglicil-seril) linker (123-137) -V-KAPPA (*Homo sapiens* IGKV4-1*01 (83.2%) -IGKJ5*01 (100%)) CDR-IMGT [12.3.9] (164-175.193-195.232-240) (138-250)] -6-mer seril-tetraglicil-seril linker (251-256) -scFv-VH-V-lambda anti-CD3E (257-505) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD)-IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (282-289.307-316.355-370) (257-381) -15-mer tris(tetraglicil-seril) linker (382-396) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%) CDR-IMGT [9.3.9] (422-430.448-450.487-495) (397-505)] -hexahistidina (506-511)], no glicosilado, producido en las células ováricas de hamster chino (CHO)

```
Heavy chain / Chaîne lourde / Cadena pesada
QVQLVQSGAE VKKPGESVKV SCKASGYTFT NYGMNWVKQA PGQGLEWMGW  50
INTYTGEPTY ADKFQGRVTM TTDTSTSTAY MEIRNLGGDD TAVYYCARWS 100
WSDGYYVYFD YWGQGTSVTV SSGGGGSGGG GSGGGGSDIV MTQSPDSLTV 150
SLGERTTINC KSSQSVLDSS TNKNSLAWYQ QKPGQPPKLL LSWASTRESG 200
IPDRFSGSGS GTDFTLTIDS PQPEDSATYY CQQSAHFPIT FGQGTRLEIK 250
SGGGGSEVQL VESGGGLVQP GGSLKLSCAA SGFTFNKYAM NWVRQAPGKG 300
LEWVARIRSK YNNYATYYAD SVKDRFTISR DDSKNTAYLQ MNNLKTEDTA 350
VYYCVRHGNF GNSYISYWAY WGQGTLVTVS SGGGGSGGGG SGGGGSQTVV 400
TQEPSLTVSP GGTVTLTCGS STGAVTSGNY PNWVQQKPGQ APRGLIGGTK 450
FLAPGTPARF SGSLLGGKAA LTLSGVQPED EAEYYCVLWY SNRWVFGGGT 500
KLTVLHHHHH H                                            511
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Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-V (C23 C104) 22-96 160-231 278-354 418-486

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
VH Q1: 1

No N-glycosylation sites / pas de sites de N-glycosylation / ningùn posición de N-glycosilación
Aglycosylated

emerfetamabum #
emerfetamab

immunoglobulin scFv-scFv-scFc, anti-[*Homo sapiens* CD33 (sialic acid binding Ig-like lectin 3, SIGLEC3, SIGLEC-3, gp67, p67)] and anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], monoclonal antibody single chain (scFv)2-scFc, bispecific;
IG scFv-scFv-scFc single chain, anti-CD33 and anti-CD3E (1-993) [scFv-VH-V-kappa anti-CD33 (1-250) [VH (*Homo sapiens* IGHV1-18*01 G49>C (44) (81.6%) -(IGHD) -IGHJ4*01 (93.3%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122) -15-mer tris(tetraglycyl-seryl) linker (123-137) -V-KAPPA (*Homo sapiens* IGKV4-1*01 (83.2%) -IGKJ5*01 Q120>C (243) (91.7%)) CDR-IMGT [12.3.9] (164-175.193-195.232-240) (138-250)] -6-mer seryl-tetraglycyl-seryl linker (251-256) -scFv-VH-V-lambda anti-CD3E (257-505) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (282-289.307-316.355-370) (257-381) -15-mer tris(tetraglycyl-seryl) linker (382-396) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (422-430.448-450.487-495) (397-505)] -4-mer tetraglycyl linker (506-509) -scFc (h-CH2-CH3)-(h-CH2-CH3) (510-993) [*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (hinge 6-15 (510-519), CH2 R83>C (581), N84.4>G (586), V85>C (591) (520-629), CH3 E12 (645), M14 (647) (630-734), CHS (735-736)) (510-736) -30-mer hexakis(tetraglycyl-seryl) linker (737-766) -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (hinge 6-15 (767-776), CH2 R83>C (838), N84.4>G (843), V85>C (848) (777-886), CH3 E12 (902), M14 (904) (887-991), CHS (992-993)) (767-993)]], non-glycosylated, produced in Chinese hamster ovary (CHO) cells

émerfétamab	immunoglobuline scFv-scFv-scFc, anti-[*Homo sapiens* CD33 (lectine 3 de type Ig-like liant l'acide sialique, SIGLEC3, SIGLEC-3, gp67, p67)], et anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], anticorps monoclonal à chaîne unique (scFv)2-scFc, bispécifique; IG scFv-scFv-scFc chaîne unique, anti-CD33 et anti-CD3E (1-993) [scFv-VH-V-kappa anti-CD33 (1-250) [VH (*Homo sapiens* IGHV1-18*01 G49>C (44) (81.6%) -(IGHD) -IGHJ4*01 (93.3%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122) -15-mer-tris(tétraglycyl-séryl) linker (123-137) -V-KAPPA (*Homo sapiens* IGKV4-1*01 (83.2%) -IGKJ5*01 Q120>C (243) (91.7%)) CDR-IMGT [12.3.9] (164-175.193-195.232-240) (138-250)] -6-mer séryl-tétraglycyl-séryl linker (251-256) -scFv-VH-V-lambda anti-CD3E (257-505) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (282-289.307-316.355-370) (257-381) -15-mer tris(tétraglycyl-séryl) linker (382-396) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (422-430.448-450.487-495) (397-505)] -4-mer-tétraglycyl linker (506-509) -scFc (h-CH2-CH3)-(h-CH2-CH3) (510-993) [*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (charnière 6-15 (510-519), CH2 R83>C (581), N84.4>G (586), V85>C (591) (520-629), CH3 E12 (645), M14 (647) (630-734), CHS (735-736)) (510-736) -30-mer hexakis(tétraglycyl-séryl) linker (737-766) -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (charnière 6-15 (767-776), CH2 R83>C (838), N84.4>G (843), V85>C (848) (777-886), CH3 E12 (902), M14 (904) (887-991), CHS (992-993)) (767-993)]], non-glycosylé, produit dans des cellules ovariennes de hamster chinois (CHO)
emerfetamab	inmunoglobulina scFv-scFv-scFc, anti-[*Homo sapiens* CD33 (lectina 3 de tipo Ig-like aglutinando el ácido siálico, SIGLEC3, SIGLEC-3, gp67, p67)], y anti-[*Homo sapiens* CD3E (CD3 épsilon, Leu-4)], anticuerpo monoclonal con cadena única (scFv)2-scFc, biespecífico; IG scFv-scFv-scFc cadena única, anti-CD33 y anti-CD3E (1-993) [scFv-VH-V-kappa anti-CD33 (1-250) [VH (*Homo sapiens* IGHV1-18*01 G49>C (44) (81.6%) -(IGHD) -IGHJ4*01 (93.3%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122) -15-mer-tris(tetraglicil-seril) linker (123-137) -V-KAPPA (*Homo sapiens* IGKV4-1*01 (83.2%) -IGKJ5*01 Q120>C (243) (91.7%)) CDR-IMGT [12.3.9] (164-175.193-195.232-240) (138-250)] -6-mer seril-tetraglicil-seril linker (251-256) -scFv-VH-V-lambda anti-CD3E (257-505) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (282-289.307-316.355-370) (257-381) -15-mer tris(tetraglicil-seril) linker (382-396) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (422-430.448-450.487-495) (397-505)] -4-mer-tetraglicil linker (506-509) -scFc (h-CH2-CH3)-(h-CH2-CH3) (510-993) [*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (bisagra 6-15 (510-519), CH2 R83>C (581), N84.4>G (586), V85>C (591) (520-629), CH3 E12 (645), M14 (647) (630-734), CHS (735-736)) (510-736) -30-mer hexakis(tetraglicil-seril) linker (737-766) -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (bisagra 6-15 (767-776), CH2 R83>C (838), N84.4>G (843), V85>C (848) (777-886), CH3 E12 (902), M14 (904) (887-991), CHS (992-993)) (767-993)]], no glicosilado, producido en las células ováricas de hamster chino (CHO)

Heavy chain / Chaîne lourde / Cadena pesada

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QVQLVQSGAE VKKPGESVKV SCKASGYTFT NYGMNWVKQA PGQCLEWMGW  50
INTYTGEPTY ADKFQGRVTM TTDTSTSTAY MEIRNLGGDD TAVYYCARWS 100
WSDGYYVYFD YWGQGTSVTV SSGGGGSGGG GSGGGGSDIV MTQSPDSLTV 150
SLGERTTINC KSSQSVLDSS TNKNSLAWYQ QKPGQPPKLL LSWASTRESG 200
IPDRFSGSGS GTDFTLTIDS PQPEDSATYY CQQSAHFPIT FGCGTRLEIK 250
SGGGGSEVQL VESGGGLVQP GGSLKLSCAA SGFTFNKYAM NWVRQAPGKG 300
LEWVARIRSK YNNYATYYAD SVKDRFTISR DDSKNTAYLQ MNNLKTEDTA 350
VYYCVRHGNF GNSYISYWAY WGQGTLVTVS SGGGGSGGGG SGGGGSQTVV 400
TQEPSLTVSP GGTVTLTCGS STGAVTSGNY PNWVQQKPGQ APRGLIGGTK 450
FLAPGTPARF SGSLLGGKAA LTLSGVQPED EAEYYCVLWY SNRWVFGGGT 500
KLTVLGGGGD KTHTCPPCPA PELLGGPSVF LFPPKPKDTL MISRTPEVTC 550
VVVDVSHEDP EVKFNWYVDG VEVHNAKTKP CEEQYGSTYR CVSVLTVLHQ 600
DWLNGKEYKC KVSNKALPAP IEKTISKAKG QPREPQVYTL PPSREEMTKN 650
QVSLTCLVKG FYPSDIAVEW ESNGQPENNY KTTPPVLDSD GSFFLYSKLT 700
VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL SLSPGKGGGG SGGGGSGGGG 750
SGGGGSGGGG SGGGGSDKTH TCPPCPAPEL LGGPSVFLFP PKPKDTLMIS 800
RTPEVTCVVV DVSHEDPEVK FNWYVDGVEV HNAKTKPCEE QYGSTYRCVS 850
VLTVLHQDWL NGKEYKCKVS NKALPAPIEK TISKAKGQPR EPQVYTLPPS 900
REEMTKNQVS LTCLVKGFYP SDIAVEWESN GQPENNYKTT PPVLDSDGSF 950
FLYSKLTVDK SRWQQGNVFS CSVMHEALHN HYTQKSLSLS PGK        993
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Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-V (C23 C104)	22-96	160-231	278-354	418-486	
Intra-C (C23-C104)	550-610	656-714	807-867	913-971	
Intra-CH2 (C83-C85)	581-591	838-848			
Inter-VH-VL (C49-C120)	44-243				
Inter-h11 (h 11 - h 11)	515-772				
Inter-h14 (h 14 - h 14)	518-775				

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
VH Q1:
1

No N-glycosylation sites / pas de sites de N-glycosylation / ningún posición de N-glicosilación
CH2 N84.4>G:
586, 843
Aglycosylated

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
CHS K2:
993

enibarcimabum

enibarcimab	immunoglobulin G1-kappa, anti-[*Homo sapiens* ADM (adrenomedullin)], monoclonal antibody; gamma1 heavy chain (1-448) [VH (*Homo sapiens* IGHV1-69*01 (86.5%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (215) (119-216), hinge 1-15 (217-231), CH2 (232-341), CH3 D12 (357), L14 (359) (342-446), CHS (447-448)) (119-448)], (221-219')-disulfide with kappa light chain (1'-219') [V-KAPPA (*Mus musculus* IGKV1-117*01 (88.0%) -IGKJ2*01 (100%)/*Homo sapiens* IGKV2-30*01 (88.0%) -IGKJ2*01 (91.7%)) CDR-IMGT [11.3.9] (27-37.55-57.94-102) (1'-112') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (158), V101 (196) (113'-219')]; dimer (227-227'':230-230'')-bisdisulfide, produced in Chinese hamster ovary (CHO)-DG44 cell line, glycoform alfa
énibarcimab	immunoglobuline G1-kappa, anti-[*Homo sapiens* ADM (adrénomédulline)], anticorps monoclonal; chaîne lourde gamma1 (1-448) [VH (*Homo sapiens* IGHV1-69*01 (86.5%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (215) (119-216), charnière 1-15 (217-231), CH2 (232-341), CH3 D12 (357), L14 (359) (342-446), CHS (447-448)) (119-448)], (221-219')-disulfure avec la chaîne légère kappa (1'-219') [V-KAPPA (*Mus musculus* IGKV1-117*01 (88.0%) -IGKJ2*01 (100%)/*Homo sapiens* IGKV2-30*01 (88.0%) -IGKJ2*01 (91.7%)) CDR-IMGT [11.3.9] (27-37.55-57.94-102) (1'-112') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (158), V101 (196) (113'-219')]; dimère (227-227'':230-230'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-DG44, glycoforme alfa

enibarcimab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* ADM (adrenomedulina)], anticuerpo monoclonal;
cadena pesada gamma1 (1-448) [VH (*Homo sapiens* IGHV1-69*01 (86.5%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (215) (119-216), bisagra 1-15 (217-231), CH2 (232-341), CH3 D12 (357), L14 (359) (342-446), CHS (447-448)) (119-448)], (221-219')-disulfuro con la cadena ligera kappa (1'-219') [V-KAPPA (*Mus musculus* IGKV1-117*01 (88.0%) -IGKJ2*01 (100%)/*Homo sapiens* IGKV2-30*01 (88.0%) -IGKJ2*01 (91.7%)) CDR-IMGT [11.3.9] (27-37.55-57.94-102) (1'-112') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (158), V101 (196) (113'-219')];
dímero (227-227":230-230")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-DG44, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

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QVQLVQSGAE VKKPGSSVKV SCKASGYTFS RYWIEWVRQA PGQGLEWIGE  50
ILPGSGSTNY NQKFQGRVTI TADTSTSTAY MELSSLRSED TAVYYCTEGY 100
EYDGFDYWGQ 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 SLSLSPGK   448
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Light chain / Chaîne légère / Cadena ligera

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DVVLTQSPLS LPVTLGQPAS ISCRSSQSIV YSNGNTYLEW YLQRPGQSPR  50
LLIYRVSNRF SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCFQGSHIP 100
YTFGGGTKLE IKRTVAAPSV FIFPPSDEQL KSGTASVVCL LNNFYPREAK 150
VQWKVDNALQ SGNSQESVTE QDSKDSTYSL SSTLTLSKAD YEKHKVYACE 200
VTHQGLSSPV TKSFNRGEC                                   219
```

Post-translational modifications
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'-93' 139'-199'
23'"-93'" 139'"-199'"
Inter-H-L (h 5-CL 126) 221-219' 221"-219'"
Inter-H-H (h 11, h 14) 227-227" 230-230"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"

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.

enomimeranum #

enomimeran

Messenger RNA encoding melanoma-associated antigen 3 (MAGE-A3).
Messenger RNA (mRNA), 5'-capped, encoding codon-optimised melanoma-associated antigen 3 (MAGE-A3, cancer/testis antigen 1.3) expressed as a fusion protein comprising a secretory signal peptide, MAGE-A3, P2P16 tetanus toxoid-derived helper epitopes and a major histocompatibility complex (MHC) class I transmembrane and cytoplasmic domain (MITD), connected by three glycine/serine-rich (GS) linker peptides, flanked by 5' and 3' untranslated regions and a 3' poly(A) tail.

énomiméran

ARN messager codant pour l'antigène 3 associé au mélanome (MAGE-A3).

	Un ARN messager (ARNm), protégé en 5', codant pour l'antigène 3 associé au mélanome (MAGE-A3, antigène 1.3 du cancer testiculaire) , avec des codons optimisés, exprimé sous la forme d'une protéine de fusion comprenant un peptide signal de sécrétion, MAGE-A3, les épitopes auxiliaires P2P16 dérivés de l'anatoxine tétanique et un domaine transmembranaire et cytoplasmique (MITD) du complexe majeur d'histocompatibilité (CMH) de classe I, reliés par trois peptides de liaison riches en glycine/sérine (GS), flanqués de régions non traduites en 5' et 3' et d'une queue poly(A) en 3'.
enomimerán	ARN mensajero que codifica para el antígeno asociado a melanoma 3 (MAGE-A3). ARN mensajero (ARNm), protegido en 5', que codifica para el antígeno asociado a melanoma 3 (MAGE-A3, antígeno de cáncer/testículo 1.3), con codones optimizados, expresado como una proteína de fusión que consta de un péptido señal de secreción, MAGE-A3, los epítopos auxiliares P2P16 derivados del toxoide tetánico y un dominio citoplásmico y transmembrana del complejo principal de histocompatibilidad (MHC) de clase I, conectados mediante tres péptidos de enlace ricos en glicina/serina (GS), flanqueado por las regiones 5' y 3' no traducidas y una cola poly(A) en 3'.

entacingenum turiparvovecum #

entacingene turiparvovec	A replication-defective adeno-associated viral vector encoding cone photoreceptor cyclic nucleotide-gated channel β3 (CNGB3). A recombinant non-replicating adeno-associated viral vector serotype 8 (rAAV8), encoding codon-optimised human cone photoreceptor cyclic nucleotide gated channel β3 (CNGB3), under the control of the human cone arrestin (hCAR) promoter and an SV40 poly(A) sequence, flanked by AAV2 inverted terminal repeats (ITR).
entacingène turiparvovec	Un vecteur adénoviral à réplication défectueuse codant pour le canal du photorécepteur conique β3 (CNGB3), dépendant des nucléotides cycliques. Un vecteur adénoviral recombinant non réplicatif de sérotype 8 (rAAV8), codant pour le canal du photorécepteur du cône humain β3 (CNGB3), dépendant des nucléotides cycliques, avec des codons optimisés, sous le contrôle du promoteur hCAR (arrestine du cône humain) et d'une séquence poly(A) SV40, flanquée de répétitions terminales inversées (ITR) AAV2.
entacingén turiparvovec	Un vector de virus adeno-asociado, deficiente de replicación, que codifica para el canal β3 regulado por nucleótidos cíclicos (CNGB3) del fotorreceptor de los conos. Un vector de virus adeno-asociado recombinante serotipo 8 (rAAV8), deficiente de replicación, que codifica para el canal β3 regulado por nucleótidos cíclicos (CNGB3) del fotorreceptor de los conos, con codones optimizados, bajo el control del promotor de la arrestina de cono humana (hCAR) y una secuencia poly(A) de SV40, flanqueado por las repeticiones invertidas terminales (ITR) del AAV2.

eplontersenum

eplontersen

all-P-ambo-5'-*O*-(28-[(2-acetamido-2-deoxy-β-D-galactopyranosyl)oxy]-16,16-bis{[3-({6-[(2-acetamido-2-deoxy-β-D-galactopyranosyl)oxy]hexyl}amino)-3-oxopropoxy]methyl}-1-hydroxy-1,10,14,21-tetraoxo-2,18-dioxa-9,15,22-triaza-1λ^5-phosphaoctacosan-1-yl)-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methylcytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyluridylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyluridylyl-(3'→5')-2'-*O*-(2-methoxyethyl)guanylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-deoxy-*P*-thioadenylyl-(3'→5')-2'-deoxy-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-deoxy-*P*-thioadenylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-deoxy-*P*-thioadenylyl-(3'→5')-2'-deoxy-*P*-thioadenylyl-(3'→5')-2'-*O*-(2-methoxyethyl)adenylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyluridylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methylcytidine

éplontersen

tout-P-ambo-5'-*O*-(28-[(2-acétamido-2-désoxy-β-D-galactopyranosyl)oxy]-16,16-bis{[3-({6-[(2-acétamido-2-désoxy-β-D-galactopyranosyl)oxy]hexyl}-amino)-3-oxopropoxy]méthyl}-1-hydroxy-1,10,14,21-tétraoxo-2,18-dioxa-9,15,22-triaza-1λ^5-phosphaoctacosan-1-yl)-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthylcytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyluridylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyluridylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)guanylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-désoxy-*P*-thioadénylyl-(3'→5')-2'-désoxy-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-désoxy-*P*-thioadénylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-2'-désoxy-*P*-thioadénylyl-(3'→5')-2'-désoxy-*P*-thioadénylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)adénylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyluridylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthylcytidine

eplontersén

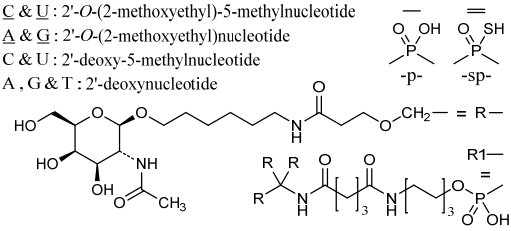
todo-P-ambo-5'-*O*-(28-[(2-acetamido-2-desoxi-β-D-galactopiranosil)oxi]-16,16-bis{[3-({6-[(2-acetamido-2-desoxi-β-D-galactopiranosil)oxi]hexil}amino)-3-oxopropoxi]metil}-1-hidroxi-1,10,14,21-tetraoxo-2,18-dioxa-9,15,22-triaza-1λ^5-fosfaoctacosan-1-il)-2'-*O*-(2-metoxietil)-5-metil-*P*-tiouridilil-(3'→5')-2'-*O*-(2-metoxietil)-5-metilcitidilil-(3'→5')-2'-*O*-(2-metoxietil)-5-metiluridilil-(3'→5')-2'-*O*-(2-metoxietil)-5-metiluridilil-(3'→5')-2'-*O*-(2-metoxietil)guanilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-*P*-tiotimidilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-*P*-tioadenilil-(3'→5')-2'-desoxi-5-metil-*P*-tiocitidilil-(3'→5')-2'-desoxi-*P*-tioadenilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-2'-desoxi-*P*-tioadenilil-(3'→5')-2'-desoxi-*P*-tioadenilil-(3'→5')-2'-*O*-(2-metoxietil)adenilil-(3'→5')-2'-*O*-(2-metoxietil)-5-metiluridilil-(3'→5')-2'-*O*-(2-metoxietil)-5-metil-*P*-tiocitidilil-(3'→5')-2'-*O*-(2-metoxietil)-5-metil-*P*-tiocitidilil-(3'→5')-2'-*O*-(2-metoxietil)-5-metilcitidina

$C_{296}H_{437}N_{77}O_{156}P_{20}S_{13}$

(3'-5') R1-U=C-U-U-G-d(G=T=T=A=C=A=T=G=A=A=)A-U-C=C=C

Legend:

C & U : 2'-*O*-(2-methoxyethyl)-5-methylnucleotide
A & G : 2'-*O*-(2-methoxyethyl)nucleotide
C & U : 2'-deoxy-5-methylnucleotide
A , G & T : 2'-deoxynucleotide



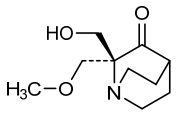
eprenetapoptum

eprenetapopt — *rac*-(2*R*)-2-(hydroxymethyl)-2-(methoxymethyl)-1-azabicyclo[2.2.2]octan-3-one

éprénétapopt — *rac*-(2*R*)-2-(hydroxyméthyl)-2-(méthoxyméthyl)-1-azabicyclo[2.2.2]octan-3-one

eprenetapopt — *rac*-(2*R*)-2-(hidroximetil)-2-(metoximetil)-1-azabiciclo[2.2.2]octan-3-ona

$C_{10}H_{17}NO_3$



and enantiomer
et énantiomère
y enantiómero

etevritamabum #

etevritamab — immunoglobulin scFv-scFv, anti-[*Homo sapiens* EGFR (epidermal growth factor receptor, receptor tyrosine-protein kinase erbB-1, ERBB1, HER1, HER-1, ERBB) variant III (EGFRvIII)] and anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], monoclonal antibody single chain, bispecific;
IG scFv-scFv single chain (1-512) [scFv-VH-V-kappa anti-EGFRvIII(1-251) [VH (*Homo sapiens* IGHV3-33*01 G49>C (44) (93.9%) -IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.17] (26-33.51-58.97-113) (1-124) -15-mer tris(tetraglycyl-seryl) linker (125-139) -V-KAPPA (*Homo sapiens* IGKV2-24*01 (92.0%) -IGKJ1*01 Q120>C (244) (90.9%)) CDR-IMGT [11.3.9] (166-176.194-196.233-241) (140-251)] -6-mer seryl-tetraglycyl-seryl linker (252-257) -scFv-VH-V-lambda anti-CD3E (258-506) [VH (*Mus musculus* IGHV10-1*02 (91.9%)-(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87.0%)-(IGHD) -IGHJ5*01 (100%)) [8.10.16] (258-382) - 15-mer tris(tetraglycyl-seryl) linker (383-397) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%) CDR-IMGT [9.3.9] (423-431.449-451.488-496) (398-506)] -hexahistidine (507-512)], non-glycosylated, produced in Chinese hamster ovary (CHO) cells

étévritamab

immunoglobuline scFv-scFv, anti-[*Homo sapiens* EGFR (récepteur du facteur de croissance épidermique, récepteur tyrosine-protéine kinase erb-1, ERBB1, HER1, HER-1, ERBB) variant III (EGFRvIII)] et anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], anticorps monoclonal à chaîne unique, bispécifique;
IG scFv-scFv chaîne unique (1-512) [scFv-VH-V-kappa anti-EGFRvIII(1-251) [VH (*Homo sapiens* IGHV3-33*01 G49>C (44) (93.9%) -IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.17] (26-33.51-58.97-113) (1-124) -15-mer tris(tétraglycyl-séryl) linker (125-139) – V-KAPPA (*Homo sapiens* IGKV2-24*01 (92.0%) -IGKJ1*01 Q120>C (244) (90.9%)) CDR-IMGT [11.3.9] (166-176.194-196.233-241) (140-251)] -6-mer séryl-tétraglycyl-séryl linker (252-257) -scFv-VH-V-lambda anti-CD3E (258-506) [VH (*Mus musculus* IGHV10-1*02 (91.9%)-(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87.0%)-(IGHD) -IGHJ5*01 (100%)) [8.10.16] (258-382) -15-mer tris(tétraglycyl-séryl) linker (383-397) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%) CDR-IMGT [9.3.9] (423-431.449-451.488-496) (398-506)] -hexahistidine (507-512)], non-glycosylé, produit dans des cellules ovariennes de hamsters chinois (CHO)

etevritamab

inmunoglobulina scFv-scFv, anti-[*Homo sapiens* EGFR (receptor del factor de crecimiento epidérmico, receptor tirosina-proteína kinasa erb-1, ERBB1, HER1, HER-1, ERBB) variante III (EGFRvIII)] y anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], anticuerpo monoclonal de cadena única, biespecífico;
IG scFv-scFv cadena única (1-512) [scFv-VH-V-kappa anti-EGFRvIII(1-251) [VH (*Homo sapiens* IGHV3-33*01 G49>C (44) (93.9%) -IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.17] (26-33.51-58.97-113) (1-124) -15-mer tris(tetraglicil-seril) linker (125-139) – V-KAPPA (*Homo sapiens* IGKV2-24*01 (92.0%) -IGKJ1*01 Q120>C (244) (90.9%)) CDR-IMGT [11.3.9] (166-176.194-196.233-241) (140-251)] -6-mer seril-tetraglicil-seril linker (252-257) -scFv-VH-V-lambda anti-CD3E (258-506) [VH (*Mus musculus* IGHV10-1*02 (91.9%)-(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87.0%)-(IGHD) -IGHJ5*01 (100%)) [8.10.16] (258-382) -15-mer tris(tetraglicil-seril) linker (383-397) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%) CDR-IMGT [9.3.9] (423-431.449-451.488-496) (398-506)] -hexahistidina (507-512)], no glicosilado, producido en las células ováricas de hámster chino (CHO)

Sequence / Séquence / Secuencia

```
QVQLVESGGG VVQSGRSLRL SCAASGFTFR NYGMHWVRQA PGKCLEWVAV  50
IWYDGSDKYY ADSVRGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARDG 100
YDILTGNPRD FDYWGQGTLV TVSSGGGGSG GGGSGGGGSD TVMTQTPLSS 150
HVTLGQPASI SCRSSQSLVH SDGNTYLSWL QQRPGQPPRL LIYRISRRFS 200
GVPDRFSGSG AGTDFTLEIS RVEAEDVGVY YCMQSTHVPR TFGCGTKVEI 250
KSGGGGSEVQ LVESGGGLVQ PGGSLKLSCA ASGFTFNKYA MNWVRQAPGK 300
GLEWVARIRS KYNNYATYYA DSVKDRFTIS RDDSKNTAYL QMNNLKTEDT 350
AVYYCVRHGN FGNSYISYWA YWGQGTLVTV SSGGGGSGGG GSGGGGSQTV 400
VTQEPSLTVS PGGTVTLTCG SSTGAVTSGN YPNWVQQKPG QAPRGLIGGT 450
KFLAPGTPAR FSGSLLGGKA ALTLSGVQPE DEAEYYCVLW YSNRWVFGGG 500
TKLTVLHHHH HH                                          512
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-chain (C23 C104):V 22-96 162-232 279-355 419-487
(C49-C120) V 44-244

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
VH Q1:
1

No N-glycosylation sites / pas de sites de N-glycosylation / ningùm posición de N-glycosilación
Aglycosylated

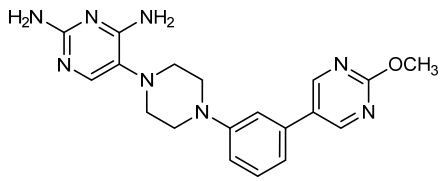
fanotaprimum

fanotaprim — 5-{4-[3-(2-methoxypyrimidin-5-yl)phenyl]piperazin-1-yl}pyrimidine-2,4-diamine

fanotaprim — 5-{4-[3-(2-méthoxypyrimidin-5-yl)phényl]pipérazin-1-yl}pyrimidine-2,4-diamine

fanotaprim — 5-{4-[3-(2-metoxipirimidin-5-il)fenil]piperazin-1-il}pirimidina-2,4-diamina

$C_{19}H_{22}N_8O$



favezelimabum #

favezelimab — immunoglobulin G4-kappa, anti-[*Homo sapiens* LAG3 (lymphocyte activating 3, lymphocyte-activation 3, CD223)], humanized monoclonal antibody;
gamma4 heavy chain humanized (1-446) [VH (*Homo sapiens* IGHV1-58*01 (85.6%) -(IGHD) -IGHJ1*01 (91.7%)) [8.8.12] (1-119) -*Homo sapiens* IGHG4*01 (CH1 (120-217), hinge 1-12 (218-229), CH2 (230-339), CH3 (340-444), CHS (445-446)) (120-446)], (133-218')-disulfide with kappa light chain humanized (1'-218') [V-KAPPA (*Homo sapiens* IGKV2D-29*01 (82.0%) -IGKJ4*01 (100%))[10.3.9] (1'-111') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (157), V101 (195) (112'-218')];
dimer (225-225'':228-228'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

favézélimab — immunoglobuline G4-kappa, anti-[*Homo sapiens* LAG3 (activateur 3 des lymphocytes, lymphocyte-activation 3, CD223)], anticorps monoclonal humanisé;
chaîne lourde gamma4 humanisée (1-446) [VH (*Homo sapiens* IGHV1-58*01 (85.6%) -(IGHD) -IGHJ1*01 (91.7%)) [8.8.12] (1-119) -*Homo sapiens* IGHG4*01 (CH1 (120-217), charnière 1-12 (218-229), CH2 (230-339), CH3 (340-444), CHS (445-446)) (120-446)], (133-218')-disulfure avec la chaîne légère kappa humanisée (1'-218') [V-KAPPA (*Homo sapiens* IGKV2D-29*01 (82.0%) -IGKJ4*01 (100%)) [10.3.9] (1'-111') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (157), V101 (195) (112'-218')];
dimère (225-225'':228-228'')-bisdisulfure, produit dans des cellules ovariennes de hamsters chinois (CHO), glycoforme alfa

favezelimab

inmunoglobulina G4-kappa, anti-[*Homo sapiens* LAG3 (activador 3 de los linfocitos, linfocito-activación 3, CD223)], anticuerpo monoclonal humanizado; cadena pesada gamma4 humanizada (1-446) [VH (*Homo sapiens* IGHV1-58*01 (85.6%) -(IGHD) - IGHJ1*01 (91.7%)) [8.8.12] (1-119) -*Homo sapiens* IGHG4*01 (CH1 (120-217), bisagra 1-12 (218-229), CH2 (230-339), CH3 (340-444), CHS (445-446)) (120-446)], (133-218')-disulfuro con la cadena ligera kappa humanizada (1'-218') [V-KAPPA (*Homo sapiens* IGKV2D-29*01 (82.0%) -IGKJ4*01 (100%)) [10.3.9] (1'-111') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (157), V101 (195) (112'-218')]; dímero (225-225":228-228")-bisdisulfuro, producido en las células ováricas de hamsters chinos (CHO), glicoforma alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QMQLVQSGPE VKKPGTSVKV SCKASGYTFT DYNVDWVRQA RGQRLEWIGD  50
INPNDGGTIY AQKFQERVTI TVDKSTSTAY MELSSLRSED TAVYYCARNY 100
RWFGAMDHWG QGTTVTVSSA STKGPSVFPL APCSRSTSES TAALGCLVKD 150
YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTKTY 200
TCNVDHKPSN TKVDKRVESK YGPPCPPCPA PEFLGGPSVF LFPPKPKDTL 250
MISRTPEVTC VVVDVSQEDP EVQFNWYVDG VEVHNAKTKP REEQFNSTYR 300
VVSVLTVLHQ DWLNGKEYKC KVSNKGLPSS IEKTISKAKG QPREPQVYTL 350
PPSQEEMTKN QVSLTCLVKG FYPSDIAVEW ESNGQPENNY KTTPPVLDSD 400
GSFFLYSRLT VDKSRWQEGN VFSCSVMHEA LHNHYTQKSL SLSLGK     446
```

Light chain / Chaîne légère / Cadena ligera

```
DIVMTQTPLS LSVTPGQPAS ISCKASQSLD YEGDSDMNWY LQKPGQPPQL  50
LIYGASNLES GVPDRFSGSG SGTDFTLKIS RVEAEDVGVY YCQQSTEDPR 100
TFGGGTKVEI KRTVAAPSVF IFPPSDEQLK SGTASVVCLL NNFYPREAKV 150
QWKVDNALQS GNSQESVTEQ DSKDSTYSLS STLTLSKADY EKHKVYACEV 200
THQGLSSPVT KSFNRGEC                                    218
```

Post-translational modifications

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

Intra-H (C23-C104) 22-96 146-202 260-320 366-424
22"-96" 146"-202" 260"-320' 366"-424"
Intra-L (C23-C104) 23'-92' 138'-198'
23'"-92"' 138'"-198'"
Inter-H-L (CH1 10-CL 126) 133-218' 133"-218'"
Inter-H-H (h 11, h 14) 225-225" 228-228"

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

H CH2 N84.4:
296, 296"

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

C-terminal lysine clipping:
H CHS K2:
446, 446"

firazorextonum

firazorexton

N-{(2*S*,3*S*)-1-(2-hydroxy-2-methylpropanoyl)-2-[(2,3',5'-trifluoro[1,1'-biphenyl]-3-yl)methyl]pyrrolidin-3-yl}methanesulfonamide

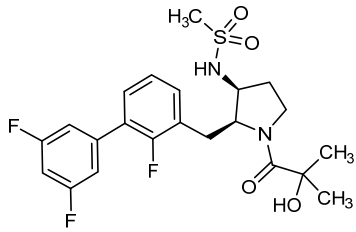
firazorexton

N-{(2*S*,3*S*)-1-(2-hydroxy-2-méthylpropanoyl)-2-[(2,3',5'-trifluoro[1,1'-biphényl]-3-yl)méthyl]pyrrolidin-3-yl}méthanesulfonamide

firazorextón

N-{(2*S*,3*S*)-1-(2-hidroxi-2-metilpropanoil)-2-[(2,3',5'-trifluoro[1,1'-bifenil]-3-il)metil]pirrolidin-3-il}metanosulfonamida

$C_{22}H_{25}F_3N_2O_4S$



flotufolastatum (^{18}F)

flotufolastat (^{18}F)

N^2-(*N*-{(4*S*)-4-carboxy-4-[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraaza-cyclododecan-1-yl]butanoyl}-3-[4-(di-*tert*-butyl(^{18}F)fluorosilyl)benzamido]-D-alanyl)-*N*^{6}-[4-(*N*^{2}-{*N*-[(L-glutamic acid-*N*-yl)carbonyl]-L-γ-glutamyl}-D-ornithin-*N*^{5}-yl)-4-oxobutanoyl]-D-lysine

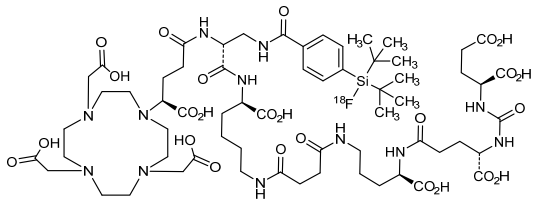
flotufolastat (^{18}F)

N^2-(*N*-{(4*S*)-4-carboxy-4-[4,7,10-tris(carboxyméthyl)-1,4,7,10-tétraaza-cyclododécan-1-yl]butanoyl}-3-[4-(di-*tert*-butyl(^{18}F)fluorosilyl)benzamido]-D-alanyl)-*N*^{6}-[4-(*N*^{2}-{*N*-[(acide L-glutamique-*N*-yl)carbonyl]-L-γ-glutamyl}-D-ornithin-*N*^{5}-yl)-4-oxobutanoyl]-D-lysine

flotufolastat (^{18}F)

N^2-(*N*-{(4*S*)-4-carboxi-4-[4,7,10-tris(carboximetil)-1,4,7,10-tetraazaciclo-dodecan-1-il]butanoil}-3-[4-(di-*terc*-butil(^{18}F)fluorosilil)benzamido]-D-alanil)-*N*^{6}-[4-(*N*^{2}-{*N*-[(ácido L-glutámico-*N*-il)carbonil]-L-γ-glutamil}-D-ornitin-*N*^{5}-il)-4-oxobutanoil]-D-lisina

$C_{63}H_{99}{}^{18}FN_{12}O_{25}Si$



flubentylosinum

flubentylosin

[(4*R*,5*S*,6*S*,7*R*,9*R*,11*E*,13*E*,15*R*,16*R*)-15-{[(6-deoxy-2,3-di-*O*-methyl-β-D-allopyranosyl)oxy]methyl}-6-{[3,6-dideoxy-4-*O*-{2,6-dideoxy-4-*O*-[(4-fluorophenyl)methyl]-3-*C*-methyl-α-L-*ribo*-hexopyranosyl}-3-(dimethylamino)-β-D-glucopyranosyl]oxy}-16-ethyl-4-hydroxy-5,9,13-trimethyl-2,10-dioxo-1-oxacyclohexadeca-11,13-dien-7-yl]acetaldehyde;
4^B-*O*-(4-fluorobenzyl)tylosin

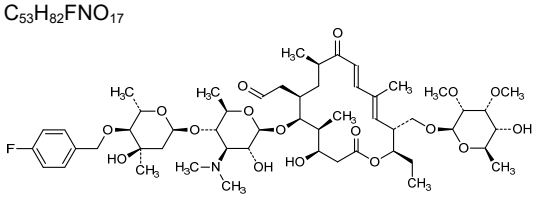
flubentylosine

[(4*R*,5*S*,6*S*,7*R*,9*R*,11*E*,13*E*,15*R*,16*R*)-15-{[(6-désoxy-2,3-di-*O*-méthyl-β-D-allopyranosyl)oxy]méthyl}-6-{[3,6-didésoxy-4-*O*-{2,6-didésoxy-4-*O*-[(4-fluorophényl)méthyl]-3-*C*-méthyl-α-L-*ribo*-hexopyranosyl}-3-(diméthylamino)-β-D-glucopyranosyl]oxy}-16-éthyl-4-hydroxy-5,9,13-triméthyl-2,10-dioxo-1-oxacyclohexadéca-11,13-dién-7-yl]acetaldehyde;
4^B-*O*-(4-fluorobenzyl)tylosine

flubentilosina

[(4*R*,5*S*,6*S*,7*R*,9*R*,11*E*,13*E*,15*R*,16*R*)-15-{[(6-desoxi-2,3-di-*O*-metil-β-D-alopiranosil)oxi]metil}-6-{[3,6-didesoxi-4-*O*-{2,6-didesoxi-4-*O*-[(4-fluorofenil)metil]-3-*C*-metil-α-L-*ribo*-hexopiranosil}-3-(dimetilamino)-β-D-glucopiranosil]oxi}-16-etil-4-hidroxi-5,9,13-trimetil-2,10-dioxo-1-oxaciclohexadeca-11,13-dien-7-il]acetaldehído; 4^B-*O*-(4-fluorobencil)tilosina

$C_{53}H_{82}FNO_{17}$



fordadistrogenum movaparvovecum #

fordadistrogene movaparvovec

A replication-defective adeno-associated viral vector encoding a codon-optimised mini-dystrophin (DMD).
A recombinant replication-defective adeno-associated viral vector serotype 9 (rAAV9), encoding a codon-optimised mini-dystrophin (DMD) gene comprising the N-terminus, hinge regions H1, H3 and H4, spectrin-like repeats R1, R2 and R22-24, and the C-terminal cysteine-rich region, under the control of a human muscle-specific synthetic enhancer/promoter and a synthetic poly(A) sequence, flanked by AAV2 inverted terminal repeats (ITR).

fordadistrogène movaparvovec

Un vecteur adénoviral à réplication défectueuse et codant pour une mini-dystrophine (DMD) avec des codons optimisés.
Un vecteur adénoviral recombinant de sérotype 9 (rAAV9) à réplication défectueuse, codant pour un gène de mini-dystrophine (DMD) avec des codons optimisés, comprenant l'extrémité N-terminale, les régions charnières H1, H3 et H4, les répétitions de type spectrine R1, R2 et R22-24, et la région C-terminale riche en cystéines, sous le contrôle d'un promoteur/amplificateur synthétique spécifique du muscle humain et d'une séquence synthétique poly(A), flanquée de répétitions terminales inversées (ITR) de l'AAV2.

fordadistrogén movaparvovec

Un vector de virus adeno-asociado, deficiente de replicación, que codifica para una mini-distrofina (DMD) con los codones optimizados.
Un vector de virus adeno-asociado recombinante de serotipo 9 (rAAV9), deficiente de replicación, que codifica para un gen de mini-distrofina (DMD) con los codones optimizados que contiene el extremo N-terminal, las regiones bisagra H1, H3 y H4, las repeticiones de tipo espectrina R1, R2 y R22-24, y la región C-terminal rica en cisteínas, bajo el control de un promotor/amplificador (enhancer) sintético específico de músculo humano y una secuencia poly(A) sintética, flanqueado por las repeticiones terminales invertidas (ITR) del AAV2.

gallium (^{68}Ga) gozetotidum

gallium (^{68}Ga) gozetotide

{*N*-[(*N*^{6}-{6-[3-(3-{[{2-[{[5-(2-carboxyethyl)-2-hydroxy-κ*O*-phenyl]methyl}(carboxy-κ*O*-methyl)amino-κ*N*]ethyl}(carboxy-κ*O*-methyl)amino-κ*N*]methyl}-4-hydroxy-κ*O*-phenyl)propanamido]hexanoyl}-L-lysin-*N*^{2}-yl)carbonyl]-L-glutamato(3−)}(^{68}Ga)gallium

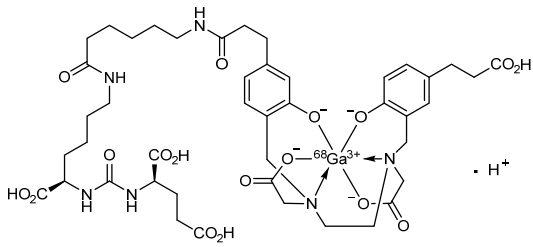
gallium (^{68}Ga) gozétotide

{*N*-[(*N*^{6}-{6-[3-(3-{[{2-[{[5-(2-carboxyéthyl)-2-hydroxy-κ*O*-phényl]méthyl}(carboxy-κ*O*-méthyl)amino-κ*N*]éthyl}(carboxy-κ*O*-méthyl)amino-κ*N*]méthyl}-4-hydroxy-κ*O*-phényl)propanamido]hexanoyl}-L-lysin-*N*^{2}-yl)carbonyl]-L-glutamato(3−)}(^{68}Ga)gallium

galio (^{68}Ga) gozetótida

{*N*-[(*N*^{6}-{6-[3-(3-{[{2-[{[5-(2-carboxietil)-2-hidroxi-κ*O*-fenil]metil}(carboxi-κ*O*-metil)amino-κ*N*]etil}(carboxi-κ*O*-metil)amino-κ*N*]metil}-4-hidroxi-κ*O*-fenil)propanamido]hexanoil}-L-lisin-*N*^{2}-il)carbonil]-L-glutamato(3−)}(^{68}Ga)galio

$C_{44}H_{59}{}^{68}GaN_6O_{17}$



garivulimabum #

garivulimab

immunoglobulin G1-kappa, anti-[*Homo sapiens* CD274 (programmed death ligand 1, PDL1, PD-L1, B7 homolog 1, B7H1)], humanized monoclonal antibody; gamma1 heavy chain humanized (1-446) [VH humanized (*Homo sapiens* IGHV3-NL1*01 (84.7%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.7.11] (26-33.51-57.96-106) (1-117) -*Homo sapiens* IGHG1*01 G1m17,1, G1v4 CH2 A114 (CH1 K120 (214) (118-215), hinge 1-15 (216-230) -CH2 V1.2>A (234), P114>A (329) (231-339), CH3 D12 (355), L14 (357) (340-444), CHS (445-446)) (118-446)], (220-215')-disulfide with kappa light chain humanized (1'-215') [V-KAPPA humanized (*Homo sapiens* IGKV1-5*03 (84.0%) -IGKJ2*01 (91.7%)) CDR-IMGT [6.3.10] (27-32.50-52.89-98) (1'-108') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (154), V101 (192) (109'-215')]; dimer (226-226":229-229")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

garivulimab

immunoglobuline G1-kappa, anti-[*Homo sapiens* CD274 (ligand 1 de mort programmée, PDL1, PD-L1, homologue 1 de B7, B7H1)], anticorps monoclonal humanisé;

chaîne lourde gamma1 humanisée (1-446) [VH humanisé (*Homo sapiens* IGHV3-NL1*01 (84.7%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.7.11] (26-33.51-57.96-106) (1-117) -*Homo sapiens* IGHG1*01 G1m17,1, G1v4 CH2 A114 (CH1 K120 (214) (118-215), charnière 1-15 (216-230) -CH2 V1.2>A (234), P114>A (329) (231-339), CH3 D12 (355), L14 (357) (340-444), CHS (445-446)) (118-446)], (220-215')-disulfure avec la chaîne légère kappa humanisée (1'-215') [V-KAPPA humanisé (*Homo sapiens* IGKV1-5*03 (84.0%) -IGKJ2*01 (91.7%)) CDR-IMGT [6.3.10] (27-32.50-52.89-98) (1'-108') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (154), V101 (192) (109'-215')]; dimère (226-226":229-229")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

garivulimab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* CD274 (ligando 1 de muerte programada, PDL1, PD-L1, homólogo 1 de B7, B7H1)], anticuerpo monoclonal humanizado; cadena pesada gamma1 humanizada (1-446) [VH humanizado (*Homo sapiens* IGHV3-NL1*01 (84.7%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.7.11] (26-33.51-57.96-106) (1-117) -*Homo sapiens* IGHG1*01 G1m17,1, G1v4 CH2 A114 (CH1 K120 (214) (118-215), bisagra 1-15 (216-230) -CH2 V1.2>A (234), P114>A (329) (231-339), CH3 D12 (355), L14 (357) (340-444), CHS (445-446)) (118-446)], (220-215')-disulfuro con la cadena ligera kappa humanizada (1'-215') [V-KAPPA humanizado (*Homo sapiens* IGKV1-5*03 (84.0%) -IGKJ2*01 (91.7%)) CDR-IMGT [6.3.10] (27-32.50-52.89-98) (1'-108') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (154), V101 (192) (109'-215')]; dímero (226-226":229-229")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGGSLRL SCAVSGFSLT SYGVHWVRQA PGKGLEWVAV  50
IWAGGSTNYA DSVKGRFTIS KDTSKNTVYL QMNSLRAEDT AVYYCAKPYG 100
TSAMDYWGQG TLVTVSSAST KGPSVFPLAP SSKSTSGGTA ALGCLVKDYF 150
PEPVTVSWNS GALTSGVHTF PAVLQSSGLY SLSSVVTVPS SSLGTQTYIC 200
NVNHKPSNTK VDKKVEPKSC DKTHTCPPCP APPAAGPSVF LFPPKPKDTL 250
MISRTPEVTC VVVDVSHEDP EVKFNWYVDG VEVHNAKTKP REEQYNSTYR 300
VVSVLTVLHQ DWLNGKEYKC KVSNKALAAP IEKTISKAKG QPREPQVYTL 350
PPSRDELTKN QVSLTCLVKG FYPSDIAVEW ESNGQPENNY KTTPPVLDSD 400
GSFFLYSKLT VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL SLSPGK     446
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Light chain / Chaîne légère / Cadena ligera

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DIQMTQSPSS LSASVGDRVT ITCKASQDVG IVVAWYQQKP GKAPKLLIYW  50
ASIRHTGVPS RFSGSGSGTE FTLTISSLQP DDFATYYCQQ YSNYPLYTFG 100
QGTKVEIKRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK 150
VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ 200
GLSSPVTKSF NRGEC                                       215
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-95 144-200 260-320 366-424
22"-95" 144"-200" 260"-320" 366"-424"
Intra-L (C23-C104) 23'-88' 135'-195'
23'"-88'" 135'"-195'"
Inter-H-L (h 5-CL 126) 220-215' 220"-215'"
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:
296, 296"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
446, 446"

garveleucelum

garveleucel	Allogeneic T cell-enriched leukocyte preparation, devoid of alloreactive T cells. The cells are derived from peripheral blood mononuclear cells (PBMCs) collected by apheresis from a haploidentical stem cell donor. The cells are lymphocyte enriched, and during processing patient and donor cells are co-cultured *ex vivo* in an MLR (mixed lymphocyte reaction) to stimulate activation of host alloreactive T-cells and subsequent depletion of these cells using a proprietary rhodamine-based photodynamic treatment. In this process, monocytes are largely eliminated from the cell mixture. The cells are primarily T cells (average ~90%) consisting of both CD4+ T-helper cells and CD8+ T-cytotoxic cells (mean CD4:CD8 ratio of 2.1), and other leucocytes (average ~10%, with B-cells (~ 6-7%) and NK cells (~ 2-3%).
garvéleucel	Préparation de leucocytes enrichis en cellules T allogéniques, dépourvus de cellules T alloréactives. Les cellules sont dérivées de cellules mononucléaires du sang périphérique (PBMC) prélevées par aphérèse chez un donneur de cellules souches partiellement compatible pour les antigènes HLA. Les cellules sont enrichies en lymphocytes et, pendant le traitement, les cellules du patient et du donneur sont co-cultivées *ex vivo* selon une RML (réaction lymphocytaire mixte) pour stimuler l'activation des cellules T allo-réactives de l'hôte et l'épuisement ultérieur de ces cellules grâce à un traitement photodynamique exclusif à base de rhodamine. Dans ce processus, les monocytes sont largement éliminés du mélange de cellules. Les cellules sont principalement des cellules T (en moyenne ~90%) composées à la fois de cellules T auxiliaires CD4+ et de cellules T cytotoxiques CD8+ (rapport moyen CD4:CD8 de 2.1), et d'autres leucocytes (en moyenne ~10%, avec des cellules B (~6-7%) et des cellules NK (~ 2-3%).
garveleucel	Preparación de leucocitos enriquecidos en células T alogénicos, desprovistos de células T aloreactivas. Las células se obtienen a partir de células mononucleares de sangre periférica (PBMCs) recogidas por aféresis de un donante de células madre haploidéntico. Las células se enriquecen en linfocitos, y durante el procesamiento, las células del paciente y del donante se co-cultivan *ex vivo* en una MLR (reacción mixta de linfocitos) para estimular la activación de células T aloreactivas frente al huésped y la subsiguiente depleción de estas células usando un tratamiento fotodinámico basado en la rodamina. En este proceso, los monocitos en su mayoría se eliminan de la mezcla celular. Las células son principalmente células T (~90% como media) y consisten en células T colaboradoras CD4+ y células T citotóxicas CD8+ (ratio medio CD4:CD8 de 2.1), y otros leucocitos (media ~10%, con células B (~6-7%) y células NK (~2-3%).

gavocabtagenum autoleucelum #

gavocabtagene autoleucel	Autologous T cells transduced *ex vivo* with a self-inactivating lentiviral vector encoding an anti-mesothelin (MSLN) chimeric antigen receptor Autologous T cells transduced *ex vivo* with a non-replicating, self-inactivating (SIN) lentiviral vector, encoding an anti-mesothelin (MSLN) single-domain antibody (sdAb) based chimeric antigen receptor with a leader sequence derived from granulocyte-macrophage colony-stimulating factor receptor alpha (GMCSFR-alpha), fused to the CD3ε subunit of the T-cell receptor (TCR) via an A3(G4S)3LE flexible linker, which is incorporated into the endogenous TCR complex upon expression. The transgene is under control of elongation factor-1 alpha (EF-1α) promoter and woodchuck hepatitis virus post-transcriptional regulatory element. The vector genome also contains a packaging signal, a partial *gag* sequence, a Rev Response Element (RRE), a central polypurine tract (cPPT) and a 3' polypurine tract (3'PPT).
gavocabtagène autoleucel	Cellules T autologues transduites *ex vivo* avec un vecteur lentiviral non réplicatif codant pour un récepteur chimérique anti-mésothéline (MSLN). Cellules T autologues transduites *ex vivo* avec un vecteur lentiviral non réplicatif et auto-inactivable (SIN), codant pour un récepteur antigénique chimérique basé sur les anticorps anti-mésothéline (MSLN) à domaine unique (sdAb). Il comprend une séquence leader dérivée du récepteur alpha du facteur de stimulation des colonies de granulocytes-macrophages (GMCSFR-alpha), fusionné à la sous-unité CD3ε du récepteur des cellules T (TCR) via un polypeptide lieur flexible nommé A3(G4)3LE, qui est incorporé dans le complexe TCR endogène lors de l'expression. Le transgène est sous le contrôle du promoteur du facteur d'élongation 1 alpha (EF-1α) ainsi que de l'élément régulateur post-transcriptionnel du virus de l'hépatite de la marmotte. Le génome du vecteur contient aussi un signal de conditionnement des gènes, une séquence *gag* partielle, un élément de réponse Rev (RRE), une région centrale avec tractus polypurin (cPPT) et un tractus polypurin 3' (3'PPT).
gavocabtagén autoleucel	Células T autólogas transducidas *ex vivo* con un vector lentiviral auto-inactivante que codifica para un receptor de antígenos quimérico anti-mesotelina (MSLN). Células T autólogas transducidas *ex vivo* con vector lentiviral auto-inactivante, no replicativo, que codifica para un receptor de antígenos quimérico basado en un anticuerpo de domino único (sdAb) anti-mesotelina (MSLN) con una secuencia líder derivada del receptor alfa del factor estimulador de colonias de granulocitos-macrófagos (GMCSFR-alfa), fusionado a la subunidad CD3ε del receptor de la célula T (TCR) mediante un conector (linker) flexible A3(G4S)3LE, que se incorpora en el complejo TCR endógeno al expresarse. El transgen está bajo el control del promotor del factor de elongación 1 alfa (EF-1α) y elemento regulador post-transcripcional del virus de la hepatitis de la marmota. El genoma del vector también contiene una señal empaquetadora, un secuencia *gag* parcial, un elemento de respuesta Rev (RRE), un segmento central de polipurinas (cPPT) y un segmento 3' de polipurinas (3'PPT).

geptanolimabum #

geptanolimab

immunoglobulin G4-kappa, anti-[*Homo sapiens* PDCD1 (programmed cell death 1, PD-1, PD1, CD279)], monoclonal antibody;
gamma4 heavy chain (1-440) [VH (*Homo sapiens*IGHV7-4-1*02 (85.7%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.7] (26-33.51-58.97-103) (1-114)-*Homo sapiens* IGHG4*01, G4v5 h P10 (CH1 (115-212), hinge 1-12 S10>P (222) (213-224), CH2 (225-334), CH3 (335-439), CHS K>del (440) (115-440)], (28-217')-disulfide with kappa light chain (1'-217') [V-KAPPA (*Mus musculus* IGKV3-5*01 (89.9%) -IGKJ1*01 (90.9%)/*Homo sapiens* IGKV3D-11*02 (64.9%) -IGKJ2*01 (100%)) CDR-IMGT [10.3.8] (27-36.54-56.93-100) (1'-110') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (156), V101 (194) (111'-217')];
dimer (220-220":223-223")-bisdisulfide, produced in Chinese hamster ovary (CHO)-S cell line, glycoform alfa

geptanolimab

immunoglobuline G4-kappa, anti-[*Homo sapiens* PDCD1 (protéine 1 de mort cellulaire programmée, PD-1, PD1, CD279)], anticorps monoclonal;
chaîne lourde gamma4 (1-440) [VH (*Homo sapiens* IGHV7-4-1*02 (85.7%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.7] (26-33.51-58.97-103) (1-114) -*Homo sapiens* IGHG4*01, G4v5 h P10 (CH1 (115-212), charnière 1-12 S10>P (222) (213-224), CH2 (225-334), CH3 (335-439), CHS K>del (440) (115-440)], (128-217')-disulfure avec la chaîne légère kappa (1'-217') [V-KAPPA (*Mus musculus* IGKV3-5*01 (89.9%) -IGKJ1*01 (90.9%)/*Homo sapiens* IGKV3D-11*02 (64.9%) -IGKJ2*01 (100%)) CDR-IMGT [10.3.8] (27-36.54-56.93-100) (1'-110') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (156), V101 (194) (111'-217')];
dimère (220-220":223-223")-bisdisulfure, produit dans des cellules ovariennes de hamsters chinois (CHO) lignée cellulaire CHO-S, glycoforme alfa

geptanolimab

inmunoglobulina G4-kappa, anti-[*Homo sapiens* PDCD1 (proteína 1 de muerte celular programada, PD-1, PD1, CD279)], anticuerpo monoclonal;
cadena pesada gamma4 (1-440) [VH (*Homo sapiens* IGHV7-4-1*02 (85.7%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.7] (26-33.51-58.97-103) (1-114) -*Homo sapiens* IGHG4*01, G4v5 h P10 (CH1 (115-212), bisagra 1-12 S10>P (222) (213-224), CH2 (225-334), CH3 (335-439), CHS K>del (440) (115-440)], (128-217')-disulfuro con la cadena ligera kappa (1'-217') [V-KAPPA (*Mus musculus* IGKV3-5*01 (89.9%) -IGKJ1*01 (90.9%)/*Homo sapiens* IGKV3D-11*02 (64.9%) -IGKJ2*01 (100%)) CDR-IMGT [10.3.8] (27-36.54-56.93-100) (1'-110') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (156), V101 (194) (111'-217')];
dímero (220-220":223-223")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-S, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QIQLVQSGSE LKKPGASVKV SCKASGYTFT NFGMNWVRQA PGQGLKWMGW  50
ISGYTREPTY AADFKGRFVI SLDTSVSTAY LQISSLKAED TAVYYCARDV 100
FDYWGQGTLV TVSSASTKGP SVFPLAPCSR STSESTAALG CLVKDYFPEP 150
VTVSWNSGAL TSGVHTFPAV LQSSGLYSLS SVVTVPSSSL GTKTYTCNVD 200
HKPSNTKVDK RVESKYGPPC PPCPAPEFLG GPSVFLFPPK PKDTLMISRT 250
PEVTCVVVDV SQEDPEVQFN WYVDGVEVHN AKTKPREEQF NSTYRVVSVL 300
TVLHQDWLNG KEYKCKVSNK GLPSSIEKTI SKAKGQPREP QVYTLPPSQE 350
EMTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL 400
YSRLTVDKSR WQEGNVFSCS VMHEALHNHY TQKSLSLSLG            440
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Light chain / Chaîne légère / Cadena ligera

```
DIVLTQSPAS LAVSPGQRAT ITCRASESVD NYGYSFMNWF QQKPGQPPKL  50
LIYRASNLES GVPARFSGSG SRTDFTLTIN PVEADDTANY YCQQSNADPT 100
FGQGTKLEIK RTVAAPSVFI FPPSDEQLKS GTASVVCLLN NFYPREAKVQ 150
WKVDNALQSG NSQESVTEQD SKDSTYSLSS TLTLSKADYE KHKVYACEVT 200
HQGLSSPVTK SFNRGEC                                     217
```

Post-translational modifications

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

Intra-H (C23-C104) 22-96 141-197 255-315 361-419
22"-96" 141"-197" 255"-315" 361"-419"
Intra-L (C23-C104) 23'-92' 137'-197'
23'"-92'" 137'"-197'"
Inter-H-L (h 10-CL 126) 128-217' 128"-217'"
Inter-H-H (h 8, h 11) 220-220" 223-223"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
291, 291"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

gindameranum #

gindameran

Messenger RNA encoding cancer/testis antigen 1 (New York oesophageal squamous cell carcinoma antigen-1).
Messenger RNA (mRNA), 5'-capped, encoding codon-optimised New York esophageal squamous cell carcinoma antigen-1 (NY-ESO-1; cancer/testis antigen 1, CTAG1A) expressed as a fusion protein comprising a secretory signal peptide, NY-ESO-1, P2P16 tetanus toxoid-derived helper epitopes and a major histocompatibility complex (MHC) class I transmembrane and cytoplasmic domain (MITD), connected by three glycine/serine-rich (GS) linker peptides, flanked by 5' and 3' untranslated regions and a 3' poly(A) tail.

gindaméran

ARN messager codant pour l'antigène 1 du cancer testiculaire (antigène 1 du carcinome squameux de l'œsophage, dit de New York).
ARN messager (ARNm), protégé en 5', codant pour l'antigène 1 du carcinome squameux de l'œsophage, dit de New York (NY-ESO-1; antigène 1 du cancer testiculaire, CTAG1A), avec des codons optimisés, exprimé sous la forme d'une protéine de fusion comprenant un peptide signal de sécrétion, NY-ESO-1, les épitopes auxiliaires P2P16 dérivés de l'anatoxine tétanique et un domaine transmembranaire et cytoplasmique (MITD) du complexe majeur d'histocompatibilité (CMH) de classe I, reliés par trois peptides de liaison riches en glycine/sérine (GS), flanqués de régions non traduites en 5' et 3' et d'une queue poly(A) en 3'.

gindamerán	ARN mensajero que codifica para el antígeno 1 de cáncer/testículo (antígeno 1 de carcinoma escamoso del esófago Nueva York). ARN mensajero (ARNm), protegido en 5', que codifica para el antígeno 1 de carcinoma escamoso del esófago Nueva York (NY-ESO-1; antígeno cáncer/testículo 1, CTAG1A) con codones optimizados, que se expresa como una proteína de fusión que consta de un péptido señal de secreción, NY-ESO-1, los epítopos auxiliares P2P16 derivados del toxoide tetánico y un dominio citoplásmico y transmembrana del complejo principal de histocompatibilidad (MHC) de clase I (MITD), conectados mediante tres péptidos de enlace ricos en glicina/serina (GS), flanqueado por las regiones 5' y 3' no traducidas y una cola poly(A) en 3'.
grisnilimabum #	
grisnilimab	immunoglobulin G2A-lambda, anti-[CD7 (CD7 antigen (p41),GP40, LEU-9, TP41, Tp40)], *Mus musculus* monoclonal antibody; gamma2a heavy chain *Mus musculus* (1-453) [VH (*Mus musculus* IGHV9-3-1*01 (98%) -(IGHD) -IGHJ2*01 (93.3%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Mus musculus* IGHG2A*01 (100%) (CH1 (124-220), hinge 1-16 (221-236), CH2 (237-346), CH3 (347-451), CHS (452-453)) (124-453)], (138-214')-disulfide with lambda light chain *Mus musculus* (1'-215') [V-LAMBDA (*Mus musculus* IGLV1*01 (98%) -IGLJ1*01 (100%)) CDR-IMGT [9.3.9] (26-34.52-54.91-99) (1'-109') -*Mus musculus* IGLC1*01 (100%) (110'-215')]; dimer (230-230":233-233":235-235")-trisdisulfide, produced in SP2/0-derived mouse myeloma cells, glycoform alfa
grisnilimab	immunoglobuline G2A-lambda, anti-[CD7 (CD7 antigène (p41), GP40, LEU-9, TP41, Tp40)], anticorps monoclonal *Mus musculus*; chaîne lourde gamma2a *Mus musculus* (1-453) [VH (*Mus musculus* IGHV9-3-1*01 (98%) -(IGHD) -IGHJ2*01 (93.3%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Mus musculus* IGHG2A*01 (100%) (CH1 (124-220), charnière 1-16 (221-236), CH2 (237-346), CH3 (347-451), CHS (452-453)) (124-453)], (138-214')-disulfure avec la chaîne légère lambda *Mus musculus* (1'-215') [V-LAMBDA (*Mus musculus* IGLV1*01 (98%) -IGLJ1*01 (100%)) CDR-IMGT [9.3.9] (26-34.52-54.91-99) (1'-109') -*Mus musculus* IGLC1*01 (100%) (110'-215')]; dimère (230-230":233-233":235-235")-trisdisulfure, produit par une ligne cellulaire derivée de myélome murin SP2/0, glycoforme alfa
grisnilimab	inmunoglobulina G2A-lambda, anti-[CD7 (CD7 antígeno (p41), GP40, LEU-9, TP41, Tp40)], anticuerpo monoclonal *Mus musculus*;

cadena pesada gamma2a *Mus musculus* (1-453) [VH (*Mus musculus* IGHV9-3-1*01 (98%) -(IGHD) -IGHJ2*01 (93.3%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Mus musculus* IGHG2A*01 (100%) (CH1 (124-220), bisagra 1-16 (221-236), CH2 (237-346), CH3 (347-451), CHS (452-453)) (124-453)], (138-214')-disulfuro con la cadena ligera lambda *Mus musculus* (1'-215') [V-LAMBDA (*Mus musculus* IGLV1*01 (98%) -IGLJ1*01 (100%)) CDR-IMGT [9.3.9] (26-34.52-54.91-99) (1'-109') -*Mus musculus* IGLC1*01 (100%) (110'-215')];
dímero (230-230":233-233":235-235")-trisdisulfuro, producido en una línea celular de mieloma murino SP2/0, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QIQLVQSGPE LKKPGETVKI SCKASGYTFT NYGMNWVKQA PGKGLMWLGW  50
INTYTGEPTY ADDFKGRFAF SLETSASTAY LQINNLKNED TATYFCARWA 100
YFYGSSPYFF DYWGQGTTLT VSSAKTTAPS VYPLAPVCGD TTGSSVTLGC 150
LVKGYFPEPV TLTWNSGSLS SGVHTFPAVL QSDLYTLSSS VTVTSSTWPS 200
QSITCNVAHP ASSTKVDKKI EPRGPTIKPC PPCKCPAPNL LGGPSVFIFP 250
PKIKDVLMIS LSPIVTCVVV DVSEDDPDVQ ISWFVNNVEV HTAQTQTHRE 300
DYNSTLRVVS ALPIQHQDWM SGKEFKCKVN NKDLPAPIER TISKPKGSVR 350
APQVYVLPPP EEEMTKKQVT LTCMVTDFMP EDIYVEWTNN GKTELNYKNT 400
EPVLDSDGSY FMYSKLRVEK KNWVERNSYS CSVVHEGLHN HHTTKSFSRT 450
PGK                                                     453
```

Light chain / Chaîne légère / Cadena ligera

```
QAVVTQESAL TTSPGETVTL TCRSSTGAVT TSNYANWVQE KPDHLFTGLI  50
GGTNNRAPGV PARFSGSLIG DKAALTITGA QTEDEAIYFC ALWCSNHLVF 100
GGGTKLTVLG QPKSSPSVTL FPPSSEELET NKATLVCTIT DFYPGVVTVD 150
WKVDGTPVTQ GMETTQPSKQ SNNKYMASSY LTLTARAWER HSSYSCQVTH 200
EGHTVEKSLS RADCS                                        215
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 150-205 267-327 373-431
22"-96" 150"-205" 267"-327" 373"-431"
Intra-L (C23-C104) 22'-90' 137'-196'
22'"-90'" 137'"-196'"
Inter-H-L (CH1 11-CL 126) 138-214' 138"-214'"
Inter-H-H (h 12, h 15, h 18) 230-230" 233-233" 235-235"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"
L VL Q1:
1', 1'"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
303, 303"
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

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
453, 453"

grisnilimabum setaritoxum #
grisnilimab setaritox

immunoglobulin G2A-lambda, anti-[CD7 (CD7 antigen (p41),GP40, LEU-9, TP41, Tp40)], *Mus musculus* monoclonal antibody conjugated to ricin toxin A (RTA); gamma2a heavy chain *Mus musculus* (1-453) [VH (*Mus musculus* IGHV9-3-1*01 (98%) -(IGHD) -IGHJ2*01 (93.3%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Mus musculus* IGHG2A*01 (100%) (CH1 (124-220), hinge 1-16 (221-236), CH2 (237-346), CH3 (347-451), CHS (452-453)) (124-453)], (138-214')-disulfide

	with lambda light chain *Mus musculus* (1'-215') [V-LAMBDA (*Mus musculus* IGLV1*01 (98%) - IGLJ1*01 (100%)) CDR-IMGT [9.3.9] (26-34.52-54.91-99) (1'-109') -*Mus musculus* IGLC1*01 (100%) (110'-215')]; dimer (230-230":233-233":235-235")-trisdisulfide, produced in SP2/0-derived mouse myeloma cells, glycoform alfa, substituted at N^6 of an average of 1.6 lysyl residues with 4-[(1*RS*)-1-{[L-methionyl-ricin toxin A-chain (Met-RTA, non-glycosylated, produced in *Escherichia coli*)-S^{260}-yl]sulfanyl}ethyl]benzoyl groups
grisnilimab sétaritox	immunoglobuline G2A-lambda, anti-[CD7 (CD7 antigène (p41), GP40, LEU-9, TP41, Tp40)], anticorps monoclonal *Mus musculus* conjugué à la toxine A de la ricine (RTA); chaîne lourde gamma2a *Mus musculus* (1-453) [VH (*Mus musculus* IGHV9-3-1*01 (98%) -(IGHD) - IGHJ2*01 (93.3%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Mus musculus* IGHG2A*01 (100%) (CH1 (124-220), charnière 1-16 (221-236), CH2 (237-346), CH3 (347-451), CHS (452-453)) (124-453)], (138-214')-disulfure avec la chaîne légère lambda *Mus musculus* (1'-215') [V-LAMBDA (*Mus musculus* IGLV1*01 (98%) -IGLJ1*01 (100%)) CDR-IMGT [9.3.9] (26-34.52-54.91-99) (1'-109') -*Mus musculus* IGLC1*01 (100%) (110'-215')]; dimère (230-230":233-233":235-235")-trisdisulfure, produit par une lignée cellulaire dérivée de myélome murin SP2/0, glycoforme alfa, substitué en N^6 sur un moyenne de 1.6 résidus lysyl par des groupes 4-[(1*RS*)-1-{[L-méthionyl-chaîne A de la toxine de ricine (Met-RTA, non-glycosylée, produite par *Escherichia coli*)-S^{260}-yl]sulfanyl}éthyl]benzoyle
grisnilimab setaritox	inmunoglobulina G2A-lambda, anti-[CD7 (CD7 antígeno (p41), GP40, LEU-9, TP41, Tp40)], anticuerpo monoclonal *Mus musculus* conjugado con la toxina A de la ricina (RTA); cadena pesada gamma2a *Mus musculus* (1-453) [VH (*Mus musculus* IGHV9-3-1*01 (98%) -(IGHD) - IGHJ2*01 (93.3%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Mus musculus* IGHG2A*01 (100%) (CH1 (124-220), bisagra 1-16 (221-236), CH2 (237-346), CH3 (347-451), CHS (452-453)) (124-453)], (138-214')-disulfuro con la cadena ligera lambda *Mus musculus* (1'-215') [V-LAMBDA (*Mus musculus* IGLV1*01 (98%) -IGLJ1*01 (100%)) CDR-IMGT [9.3.9] (26-34.52-54.91-99) (1'-109') -*Mus musculus* IGLC1*01 (100%) (110'-215')]; dímero (230-230":233-233":235-235")-trisdisulfuro, producido en una línea celular de mieloma murino SP2/0, forma glicosilada alfa, sustituída en N^6 de un promedio de 1,6 residuos de lisilo con grupos de 4-[(1*RS*)-1-{[L-metionil-cadena A de toxina de ricina (Met-RTA, no glicosilada, producida por *Escherichia coli*)-S^{260}-il]sulfanil}etil]benzoilo

Heavy chain / Chaîne lourde / Cadena pesada

```
QIQLVQSGPE LKKPGETVKI SCKASGYTFT NYGMNWVKQA PGKGLMWLGW  50
INTYTGEPTY ADDFKGRFAF SLETSASTAY LQINNLKNED TATYFCARWA 100
YFYGSSPYFF DYWGQGTTLT VSSAKTTAPS VYPLAPVCGD TTGSSVTLGC 150
LVKGYFPEPV TLTWNSGSLS SGVHTFPAVL QSDLYTLSSS VTVTSSTWPS 200
QSITCNVAHP ASSTKVDKKI EPRGPTIKPC PPCKCPAPNL LGGPSVFIFP 250
PKIKDVLMIS LSPIVTCVVV DVSEDDPDVQ ISWFVNNVEV HTAQTQTHRE 300
DYNSTLRVVS ALPIQHQDWM SGKEFKCKVN NKDLPAPIER TISKPKGSVR 350
APQVYVLPPP EEEMTKKQVT LTCMVTDFMP EDIYVEWTNN GKTELNYKNT 400
EPVLDSDGSY FMYSKLRVEK KNWVERNSYS CSVVHEGLHN HHTTKSFSRT 450
PGK                                                     453
```

Light chain / Chaîne légère / Cadena ligera

```
QAVVTQESAL TTSPGETVTL TCRSSTGAVT TSNYANWVQE KPDHLFTGLI  50
GGTNNRAPGV PARFSGSLIG DKAALTITGA QTEDEAIYFC ALWCSNHLVF 100
GGGTKLTVLG QPKSSPSVTL FPPSSEELET NKATLVCTIT DFYPGVVTVD 150
WKVDGTPVTQ GMETTQPSKQ SNNKYMASSY LTLTARAWER HSSYSCQVTH 200
EGHTVEKSLS RADCS                                        215
```

Met-Ricin A chain / Met-chaîne A de la Ricine / Met-cadena A de la Ricina

```
MIFPKQYPII NFTTAGATVQ SYTNFIRAVR GRLTTGADVR HDIPVLPNRV 50
GLPINQRFIL VELSNHAELS VTLALDVTNA YVVGYRAGNS AYFFHPDNQE 100
DAEAITHLFT DVQNRYTFAF GGNYDRLEQL AGNLRENIEL GNGPLEEAIS 150
ALYYYSTGGT QLPTLARSFI ICIQMISEAA RFQYIEGEMR TRIRYNRRSA 200
PDPSVITLEN SWGRLSTAIQ ESNQGAFASP IQLQRRNGSK FSVYDVSILI 250
PIIALMVYRC APPPSSQF                                     268
```

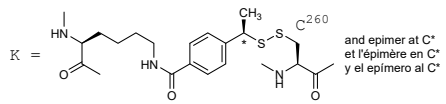
Post-translational modifications

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

Intra-H (C23-C104) 22-96 150-205 267-327 373-431
22"-96" 150"-205" 267"-327" 373"-431"
Intra-L (C23-C104) 22'-90' 137'-196'
22'"-90'" 137'"-196'"
Inter-H-L (CH1 11-CL 126) 138-214' 138"-214'"
Inter-H-H (h 12, h 15, h 18) 230-230" 233-233" 235-235"
heterogeneous patterns involving 94' and 94'" e.g.:
96-94' 138-94' 150-94' 94'-137'
96"-94'" 138"-94'" 150"-94'" 94'"-137'"
Met-RTA: C172 = Cys-SH, C260 = Cys-S-S-CH(CH3)-p-C6H4-CO-[N6-Lys(H,L)]

Conjugation sites / Sites de conjugaison / Posiciones de coniugación

major: K87 K228 K72' K113'
K87" K228" K72'" K113'"
minor: K43 K215 K323 K332 K398 K421 K132'
K43" K215" K323" K332" K398" K421" K132'"



N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)

H VH Q1:
1, 1"
L VL Q1:
1', 1'"

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

H CH2 N84.4:
303, 303"
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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal

H CHS K2:
453, 453"

hepcidinum

hepcidin — hepcidin (human) (hepatical bactericidal protein, hepcidin-25, liver-expressed antimicrobial peptide 1, LEAP-1, hepatic antimicrobial peptide, HAMP, ferroportin regulator protein): *S*^{7},*S*^{23}:*S*^{10},*S*^{13}:*S*^{11},*S*^{19}:*S*^{14},*S*^{22}-tetracyclo(L-α-aspartyl-L-threonyl-L-histidyl-L-phenylalanyl-L-prolyl-L-isoleucyl-L-cysteinyl-L-isoleucyl-L-phenylalanyl-L-cysteinyl-L-cysteinylglycyl-L-cysteinyl-L-cysteinyl-L-histidyl-L-arginyl-L-seryl-L-lysyl-L-cysteinylglycyl-L-methionyl-L-cysteinyl-L-cysteinyl-L-lysyl-L-threonine)

hepcidine — hepcidine (humaine) (protéine bactéricide hépatique, hepcidine-25, peptide antimicrobien exprimé par le foie 1, LEAP-1, peptide antimicrobien hépatique, HAMP, protéine régulatrice de la ferroportine):

S^{7},*S*^{23}:*S*^{10},*S*^{13}:*S*^{11},*S*^{19}:*S*^{14},*S*^{22}-tétracyclo(L-α-aspartyl-L-thréonyl-L-histidyl-L-phénylalanyl-L-prolyl-L-isoleucyl-L-cystéinyl-L-isoleucyl-L-phénylalanyl-L-cystéinyl-L-cystéinylglycyl-L-cystéinyl-L-cystéinyl-L-histidyl-L-arginyl-L-séryl-L-lysyl-L-cystéinylglycyl-L-méthionyl-L-cystéinyl-L-cystéinyl-L-lysyl-L-thréonine)

hepcidina

hepcidina (humana) (proteína bactericida hepática, hepcidina-25, péptido antimicrobiano expresado en el hígado 1, LEAP-1, péptido antimicrobiano hepático, HAMP, proteína reguladora de ferroportina): *S*^{7},*S*^{23}:*S*^{10},*S*^{13}:*S*^{11},*S*^{19}:*S*^{14},*S*^{22}-tetraciclo(L-α-aspartil-L-treonil-L-histidil-L-fenilalanil-L-prolil-L-isoleucil-L-cisteinil-L-isoleucil-L-fenilalanil-L-cisteinil-L-cisteinilglicil-L-cisteinil-L-cisteinil-L-histidil-L-arginil-L-seril-L-lisil-L-cisteinilglicil-L-metionil-L-cisteinil-L-cisteinil-L-lisil-L-treonina)

$C_{113}H_{170}N_{34}O_{31}S_9$

Sequence / Séquence / Secuencia
DTHFPICIFC CGCCHRSKCG MCCKT 25

Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
7-23, 10-13, 11-19, 14-22

ibezapolstatum

ibezapolstat

2-{[(3,4-dichlorophenyl)methyl]amino}-7-[2-(morpholin-4-yl)ethyl]-1,7-dihydro-6*H*-purin-6-one

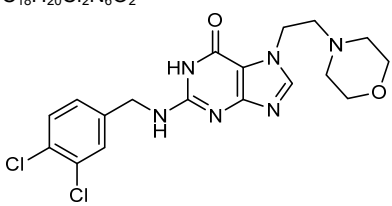
ibézapolstat

2-{[(3,4-dichlorophényl)méthyl]amino}-7-[2-(morpholin-4-yl)éthyl]-1,7-dihydro-6*H*-purin-6-one

ibezapolstat

2-{[(3,4-diclorofenil)metil]amino}-7-[2-(morfolin-4-il)etil]-1,7-dihidro-6*H*-purin-6-ona

$C_{18}H_{20}Cl_2N_6O_2$



icapamespibum

icapamespib

9-{2-[(2,2-dimethylpropyl)amino]ethyl}-8-[(6-iodo-2*H*-1,3-benzodioxol-5-yl)sulfanyl]-9*H*-purin-6-amine

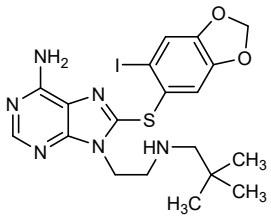
icapamespib

9-{2-[(2,2-diméthylpropyl)amino]éthyl}-8-[(6-iodo-2*H*-1,3-benzodioxol-5-yl)sulfanyl]-9*H*-purin-6-amine

icapamespib

9-{2-[(2,2-dimetilpropil)amino]etil}-8-[(6-iodo-2*H*-1,3-benzodioxol-5-il)sulfanil]-9*H*-purin-6-amina

$C_{19}H_{23}IN_6O_2S$



idactamabum #

idactamab	immunoglobulin G1-kappa, anti-[*Homo sapiens* SLC1A5 (solute carrier family 1 member 5,neutral amino acid transporter, RDRC, M7V1,AAAT, ASCT2)], *Homo sapiens* monoclonal antibody; gamma1 heavy chain *Homo sapiens* (1-452) [VH (*Homo sapiens* IGHV4-34*01 (96.9%) -(IGHD) -IGHJ4*01 (100%)) [8.7.15] (1-121) -*Homo sapiens* IGHG1*03 G1m3, nG1m1 (CH1 R120 (218) (122-219), hinge 1-15 (220-234), CH2 3^4>ins^cysteinyl (244) (235-345), CH3 E12 (361), M14 (363) (346-450), CHS (451-452))(122-452)], (224-214')-disulfide with kappa light chain *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-5*03 (94.7%) -IGKJ1*01 (100%)) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dimer (230-230'':233-233'')-bisdisulfide, produced in a Chinese hamster ovary (CHO) cell line derived from CHO-K1, glycoform alfa
idactamab	immunoglobuline G1-kappa, anti-[*Homo sapiens* SLC1A5 (famille du porteur soluté 1 membre 5, transporteur d'acide aminé neutre, RDRC, M7V1, AAAT, ASCT2)], anticorps monoclonal *Homo sapiens;* chaîne lourde gamma1 *Homo sapiens* (1-452) [VH (*Homo sapiens* IGHV4-34*01 (96.9%) -(IGHD) -IGHJ4*01 (100%)) [8.7.15] (1-121) -*Homo sapiens* IGHG1*03 G1m3, nG1m1 (CH1 R120 (218) (122-219), charnière 1-15 (220-234), CH2 3^4>ins^cysteinyl (244) (235-345), CH3 E12 (361), M14 (363) (346-450), CHS (451-452)) (122-452)], (224-214')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-5*03 (94.7%) -IGKJ1*01 (100%)) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dimère (230-230'':233-233'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) dérivant de la lignée cellulaire CHO-K1, glycoforme alfa
idactamab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* SLC1A5 (familia del portador de soluto 1 miembro 5, transportador de ácido amino neutral, RDRC, M7V1, AAAT, ASCT2)], anticuerpo monoclonal *Homo sapiens*; cadena pesada gamma1 *Homo sapiens* (1-452) [VH (*Homo sapiens* IGHV4-34*01 (96.9%) -(IGHD) -IGHJ4*01 (100%)) [8.7.15] (1-121) -*Homo sapiens* IGHG1*03 G1m3, nG1m1 (CH1 R120 (218) (122-219), bisagra 1-15 (220-234), CH2 3^4>ins^cisteinil (244) (235-345), CH3 E12 (361), M14 (363) (346-450), CHS (451-452)) (122-452)], (224-214')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-5*03 (94.7%) -IGKJ1*01 (100%)) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dímero (230-230'':233-233'')-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular derivada de CHO-K1, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLQQWGAG LLKPSETLSL TCAVYGGSFS GYYWSWIRQP PGKGLEWIGE  50
IHHSGGANYN PSLKSRVTIS VDTSKNQFSL KLSSVTAADT AVYYCARGQG 100
KNWHYDYFDY WGQGTLVTVS SASTKGPSVF PLAPSSKSTS GGTAALGCLV 150
KDYFPEPVTV SWNSGALTSG VHTFPAVLQS SGLYSLSSVV TVPSSSLGTQ 200
TYICNVNHKP SNTKVDKRVE PKSCDKTHTC PPCPAPELLG GPSCVFLFPP 250
KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NWYVDGVEVH NAKTKPREEQ 300
YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQPRE 350
PQVYTLPPSR EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP 400
PVLDSDGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP 450
GK                                                      452
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPST LSASVGDRVT ITCRASQSIR SWLAWYQQKP GKAPKLLIYK  50
ASILKIGVPS RFSGSGSGTE FTLTISSLQP DDFATYYCQQ YYSYSRTFGQ 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Post-translational modifications

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

Intra-H (C23-C104) 22-95 148-204 266-326 372-430
22"-95" 148"-204" 266"-326" 372"-430"

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"

Cysteinyl inserted for conjugation capped by a cysteinyl
H CH2 C3^4):
244, 244"

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.

C-terminal lysine clipping:
H CHS K2:
452, 452"

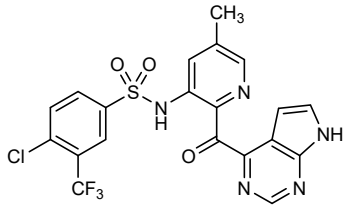
ilacirnonum

ilacirnon — 4-chloro-*N*-[5-methyl-2-(7*H*-pyrrolo[2,3-*d*]pyrimidine-4-carbonyl)pyridin-3-yl]-3-(trifluoromethyl)benzene-1-sulfonamide

ilacirnon — 4-chloro-*N*-[5-méthyl-2-(7*H*-pyrrolo[2,3-*d*]pyrimidine-4-carbonyl)pyridin-3-yl]-3-(trifluorométhyl)benzène-1-sulfonamide

ilacirnón — 4-cloro-*N*-[5-metil-2-(7*H*-pirrolo[2,3-*d*]pirimidina-4-carbonil)piridin-3-il]-3-(trifluorometil)benceno-1-sulfonamida

$C_{20}H_{13}ClF_3N_5O_3S$



insulinum icodecum

insulin icodec — human insulin A-chain (1-21) variant (Y>E^{14}), human insulin B-chain (1-29) variant (Y>H^{16}, F>H^{25}) conjugated at K^{29B} at its N^6 to (22*S*)-22,42-dicarboxy-10,19,24-trioxo-3,6,12,15-tetraoxa-9,18,23-triazadotetracontan-1-oyl; $N^{6.29B}$-[(22*S*)-22,42-dicarboxy-10,19,24-trioxo-3,6,12,15-tetraoxa-9,18,23-triazadotetracontan-1-oyl]-[Tyr14^A>Glu, Tyr16^B>His, Phe25^B>His]-des-Thr30^B-human insulin

insuline icodec

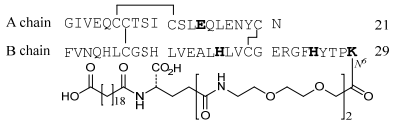
chaîne A de l'insuline humaine (1-21) variant (Y>E^{14}), chaîne B de l'insuline humaine (1-29) variant (Y>H^{16}, F>H^{25}), conjuguée en K^{29B} par son *N*^{6} à (22*S*)-22,42-dicarboxy-10,19,24-trioxo-3,6,12,15-tétraoxa-9,18,23-triazadotétracontan-1-oyle; *N*$^{6.29B}$-[(22*S*)-22,42-dicarboxy-10,19,24-trioxo-3,6,12,15-tétraoxa-9,18,23-triazadotétracontan-1-oyl]-[Tyr14^{A}>Glu, Tyr16^{B}>His, Phé25^{B}>His]-des-Thr30^{B}-insuline humaine

insulina icodec

insulina humana cadena-A (1-21) variante (Y>E^{14}), insulina humana cadena-B (1-29) variante (Y>H^{16}, F>H^{25}) conjugada con K^{29B} con su *N*^{6} al (22*S*)-22,42-dicarboxi-10,19,24-trioxo-3,6,12,15-tetraoxa-9,18,23-triazadotetracontan-1-oilo; *N*$^{6.29B}$-[(22*S*)-22,42-dicarboxi-10,19,24-trioxo-3,6,12,15-tetraoxa-9,18,23-triazadotetracontan-1-oil]-[Tir14^{A}>Glu, Tir16^{B}>His, Fen25^{B}>His]-des-Tre30^{B}-insulina humana

$C_{280}H_{435}N_{71}O_{87}S_6$

Sequences / Séquences / Secuencias



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

Intra-chain 6^{A}-11^{A}

Inter-chain 7^{A}-7^{B}, 20^{A}-19^{B}

Modifications / Modifications / Modificaciones

$Lys29^{B}$ conjugated at N^{6}

inupadenantum

inupadenant

(+)-5-amino-3-{2-[4-(2,4-difluoro-5-{2-[(*S*)-methanesulfinyl]ethoxy}phenyl)piperazin-1-yl]ethyl}-8-(furan-2-yl)[1,3]thiazolo[5,4-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-2(3*H*)-one

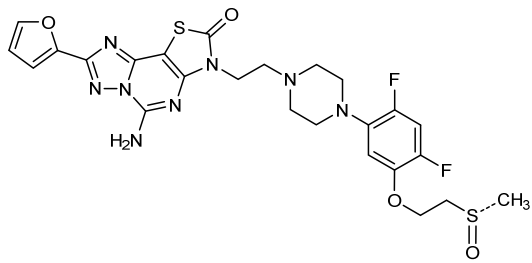
inupadénant

(+)-5-amino-3-{2-[4-(2,4-difluoro-5-{2-[(*S*)-méthanesulfinyl]éthoxy}phényl)pipérazin-1-yl]éthyl}-8-(furan-2-yl)[1,3]thiazolo[5,4-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-2(3*H*)-one

inupadenant

(+)-5-amino-3-{2-[4-(2,4-difluoro-5-{2-[(*S*)-metanosulfinil]etoxi}fenil)piperazin-1-il]etil}-8-(furan-2-il)[1,3]tiazolo[5,4-*e*][1,2,4]triazolo[1,5-*c*]pirimidin-2(3*H*)-ona

$C_{25}H_{26}F_2N_8O_4S_2$



invimestrocelum

invimestrocel	Allogeneic human multipotent adult progenitor cells (MAPC) derived from bone marrow and isolated by density gradient centrifugation. The cells are expanded *ex vivo* on fibronectin-coated surfaces under low-oxygen conditions and in the presence of growth media for the creation of a master cell bank (passage 4), a working cell bank (passage 6) and active substance (passage 9). The cells are adherent, secrete proangiogenic factors (including VEGF, IL-8 and CXCL5) and of mesenchymal progenitor lineage (*in vitro* differentiation to endothelial, hepatic and neuronal lineages). The cells express CD49c and CD90 (≥ 95% of the cells), and lack expression of CD45 and HLA II (< 5%). Additional markers include >90% CD13, CD44, CD73, CD105 and <5% CD34. The cells have also been shown to induce T cell suppression.
invimestrocel	Cellules humaines adultes progénitrices multipotentes qui sont allogéniques (MAPC), dérivées de la moelle osseuse et isolées par centrifugation à gradient de densité. Les cellules sont amplifiées *ex vivo* sur des surfaces recouvertes de fibronectine dans des conditions de faible teneur en oxygène et en présence de milieux de croissance pour la création d'une banque de cellules primaires (passage 4) et d'une banque de cellules de travail (passage 6) et d'une substance active produit fini (passage 9). Les cellules sont adhérentes, sécrètent des facteurs pro-angiogéniques (notamment le VEGF, l'IL-8 et la CXCL5) et sont de la lignée progénitrice mésenchymateuse (différenciation *in vitro* en lignées endothéliales, hépatiques et neuronales). Les cellules expriment CD49c et CD90 (≥ 95% des cellules), et sont négatives pour CD45 et HLA II (< 5%). Les marqueurs supplémentaires comprennent > 90 % de CD13, CD44, CD73, CD105 et < 5 % de CD34. Il a également été démontré que les cellules induisent la suppression des lymphocytes T.
invimestrocel	Células progenitoras adultas multipotentes humanas alogénicas (MAPC) derivadas de médula ósea y aisladas mediante centrifugación en gradiente de densidad. Las células se expanden *ex vivo* en superficies cubiertas de fibronectina en condiciones de oxígeno bajo y en presencia de medio de crecimiento para la creación de un banco de células maestro (pase 4) y un banco de células de trabajo (pase 6) y el principio activo (pase 9). Las células son adherentes, secretan factores proangiogénicos (incluyendo VEGF, IL-8 y CXCL5) y son de la línea progenitora mesenquimal (diferenciación *in vitro* a las líneas endotelial, hepática y neuronal). Las células expresan CD49c (≥ 95% de las células), y carecen de expresión de CD45 y HLA II (<5%). Otros marcadores adicionales incluyen >90% de CD13, CD44, CD73, CD105 y <5% de CD34. Se ha demostrado también que las células inducen supresión de linfocitos T.

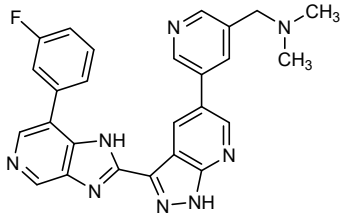
ipivivintum

ipivivint — 1-(5-{3-[7-(3-fluorophenyl)-1*H*-imidazo[4,5-*c*]pyridin-2-yl]-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl}pyridin-3-yl)-*N*,*N*-dimethylmethanamine

ipivivint — 1-(5-{3-[7-(3-fluorophényl)-1*H*-imidazo[4,5-*c*]pyridin-2-yl]-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl}pyridin-3-yl)-*N*,*N*-diméthylméthanamine

ipivivint — 1-(5-{3-[7-(3-fluorofenil)-1*H*-imidazo[4,5-*c*]piridin-2-il]-1*H*-pirazolo[3,4-*b*]piridin-5-il}piridin-3-il)-*N*,*N*-dimetilmetanamina

$C_{26}H_{21}FN_8$



izuralimabum #

izuralimab — immunoglobulin half-IG G1-kappa/scFv-h-CH2-CH3, anti-[*Homo sapiens* ICOS (inductible T-cell costimulatory, activation-inducible lymphocyte immunomediatory molecule, AILIM, CD278)] and anti-[*Homo sapiens* PDCD1 (programmed cell death 1, PD-1, PD1, CD279)], monoclonal antibody, bispecific; gamma1 heavy chain anti-ICOS (1-454) [VH (*Homo sapiens* IGHV1-2*02 (99%) -(IGHD) -IGHJ3*02 (100%)) CDR-IMGT [8.8.18] (26-33.51-58.97-114) (1-125) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 N114>D (216) R120>K (222) (126-223), hinge 1-15 (224-238), CH2 E1.4,L1.3>P (241), L1.2>V (242), G1.1>A (243), S29>K (274), Q84.2>E (302) (239-347), CH3 E12 (363), M14 (365), L24>D (375), K26>S (377), N44>D (391), Q97>E (425), N100>D (428), M107>L (435), N114>S (441) (348-452), CHS (453-454)) (126-454)], (228-214')-disulfide with kappa light chain anti-ICOS (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (96.8%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')];
IG scFv-h-CH2-CH3 single chain, anti-PDCD1 (1"-480") [scFv-V-kappa-VH anti-PDCD1 (1"-249")[V-KAPPA (*Homo sapiens* IGKV3-15*01 (80.0%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1"-107") -20-mer tetrakis(glycyl-lysyl-prolyl-glycyl-seryl) linker (108"-127") -VH (*Mus musculus* IGHV6-6*02 (87.0%) -(IGHD) -IGHJ1*03 (86.7%)/*Homo sapiens* IGHV3-15*07 (81.8%) -(IGHD) -IGHJ2*01 (93.3%)) CDR-IMGT [8.10.13] (153-160.178-187.226-238) (128"-249")] -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (250"-480") [hinge 1-15 C5>S (254) (250-264) -CH2 E1.4,L1.3>P (267), L1.2>V (268), G1.1>A (269), S29>K (300) (265-373),CH3 E12 (389), E13>Q (390), M14 (391), S20>K (397), M107>L (461), N114>S (467) (374-478), CHS (479-480)]];
dimer (234-260":237-263")-bisdisulfide, produced in Chinese hamster ovary (CHO)-S cell line, glycoform alfa

izuralimab	immunoglobuline demi-IG G1-kappa/scFv-h-CH2-CH3, anti-[*Homo sapiens* ICOS (costimulateur inductible du lymphocyte T, molécule immunomédiateur lymphocytaire inductible par activation, AILIM, CD278)] et anti-[*Homo sapiens* PDCD1 (protéine 1 de mort cellulaire programmée, PD-1, PD1, CD279)], anticorps monoclonal, bispécifique; chaîne lourde gamma1 anti-ICOS (1-454) [VH (*Homo sapiens* IGHV1-2*02 (99%) -(IGHD) -IGHJ3*02 (100%)) CDR-IMGT [8.8.18] (26-33.51-58.97-114) (1-125) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 N114>D (216) R120>K (222) (126-223), charnière 1-15 (224-238), CH2 E1.4,L1.3>P (241), L1.2>V (242), G1.1>A (243), S29>K (274), Q84.2>E (302) (239-347), CH3 E12 (363), M14 (365), L24>D (375), K26>S (377), N44>D (391), Q97>E (425), N100>D (428), M107>L (435), N114>S (441) (348-452), CHS (453-454)) (126-454)], (228-214')-disulfure avec la chaîne légère kappa anti-ICOS (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (96.8%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; IG scFv-h-CH2-CH3 chaîne unique, anti-PDCD1 (1"-480") [scFv V-kappa-VH anti-PDCD1 (1"-249") [V-KAPPA (*Homo sapiens* IGKV3-15*01 (80.0%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1"-107") -20-mer tétrakis(glycyl-lysyl-prolyl-glycyl-séryl) linker (126"-145") -VH (*Mus musculus* IGHV6-6*02 (87.0%) -(IGHD) -IGHJ1*03 (86.7%)/*Homo sapiens* IGHV3-15*07 (81.8%) -(IGHD) -IGHJ2*01 (93.3%)) CDR-IMGT [8.10.13] (153-160.178-187.226-238) (128"-249")] -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (250"-480") [charnière 1-15 C5>S (254) (250-264) -CH2 E1.4,L1.3>P (267), L1.2>V (268), G1.1>A (269), S29>K (300) (265-373), CH3 E12 (389), E13>Q (390), M14 (391), S20>K (397), M107>L (461), N114>S (467) (374-478), CHS (479-480)]]; dimère (234-260":237-263")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-S, glycoforme alfa
izuralimab	inmunoglobulina demi-IG G1-kappa/scFv-h-CH2-CH3, anti-[*Homo sapiens* ICOS (coestimulador inducible del linfocito T, molécula inmunomediadora linfocitaria inducible por activación, AILIM, CD278)] y anti-[*Homo sapiens* PDCD1 (proteína 1 de muerte celular programada, PD-1, PD1, CD279)], anticuerpo monoclonal, biespecífico; cadena pesada gamma1 anti-ICOS (1-454) [VH (*Homo sapiens* IGHV1-2*02 (99%) -(IGHD) -IGHJ3*02 (100%)) CDR-IMGT [8.8.18] (26-33.51-58.97-114) (1-125) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 N114>D (216) R120>K (222) (126-223), bisagra 1-15 (224-238), CH2 E1.4,L1.3>P (241), L1.2>V (242), G1.1>A (243), S29>K (274), Q84.2>E (302) (239-347), CH3 E12 (363), M14 (365), L24>D (375), K26>S (377), N44>D (391), Q97>E (425), N100>D (428), M107>L (435), N114>S (441) (348-452), CHS (453-454)) (126-454)], (228-214')-disulfuro con la cadena ligera kappa anti-ICOS (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (96.8%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; IG scFv-h-CH2-CH3 cadena única, anti-PDCD1 (1"-480") [scFv V-kappa-VH anti-PDCD1 (1"-249") [V-KAPPA (*Homo sapiens* IGKV3-15*01 (80.0%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1"-107") -20-mer tetrakis(glicil-lisil-prolil-glicil-seril) linker (126"-145") -VH (*Mus musculus* IGHV6-6*02 (87.0%) -(IGHD) -IGHJ1*03 (86.7%)/*Homo sapiens* IGHV3-15*07 (81.8%) -(IGHD) -IGHJ2*01 (93.3%)) CDR-IMGT [8.10.13] (153-160.178-187.226-238) (128"-249")] -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (250"-480") [bisagra 1-15 C5>S (254) (250-264) -CH2 E1.4,L1.3>P (267), L1.2>V (268), G1.1>A (269), S29>K (300) (265-373), CH3 E12 (389), E13>Q (390), M14 (391), S20>K (397), M107>L (461), N114>S (467) (374-478), CHS (479-480)]]; dímero (234-260":237-263")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-S, forma glicosilada alfa

1.Heavy chain / Chaîne lourde / Cadena pesada (anti-ICOS)

```
QVQLVQSGAE VKKPGASVKV SCKASGYTFT GYYMHWVRQA PGQGLEWMGW  50
INPHSGGTNY AQKFQGRVTM TRDTSISTAY MELSRLRSDD TAVYYCARTY 100
YYDSSGYYHD AFDIWGQGTM VTVSSASTKG PSVFPLAPSS KSTSGGTAAL 150
GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL SSVVTVPSSS 200
LGTQTYICNV NHKPSDTKVD KKVEPKSCDK THTCPPCPAP PVAGPSVFLF 250
PPKPKDTLMI SRTPEVTCVV VDVKHEDPEV KFNWYVDGVE VHNAKTKPRE 300
EEYNSTYRVV SVLTVLHQDW LNGKEYKCKV SNKALPAPIE KTISKAKGQP 350
REPQVYTLPP SREEMTKNQV SLTCDVSGFY PSDIAVEWES DGQPENNYKT 400
TPPVLDSDGS FFLYSKLTVD KSRWEQGDVF SCSVLHEALH SHYTQKSLSL 450
SPGK                                                    454
```

2. Light chain / Chaîne légère / Cadena ligera (anti-ICOS)

```
DIQMTQSPSS VSASVGDRVT ITCRASQGIS RLLAWYQQKP GKAPKLLIYV  50
ASSLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ ANSFPWTFGQ 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

3. Chain / Chaîne / Cadena IG scFv-h-CH2-CH3 (anti-PDCD1)

```
EIVLTQSPAT LSASPGERVT LTCRASQSVG NDVAWYQQKP GQAPRLLINY  50
ASHRYTGVPD RFTGSGYGTE FTLTISSVQS EDFGVYYCQQ DFSSPRTFGG 100
GTKVEIKGKP GSGKPGSGKP GSGKPGSEVQ LVESGGGLVK PGGSLRLSCV 150
ASGFTFSNYW MNWVRQAPGK GLEWVAEIRL YSNNYATHYA ESVKGRFTIS 200
RDDSKSTLYL QMNNLKTEDT GVYYCTRYYG NYGGYFDVWG RGTLVTVSSE 250
PKSSDKTHTC PPCPAPPVAG PSVFLFPPKP KDTLMISRTP EVTCVVVDVK 300
HEDPEVKFNW YVDGVEVHNA KTKPREEQYN STYRVVSVLT VLHQDWLNGK 350
EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ VYTLPPSREQ MTKNQVKLTC 400
LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW 450
QQGNVFSCSV LHEALHSHYT QKSLSLSPGK                       480
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 152-208 268-328 374-432
Intra-L (C23-C104) 23'-88' 134'-194'
Intra-chain 3 23"-88" 149"-225" 294"-354" 400"-458"
Inter-H-L (h 5-CL 126) 228-214'
Inter-H-chain 3 (h 11, h 14) 234-260" 237-263"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
304, 330"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

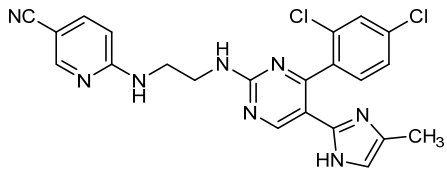
laduviglusibum

laduviglusib — 6-[(2-{[4-(2,4-dichlorophenyl)-5-(4-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl]amino}ethyl)amino]pyridine-3-carbonitrile

laduviglusib — 6-[(2-{[4-(2,4-dichlorophényl)-5-(4-méthyl-1*H*-imidazol-2-yl)pyrimidin-2-yl]amino}éthyl)amino]pyridine-3-carbonitrile

laduviglusib — 6-[(2-{[4-(2,4-diclorofenil)-5-(4-metil-1*H*-imidazol-2-il)pirimidin-2-il]amino}etil)amino]piridina-3-carbonitrilo

$C_{22}H_{18}Cl_2N_8$



lazucirnonum

lazucirnon — (4^2*R*)-1^4-chloro-*N*,*N*,1^3,7^6-tetramethyl-4^5,5-dioxo-6-aza-7(2)-pyridina-3(1,4)-piperidina-4(1,2)-pyrrolidina-1(1)-benzenaheptaphane-7^4-carboxamide

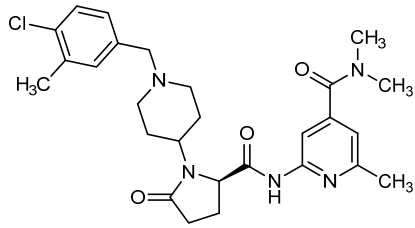
lazucirnon

(4^2*R*)-1^4-chloro-*N*,*N*,1^3,7^6-tétraméthyl-4^5,5-dioxo-6-aza-7(2)-pyridina-3(1,4)-pipéridina-4(1,2)-pyrrolidina-1(1)-benzénaheptaphane-7^4-carboxamide

lazucirnón

(4^2*R*)-1^4-cloro-*N*,*N*,1^3,7^6-tetrametil-4^5,5-dioxo-6-aza-7(2)-piridina-3(1,4)-piperidina-4(1,2)-pirrolidina-1(1)-bencenaheptafano-7^4-carboxamida

$C_{27}H_{34}ClN_5O_3$



lerodalcibepum #

lerodalcibep

engineered binding protein (1-96) anti-(human proprotein convertase subtilisin/kexin type 9), derived from human tenth fibronectin type III domain, fused via peptidyl linker (^{97}GSGSGS^{102}) to human serum albumin (103-687), variant (C^{34}>A^{136}), produced in Chinese hamster ovary (CHO) cells;
human fibronectin tenth type III domain variant anti-[human PCSK9 (pro-protein convertase subtilisin/kexin type 9, neural apoptosis-regulated convertase 1, NARC-1, proprotein convertase 9, PC9)] (1-96) fused via a $(GS)_3$ peptide linker (97-102) with [Cys^{34}>Ala (136)]-human serum albumin (HSA) (103-687), produced in Chinese hamster ovary (CHO) cells, non-glycosylated

lérodalcibep

protéine de liaison mise au point (1-96) anti-(proprotéine convertase subtilisine/kexine type 9), dérivée du dixième domaine de la fibronectine humaine de type III, fusionnée via un peptide de liaison (^{97}GSGSGS^{102}) à l'albumine sérique humaine (103-687), variant (C^{34}>A^{136}), produit dans des cellules ovariennes de hamster chinois (CHO);
peptide variant du dixième domaine de la fibronectine humaine de type III anti-[PCSK9 humain (proprotéine convertase subtilisine/kexine type 9, convertase 1 régulée par l'apoptose neuronale, NARC-1, proprotéine convertase 9, PC9)] (1-96) fusionné via un peptide $(GS)_3$ (97-102) à la [Cys^{34}>Ala (136)]-albumine sérique humaine (ASH) (103-687), produit dans des cellules ovariennes de hamsters chinois (CHO), non-glycosylé

lerodalcibep

proteína de unión diseñada (1-96) anti-(proproteína convertasa humana subtilisina/kexina tipo 9), derivada del décimo dominio de la fibronectina humana del tipo III, fusionada a través de un conector peptidil (^{97}GSGSGS^{102}) a la albúmina sérica humana (103-687), variante (C^{34}>A^{136}), producido en células ováricas de hámster Chino (CHO);

variante del décimo dominio de la fibronectina humana del tipo III anti-[PCSK9 humano (proproteína convertasa subtilisina/kexina tipo 9, convertasa 1 regulada por la apoptosa neuronal, NARC-1, proproteína convertasa 9, PC9)] fusionada mediante un péptido $(GS)_3$ (97-102) a la [Cis^{34}>Ala (136)]-albúmina sérica humana (ASH) (103-687), producido en células ováricas de hámster Chino (CHO), no glicosilado

Sequence / Séquence / Secuencia

```
VSDVPRDLEV VAATPTSLLI SWDAPAEGYG YYRITYGETG GNSPVQEFTV   50
PVSKGTATIS GLKPGVDYTI TVYAVEFDFP GAGYYHRPIS INYRTEGSGS  100
GSDAHKSEVA HRFKDLGEEN FKALVLIAFA QYLQQAPFED HVKLVNEVTE  150
FAKTCVADES AENCDKSLHT LFGDKLCTVA TLRETYGEMA DCCAKQEPER  200
NECFLQHKDD NPNLPRLVRP EVDVMCTAFH DNEETFLKKY LYEIARRHPY  250
FYAPELLFFA KRYKAAFTEC CQAADKAACL LPKLDELRDE GKASSAKQRL  300
KCASLQKFGE RAFKAWAVAR LSQRFPKAEF AEVSKLVTDL TKVHTECCHG  350
DLLECADDRA DLAKYICENQ DSISSKLKEC CEKPLLEKSH CIAEVENDEM  400
PADLPSLAAD FVESKDVCKN YAEAKDVFLG MFLYEYARRH PDYSVVLLLR  450
LAKTYETTLE KCCAAADPHE CYAKVFDEFK PLVEEPQNLI KQNCELFEQL  500
GEYKFQNALL VRYTKKVPQV STPTLVEVSR NLGKVGSKCC KHPEAKRMPC  550
AEDYLSVVLN QLCVLHEKTP VSDRVTKCCT ESLVNRRPCF SALEVDETYV  600
PKEFNAETFT FHADICTLSE KERQIKKQTA LVELVKHKPK ATKEQLKAVM  650
DDFAAFVEKC CKADDKETCF AEEGKKLVAA SQAALGL                687
```

Mutation / Mutation / Mutación

C^{136}>**A**

Post-translational modifications

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

155-164, 177-192, 193-203, 226-270, 271-279, 302-347, 348-355, 367-380, 381-391, 418-462, 463-471, 494-539, 540-550, 563-578, 579-589, 616-660, 661-669

Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación

none / aucune / ninguna

letaplimabum #

letaplimab

immunoglobulin G4-kappa, anti-[*Homo sapiens* CD47 (integrin associated protein, IAP, MER6, OA3)], *Homo sapiens* monoclonal antibody;
gamma4 heavy chain *Homo sapiens* (1-441) [VH (*Homo sapiens* IGHV4-59*01 (100%) -(IGHD) -IGHJ1*01 (100%)) CDR-IMGT [8.7.9] (26-33.51-57.96-104) (1-115)-*Homo sapiens* IGHG4*01, G4v4 CH2 A1.3, A1.2 (CH1 (116-213), hinge 1-12 S10>P (223) (214-225), CH2 F1.3>A (229), L1.2>A (230) (226-335), CH3 (336-440), CHS K>del (441) (116-441)], (129-214')-disulfide with kappa light chain *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (96.8%) -IGKJ4*01 (91.7%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dimer (221-221":224-224")-bisdisulfide, produced in Chinese hamster ovary (CHO)-S cell line, glycoform alfa

létaplimab

immunoglobuline G4-kappa, anti-[*Homo sapiens* CD47 (protéine associée à l'intégrine, IAP, MER6, OA3)], anticorps monoclonal *Homo sapiens*;

chaîne lourde gamma4 *Homo sapiens*(1-441) [VH (*Homo sapiens* IGHV4-59*01 (100%) -(IGHD) - IGHJ1*01 (100%)) CDR-IMGT [8.7.9] (26-33.51-57.96-104) (1-115) -*Homo sapiens* IGHG4*01, G4v4 CH2 A1.3, A1.2 (CH1 (116-213), charnière 1-12 S10>P (223) (214-225), CH2 F1.3>A (229), L1.2>A (230) (226-335), CH3 (336-440), CHS K>del (441) (116-441)], (129-214')-disulfure avec la chaîne légère kappa *Homo sapiens*(1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (96.8%) -IGKJ4*01 (91.7%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dimère (221-221":224-224")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-S, glycoforme alfa

letaplimab

inmunoglobulina G4-kappa, anti-[*Homo sapiens* CD47 (proteína asociada a la integrina, IAP, MER6, OA3)], anticuerpo monoclonal *Homo sapiens;*
cadena pesada gamma4 *Homo sapiens*(1-441) [VH (*Homo sapiens* IGHV4-59*01 (100%) -(IGHD) - IGHJ1*01 (100%)) CDR-IMGT [8.7.9] (26-33.51-57.96-104) (1-115) -*Homo sapiens* IGHG4*01, G4v4 CH2 A1.3, A1.2 (CH1 (116-213), bisagra 1-12 S10>P (223) (214-225), CH2 F1.3>A (229), L1.2>A (230) (226-335), CH3 (336-440), CHS K>del (441) (116-441)], (129-214')-disulfuro con la cadena ligera kappa *Homo sapiens*(1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (96.8%) -IGKJ4*01 (91.7%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dímero (221-221":224-224")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-S, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLQESGPG LVKPSETLSL TCTVSGGSIS SYYWSWIRQP PGKGLEWIGY  50
IYYSGSTNYN PSLKSRVTIS VDTSKNQFSL KLSSVTAADT AVYYCARGKT 100
GSAAWGQGTL VTVSSASTKG PSVFPLAPCS RSTSESTAAL GCLVKDYFPE 150
PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL SSVVTVPSSS LGTKTYTCNV 200
DHKPSNTKVD KRVESKYGPP CPPCPAPEAA GGPSVFLFPP KPKDTLMISR 250
TPEVTCVVVD VSQEDPEVQF NWYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ 350
EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDSDGSFF 400
LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL G          441
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS VSASVGDRVT ITCRASQGIS RWLAWYQQKP GKAPKLLIYA  50
ASSLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ TVSFPITFGG 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-95 142-198 256-316 362-420
22"-95" 142"-198" 256"-316" 362"-420"
Intra-L (C23-C104) 23'-88' 134'-194'
23'"-88'" 134'"-194'"
Inter-H-L (CH1 10-CL 126) 129-214' 129"-214'"
Inter-H-H (h 8, h 11) 221-221" 224-224"

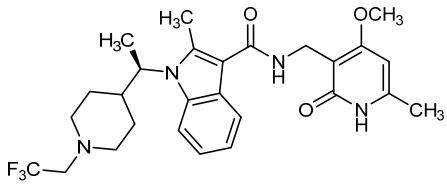
N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
L VH Q1:
1, 1"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
292, 292"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

lirametostatum

lirametostat	*N*-[(4-methoxy-6-methyl-2-oxo-1,2-dihydropyridin-3-yl)methyl]-2-methyl-1-{(1*R*)-1-[1-(2,2,2-trifluoroethyl)piperidin-4-yl]ethyl}-1*H*-indole-3-carboxamide
liramétostat	*N*-[(4-méthoxy-6-méthyl-2-oxo-1,2-dihydropyridin-3-yl)méthyl]-2-méthyl-1-{(1*R*)-1-[1-(2,2,2-trifluoroéthyl)pipéridin-4-yl]éthyl}-1*H*-indole-3-carboxamide
lirametostat	2-metil-*N*-[(6-metil-4-metoxi-2-oxo-1,2-dihidropiridin-3-il)metil]-1-{(1*R*)-1-[1-(2,2,2-trifluoroetil)piperidin-4-il]etil}-1*H*-indol-3-carboxamida

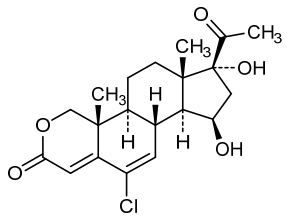
$C_{27}H_{33}F_3N_4O_3$



ludateronum

ludaterone	6-chloro-15β,17-dihydroxy-2-oxapregna-4,6-diene-3,20-dione
ludatérone	6-chloro-15β,17-dihydroxy-2-oxaprégna-4,6-diène-3,20-dione
ludaterona	6-cloro-15β,17-dihidroxi-2-oxapregna-4,6-dieno-3,20-diona

$C_{20}H_{25}ClO_5$



lutetium (^{177}Lu) vipivotidum tetraxetanum

lutetium (^{177}Lu) vipivotide tetraxetan	{*N*-[(N^6-{3-(naphthalen-2-yl)-*N*-[*trans*-4-({2-[4,7,10-tris(carboxy-κ$^3O^4$,O^7,O^{10}-methyl)-1,4,7,10-tetraazacyclododecan-1-yl-κ$^4N^1$,N^4,N^7,N^{10}]acetamido-κ*O*}methyl)cyclohexane-1-carbonyl]-L-alanyl}-L-lysin-N^2-yl)carbonyl]-L-glutamato(3−)}(^{177}Lu)lutetium

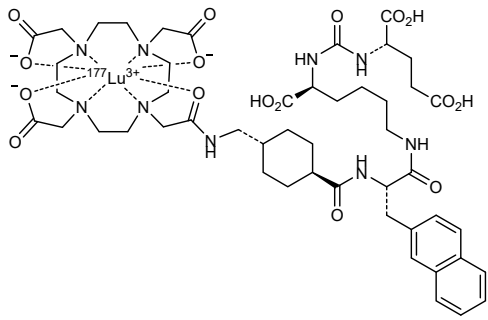
lutécium (^{177}Lu) vipivotide tétraxetan

{*N*-[(*N*^{6}-{3-(naphtalén-2-yl)-*N*-[*trans*-4-({2-[4,7,10-tris(carboxy-κ^3*O*^{4},*O*^{7},*O*^{10}-méthyl)-1,4,7,10-tétraazacyclododécan-1-yl-κ^4*N*^{1},*N*^{4},*N*^{7},*N*^{10}]acétamido-κ*O*}méthyl)cyclohexane-1-carbonyl]-L-alanyl}-L-lysin-*N*^{2}-yl)carbonyl]-L-glutamato(3−)}(^{177}Lu)lutecium

lutecio (^{177}Lu) vipivotida tetraxetán

{*N*-[(*N*^{6}-{3-(naftalen-2-il)-*N*-[*trans*-4-({2-[4,7,10-tris(carboxi-κ^3*O*^{4},*O*^{7},*O*^{10}-metil)-1,4,7,10-tetraazaciclododecan-1-il-κ^4*N*^{1},*N*^{4},*N*^{7},*N*^{10}]acetamido-κ*O*}metil)ciclohexano-1-carbonil]-L-alanil}-L-lisin-*N*^{2}-il)carbonil]-L-glutamato(3−)}(^{177}Lu)lutecio

$C_{49}H_{68}{}^{177}LuN_9O_{16}$



melrilimabum #

melrilimab

immunoglobulin G2-kappa, anti-[*Homo sapiens* IL1RL1 (interleukin 1 receptor like 1, DER4, FIT-1, growth stimulation expressed 2 gene, ST2, IL33R)], *Homo sapiens* monoclonal antibody;
gamma2 heavy chain *Homo sapiens* (1-449) [VH (*Homo sapiens* IGHV3-23*01 (91.8%) -(IGHD) -IGHJ4*01(92.9%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Homo sapiens* IGHG2*02v G2m23>G2m.., G2v3 CH2 A1.2, A1, S2, A30, L92, S115, S116 (CH1 T92 (195) (124-221), hinge 1-12 (222-233), CH2 V1.2>A (237), G1>A (239), P2>S (240), H30>A (270), M45.1>V (284), V92>L (311), A115>S (332), P116>S (333) (234-342), CH3 (343-447), CHS (448-449)) (124-449)], (137-214')-disulfide with kappa light chain *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV3D-11*02 (95.6%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')];
dimer (225-225":226-226":229-229":232-232")-tetrakisdisulfide, produced in Chinese hamster ovary (CHO)-K1SV cell line lacking the Glutamine Synthetase (GS) gene, glycoform alfa

melrilimab

immunoglobuline G2-kappa, anti-[*Homo sapiens* IL1RL1 (récepteur like 1 de l'interleukine 1, DER4, FIT1, gène 2 exprimé lors de la stimulation de la croissance, ST2, IL33R)], anticorps monoclonal *Homo sapiens*;

chaîne lourde gamma2 *Homo sapiens* (1-449) [VH (*Homo sapiens* IGHV3-23*01 (91.8%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Homo sapiens* IGHG2*02v G2m23>G2m.., G2v3 CH2 A1.2, A1, S2, A30, L92, S115, S116 (CH1 T92 (195) (124-221), charnière 1-12 (222-233), CH2 V1.2>A (237), G1>A (239), P2>S (240), H30>A (270), M45.1>V (284), V92>L (311), A115>S (332), P116>S (333) (234-342), CH3 (343-447), CHS (448-449)) (124-449)], (137-214')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV3D-11*02 (95.6%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dimère (225-225":226-226":229-229":232-232")-tétrakisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-K1SV ne présentant pas le gène de la glutamine synthétase, glycoforme alfa

melrilimab

inmunoglobulina G2-kappa, anti-[*Homo sapiens* IL1RL1 (receptor like 1 de la interleukina 1, DER4, FIT1, gen 2 expresado durante la estimulación del crecimiento, ST2, IL33R)], anticuerpo monoclonal *Homo sapiens*; cadena pesada gamma2 *Homo sapiens* (1-449) [VH (*Homo sapiens* IGHV3-23*01 (91.8%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Homo sapiens* IGHG2*02v G2m23>G2m.., G2v3 CH2 A1.2, A1, S2, A30, L92, S115, S116 (CH1 T92 (195) (124-221), bisagra 1-12 (222-233), CH2 V1.2>A (237), G1>A (239), P2>S (240), H30>A (270), M45.1>V (284), V92>L (311), A115>S (332), P116>S (333) (234-342), CH3 (343-447), CHS (448-449)) (124-449)], (137-214')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV3D-11*02 (95.6%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dímero (225-225":226-226":229-229":232-232")-tetrakisdisulfuro, producido en las células ováricas de hámsters chinos (CHO) línea celular CHO-K1SV en ausencia del gen Glutamina Sintetasa (GS)forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLLESGGG LVQPGGSLRL SCAASGFTFS IYDMIWVRQA PGKGLEWVSS  50
IRGEGGGTYY ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARDP 100
WSTEGSFFVL DYWGQGTLVT VSSASTKGPS VFPLAPCSRS TSESTAALGC 150
LVKDYFPEPV TVSWNSGALT SGVHTFPAVL QSSGLYSLSS VVTVTSSNFG 200
TQTYTCNVDH KPSNTKVDKT VERKCCVECP PCPAPPAAAS SVFLFPPKPK 250
DTLMISRTPE VTCVVVDVSA EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TFRVVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK TKGQPREPQV 350
YTLPPSREEM TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPML 400
DSDGSFFLYS KLTVDKSRWQ QGNVFSCSVM HEALHNHYTQ KSLSLSPGK  449
```

Light chain / Chaîne légère / Cadena ligera

```
EIVLTQSPAT LSLSPGERAT LSCRASQSVD DDLAWYQQKP GQAPRLLIYD  50
ASNRATGIPA RFSGSGSGTD FTLTISSLEP EDFAVYYCQQ YITAPLTFGQ 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

```
Intra-H (C23-C104)   22-96     150-206  263-323  369-427
                    22"-96"  150"-206"  263"-323"  369"-427"
Intra-L (C23-C104)   23'-88'    134'-194'
                    23'"-88'"  134'"-194'"
Inter-H-L (CH1 10-CL 126)*    137-214'  137"-214'"
Inter-H-H (h 4, h 5, h 8, h 11)*  225-225"  226-226"  229-229"  232-232"
```

*In addition to the isoform A, isoform A/B characterized by an inter-H-H (h 4 - CH1 10) 225-137'" and an inter-H-L (h 4- CL 126) 225"-214'", instead of the inter-H-H (h 4 - h 4) 225-225" and of one of the two inter-H-L (CH1 10-CL 126) 137"-214'"; isoform B characterized by an inter-H-H (h 5 - CH1 10) 226-137 and an inter-H-L (h 5- CL 126) 226"-214', instead of the inter-H-H (h 5 - h 5) 226-226" and of the inter-H-L (CH1 10-CL 126) 137-214'.
* En plus de l'isoforme A, isoforme A/B caractérisée par un inter-H-H (h 4 - CH1 10) 225-137" et un inter-H-L (h 4- CL 126) 225"-214'", au lieu de l'inter-H-H (h 4 - h 4) 225-225" et de l'un des deux inter-H-L (CH1 10-CL 126) 137"-214'"; isoforme B caractérisée par un inter-H-H (h 5 - CH1 10) 226-137 et un inter-H-L (h 5- CL 126) 226"-214', au lieu de l'inter-H-H (h 5 - h 5) 226-226" et de l'inter-H-L (CH1 10-CL 126) 137-214'.
* Además de la isoforma A, isoforma A/B caracterizado por un inter-H-H (h 4 - CH1 10) 225-137'" y un inter-H-L (h 4- CL 126) 225"-214'", enlugar del inter-H-H (h 4 - h 4) 225-225" y uno de los dos inter-H-L (CH1 10-CL 126) 137"-214'"; isoforma B caracterizado por un inter-H-H (h 5 - CH1 10) 226-137 y un inter-H-L (h 5- CL 126) 226"-214', en lugar del inter-H-H (h 5 - h 5) 226-226" y del inter-H-L (CH1 10-CL 126) 137-214'.

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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal

```
H CHS K2:
449, 449'"
```

milvexianum

milvexian

(5*R*,9*S*)-9-{4-[5-chloro-2-(4-chloro-1*H*-1,2,3-triazol-1-yl)phenyl]-6-oxopyrimidin-1(6*H*)-yl}-2^2-(difluoromethyl)-5-methyl-2^2*H*-3-aza-1(4,2)-pyridina-2(3,4)-pyrazolacyclononaphan-4-one

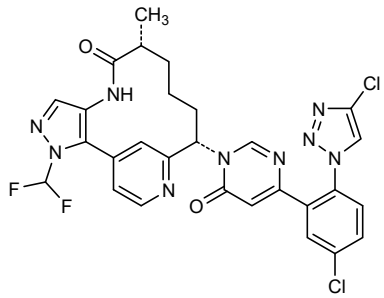
milvexian

(5*R*,9*S*)-9-{4-[5-chloro-2-(4-chloro-1*H*-1,2,3-triazol-1-yl)phényl]-6-oxopyrimidin-1(6*H*)-yl}-2^2-(difluorométhyl)-5-méthyl-2^2*H*-3-aza-1(4,2)-pyridina-2(3,4)-pyrazolacyclononaphan-4-one

milvexián

(5*R*,9*S*)-9-{4-[5-cloro-2-(4-cloro-1*H*-1,2,3-triazol-1-il)fenil]-6-oxopirimidin-1(6*H*)-il}-2^2-(difluorometil)-5-metil-2^2*H*-3-aza-1(4,2)-piridina-2(3,4)-pirazolaciclononafan-4-ona

$C_{28}H_{23}Cl_2F_2N_9O_2$



mipasetamabum #

mipasetamab

immunoglobulin G1-kappa, anti-[*Homo sapiens* AXL (AXL receptor tyrosine kinase, tyrosine-protein kinase receptor UFO)], humanized monoclonal antibody; gamma1 heavy chain humanized (1-451) [VH humanized (*Homo sapiens* IGHV3-30*03 (92.9%) -(IGHD) -IGHJ4*01 (92.3%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122) -*Homo sapiens* IGHG1*03, G1m3>G1m17, nG1m1 (CH1 R>K 120 (219) (123-220), hinge 1-15 (221-235), CH2 (236-345), CH3 E12 (361), M14 (363) (346-450), CHS K>del (451)) (123-451)], (225-215')-disulfide with kappa light chain humanized (1'-215') [V-KAPPA humanized (*Homo sapiens* IGKV3-11*01 (84.4%) -IGKJ4*01 (90.9%)) CDR-IMGT [7.3.9] (27-33.51-53.90-98) (1'-108') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (154), V101 (192) (109'-215')];
dimer (231-231''':234-234'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

mipasétamab

immunoglobuline G1-kappa, anti-[*Homo sapiens* AXL (récepteur tyrosine kinase AXL, récepteur tyrosine-protéine kinase UFO)], anticorps monoclonal humanisé;

chaîne lourde gamma1 humanisée (1-451) [VH humanisé (*Homo sapiens* IGHV3-30*03 (92.9%) -(IGHD) -IGHJ4*01 (92.3%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122) -*Homo sapiens* IGHG1*03, G1m3>G1m17, nG1m1 (CH1 R>K 120 (219) (123-220), charnière 1-15 (221-235), CH2 (236-345), CH3 E12 (361), M14 (363) (346-450), CHS K>del (451)) (123-451)], (225-215')-disulfure avec la chaîne légère kappa humanisée (1'-215') [V-KAPPA humanisé (*Homo sapiens* IGKV3-11*01 (84.4%) -IGKJ4*01 (90.9%)) CDR-IMGT [7.3.9] (27-33.51-53.90-98) (1'-108') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (154), V101 (192) (109'-215')]; dimère (231-231":234-234")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

mipasetamab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* AXL (receptor tirosina kinasa AXL, receptor tirosina-proteína kinasa UFO)], anticuerpo monoclonal humanizado; cadena pesada gamma1 humanizada (1-451) [VH humanizado (*Homo sapiens* IGHV3-30*03 (92.9%) -(IGHD) -IGHJ4*01 (92.3%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122) -*Homo sapiens* IGHG1*03, G1m3>G1m17, nG1m1 (CH1 R>K 120 (219) (123-220), bisagra 1-15 (221-235), CH2 (236-345), CH3 E12 (361), M14 (363) (346-450), CHS K>del (451)) (123-451)], (225-215')-disulfuro con la cadena ligera kappa humanizada (1'-215') [V-KAPPA humanizado (*Homo sapiens* IGKV3-11*01 (84.4%) -IGKJ4*01 (90.9%)) CDR-IMGT [7.3.9] (27-33.51-53.90-98) (1'-108') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (154), V101 (192) (109'-215')]; dímero (231-231":234-234")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVESGGG VVQPGRSLRL SCAASGFTFS SYGMSWVRQA PGKGLEWVAT  50
ISSGGSYTYY PDSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARHP 100
IYYTYDDTMD YWGQGTTVTV SSASTKGPSV FPLAPSSKST SGGTAALGCL 150
VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ SSGLYSLSSV VTVPSSSLGT 200
QTYICNVNHK PSNTKVDKKV EPKSCDKTHT CPPCPAPELL GGPSVFLFPP 250
KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NWYVDGVEVH NAKTKPREEQ 300
YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQPRE 350
PQVYTLPPSR EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP 400
PVLDSDGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP 450
G                                                       451
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Light chain / Chaîne légère / Cadena ligera

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EIVLTQSPGT LSLSPGERAT LSCSASSSVS SGNFHWYQQK PGLAPRLLIY  50
RTSNLASGIP ARFSGSGSGT DFTLTISSLE PEDFAVYYCQ QWSGYPWTFG 100
GGTKLEIKRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK 150
VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ 200
GLSSPVTKSF NRGEC                                       215
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 149-205 266-326 372-430
22"-96" 149"-205" 266"-326" 372"-430"
Intra-L (C23-C104) 23'-89' 135'-195'
23'"-89"' 135'"-195'"
Inter-H-L (h 5-CL 126) 225-215' 225"-215'"
Inter-H-H (h 11, h 14) 231-231" 234-234"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4 [glycoengineered GalNAcN3 (*N*-azidoacetyl-D-galactosamine)]:
302, 302"-bis[*N*-[*O*-2-(acetylamino)-6-azido-2,6-dideoxy- β-D-galactopyranosyl-(1->4)-*O*-[6-deoxy-α-L-galactopyranosyl-(1->6)]-2-(acetylamino)-2-deoxy- β-D-glucopyranosyl]-L-asparagine]

mipasetamabum uzoptirinum #

mipasetamab uzoptirine	immunoglobulin G1-kappa, anti-[*Homo sapiens* AXL (AXL receptor tyrosine kinase, tyrosine-protein kinase receptor UFO)], humanized monoclonal antibody conjugated to the pyrrolobenzodiazepine (PBD) dimer, SG3199; gamma1 heavy chain humanized (1-451) [VH humanized (*Homo sapiens* IGHV3-30*03 (92.9%) -(IGHD) -IGHJ4*01 (92.3%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122) -*Homo sapiens* IGHG1*03 nG1m1 (CH1 R120>K (219) (123-220), hinge 1-15 (221-235), CH2 (236-345), CH3 E12 (361), M14 (363) (346-450), CHS K>del (451)) (123-451)], (225-215')-disulfide with kappa light chain humanized (1'-215') [V-KAPPA (*Homo sapiens* IGKV3-11*01 (84.4%) -IGKJ4*01 (90.9%)) CDR-IMGT [7.3.9] (27-33.51-53.90-98) (1'-108') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (154), V101 (192) (109'-215')]; dimer (231-231":234-234")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa; conjugated on the two glycoengineered N84.4, via a spacer and a cleavable valine-alanine linker, to the cytotoxic pyrrolobenzodiazepine (PBD) dimer, SG3199
mipasétamab uzoptirine	immunoglobuline G1-kappa, anti-[*Homo sapiens* AXL (récepteur tyrosine kinase AXL, récepteur tyrosine-protéine kinase UFO)], anticorps monoclonal humanisé conjugué au dimère de pyrrolobenzodiazépine (PBD), SG3199; chaîne lourde gamma1 humanisée (1-451) [VH (*Homo sapiens* IGHV3-30*03 (92.9%) -(IGHD) -IGHJ4*01 (92.3%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122) -*Homo sapiens* IGHG1*03 nG1m1 (CH1 R120>K (219) (123-220), charnière 1-15 (221-235), CH2 (236-345), CH3 E12 (361), M14 (363) (346-450), CHS K>del (451)) (123-451)], (225-215')-disulfure avec la chaîne légère kappa humanisée (1'-215') [V-KAPPA (*Homo sapiens* IGKV3-11*01 (84.4%) -IGKJ4*01 (90.9%)) CDR-IMGT [7.3.9] (27-33.51-53.90-98) (1'-108') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (154), V101 (192) (109'-215')]; dimère (231-231":234-234")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa; conjugué sur les deux N84.4 glycomodifiés, via un espaceur et un linker clivable valine-alanine, au dimère pyrrolobenzodiazépine (PBD) cytotoxique, SG3199
mipasetamab uzoptirina	inmunoglobulina G1-kappa, anti-[*Homo sapiens* AXL (receptor tirosina kinasa AXL, receptor tirosina-proteína kinasa UFO)], anticuerpo monoclonal humanizado conjugado con el dímero de pirrolobenzodiazepina (PBD), SG3199; cadena pesada gamma1 humanizada (1-451) [VH (*Homo sapiens* IGHV3-30*03 (92.9%) -(IGHD) -IGHJ4*01 (92.3%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122) -*Homo sapiens* IGHG1*03 nG1m1 (CH1 R120>K (219) (123-220), bisagra 1-15 (221-235), CH2 (236-345), CH3 E12 (361), M14 (363) (346-450), CHS K>del (451)) (123-451)], (225-215')-disulfuro con la cadena ligera kappa humanizada (1'-215') [V-KAPPA (*Homo sapiens* IGKV3-11*01 (84.4%) -IGKJ4*01 (90.9%)) CDR-IMGT [7.3.9] (27-33.51-53.90-98) (1'-108') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (154), V101 (192) (109'-215')];

dímero (231-231":234-234")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa; conjugado sobre los dos N84.4 glicomodificados, mediante un espaciador y un conector escindible valina-alanina, al dímero pirrolobenzodiazepina (PBD) citotóxico, SG3199

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVESGGG VVQPGRSLRL SCAASGFTFS SYGMSWVRQA PGKGLEWVAT  50
ISSGGSYTYY PDSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARHP 100
IYYTYDDTMD YWGQGTTVTV SSASTKGPSV FPLAPSSKST SGGTAALGCL 150
VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ SSGLYSLSSV VTVPSSSLGT 200
QTYICNVNHK PSNTKVDKKV EPKSCDKTHT CPPCPAPELL GGPSVFLFPP 250
KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NWYVDGVEVH NAKTKPREEQ 300
YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQPRE 350
PQVYTLPPSR EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP 400
PVLDSDGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP 450
G                                                       451
```

Light chain / Chaîne légère / Cadena ligera

```
EIVLTQSPGT LSLSPGERAT LSCSASSSVS SGNFHWYQQK PGLAPRLLIY  50
RTSNLASGIP ARFSGSGSGT DFTLTISSLE PEDFAVYYCQ QWSGYPWTFG 100
GGTKLEIKRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK 150
VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ 200
GLSSPVTKSF NRGEC                                       215
```

Post-translational modifications

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

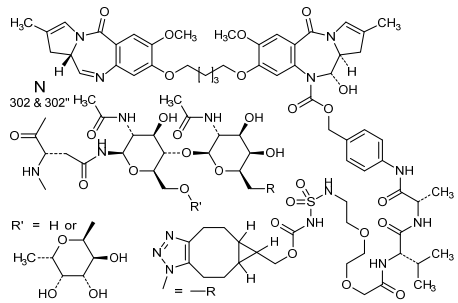
Intra-H (C23-C104) 22-96 149-205 266-326 372-430
22"-96" 149"-205" 266"-326" 372"-430"
Intra-L (C23-C104) 23'-89' 135'-195'
23'"-89'" 135'"-195'"
Inter-H-L (h 5-CL 126) 225-215' 225"-215'"
Inter-H-H (h 11, h 14) 231-231" 234-234"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)

H VH Q1:
1, 1"

Chemically modified N-glycosylation sites / Sites de N-glycosylation chimiquement modifiés / Posiciones de N-glicosilación modificadas químicamente

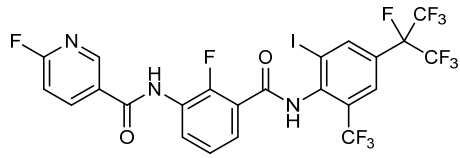
H CH2 N84.4:
302, 302"



modoflanerum

modoflaner	6-fluoro-*N*-(2-fluoro-3-{[4-(heptafluoropropan-2-yl)-2-iodo-6-(trifluoromethyl)phenyl]carbamoyl}phenyl)pyridine-3-carboxamide
modoflaner	6-fluoro-*N*-(2-fluoro-3-{[4-(heptafluoropropan-2-yl)-2-iodo-6-(trifluorométhyl)phényl]carbamoyl}phényl)pyridine-3-carboxamide
modoflaner	6-fluoro-*N*-(2-fluoro-3-{[4-(heptafluoropropan-2-il)-2-iodo-6-(trifluorometil)fenil]carbamoil}fenil)piridina-3-carboxamida

$C_{23}H_{10}F_{12}IN_3O_2$



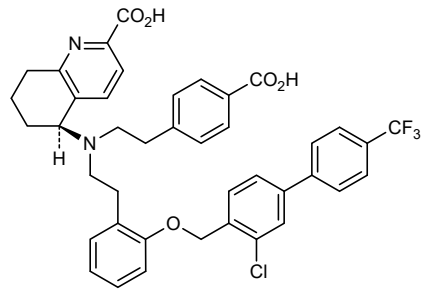
mosliciguatum

mosliciguat — (9^5*S*)-8-[2-(4-carboxyphenyl)ethyl]-2^3-chloro-1^4-(trifluoromethyl)-9^{5,6,7,8}-tetrahydro-4-oxa-8-aza-9(5)-quinolina-1(1),2(1,4),5(1,2)-tribenzenanonaphane-9^2-carboxylic acid

mosliciguat — acide (9^5*S*)-8-[2-(4-carboxyphényl)éthyl]-2^3-chloro-1^4-(trifluorométhyl)-9^{5,6,7,8}-tétrahydro-4-oxa-8-aza-9(5)-quinoléina-1(1),2(1,4),5(1,2)-tribenzénanonaphane-9^2-carboxylique

mosliciguat — ácido (9^5*S*)-8-[2-(4-carboxifenil)etil]-2^3-cloro-1^4-(trifluorometil)-9^{5,6,7,8}-tetrahidro-4-oxa-8-aza-9(5)-quinoleína-1(1),2(1,4),5(1,2)-tribencenanonafano-9^2-carboxílico

$C_{41}H_{36}ClF_3N_2O_5$



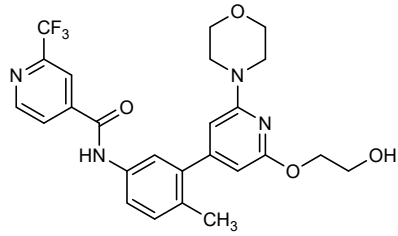
naporafenibum

naporafenib — *N*-{3-[2-(2-hydroxyethoxy)-6-(morpholin-4-yl)pyridin-4-yl]-4-methylphenyl}-2-(trifluoromethyl)pyridine-4-carboxamide

naporafénib — *N*-{3-[2-(2-hydroxyéthoxy)-6-(morpholin-4-yl)pyridin-4-yl]-4-méthylphényl}-2-(trifluorométhyl)pyridine-4-carboxamide

naporafenib — *N*-{3-[2-(2-hidroxietoxi)-6-(morfolin-4-il)piridin-4-il]-4-metilfenil}-2-(trifluorometil)piridina-4-carboxamida

$C_{25}H_{25}F_3N_4O_4$



nedosiranum

nedosiran

all-P-ambo-2'-*O*-methyl-*P*-thioadenylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-deoxy-2'-fluoroguanylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(3'→5')-2'-deoxy-2'-fluorouridylyl-(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*-methyluridylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-{[2-(2-{5-[(2-acetamido-2-deoxy-β-D-galactopyranosyl)oxy]pentanamido}ethoxy)ethoxy]methyl}guanylyl-(3'→5')-2'-*O*-{[2-(2-{5-[(2-acetamido-2-deoxy-β-D-galactopyranosyl)oxy]pentanamido}ethoxy)ethoxy]methyl}adenylyl-(3'→5')-2'-*O*-{[2-(2-{5-[(2-acetamido-2-deoxy-β-D-galactopyranosyl)oxy]pentanamido}ethoxy)ethoxy]methyl}adenylyl-(3'→5')-2'-*O*-{[2-(2-{5-[(2-acetamido-2-deoxy-β-D-galactopyranosyl)oxy]pentanamido}ethoxy)ethoxy]methyl}adenylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylcytidine
duplex with *all-P-ambo*-2'-*O*-methyl-*P*-thioguanylyl-(5'→3')-2'-*O*-methyl-*P*-thioguanylyl-(5'→3')-2'-*O*-methyluridylyl-(5'→3')-2'-*O*-methyladenylyl-(5'→3')-2'-deoxy-2'-fluorocytidylyl-(5'→3')-2'-*O*-methyladenylyl-(5'→3')-2'-deoxy-2'-fluoroadenylyl-(5'→3')-2'-*O*-methylcytidylyl-(5'→3')-2'-deoxy-2'-fluoroadenylyl-(5'→3')-2'-*O*-methylguanylyl-(5'→3')-2'-*O*-methylguanylyl-(5'→3')-2'-*O*-methyladenylyl-(5'→3')-2'-deoxy-2'-fluoroadenylyl-(5'→3')-2'-deoxy-2'-fluoroadenylyl-(5'→3')-2'-*O*-methyladenylyl-(5'→3')-2'-deoxy-2'-fluoroadenylyl-(5'→3')-2'-*O*-methyluridylyl-(5'→3')-2'-deoxy-2'-fluoroadenylyl-(5'→3')-2'-deoxy-2'-fluoro-*P*-thioguanylyl-(5'→3')-2'-deoxy-2'-fluoro-*P*-thioadenylyl-(5'→3')-2'-deoxy-2'-fluoro-*P*-thiocytidylyl-(5'→3')-methyl hydrogen 2'-*O*-methyl-5'-oxa-*O*-5'-carba-5'-uridylate

nédosiran

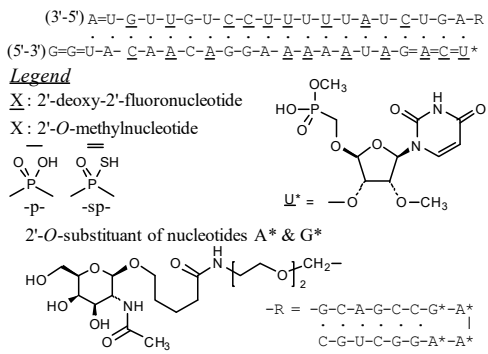
tout-P-ambo-2'-*O*-méthyl-*P*-thioadénylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-désoxy-2'-fluoroguanylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-désoxy-2'-fluorouridylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-désoxy-2'-fluorocytidylyl-(3'→5')-2'-désoxy-2'-fluorocytidylyl-(3'→5')-2'-désoxy-2'-fluorouridylyl-(3'→5')-2'-désoxy-2'-fluorouridylyl-(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*-méthyluridylyl-(3'→5')-2'-désoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthylcytidylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthylcytidylyl-(3'→5')-2'-*O*-méthylcytidylyl-(3'→5')-2'-*O*-{[2-(2-{5-[(2-acétamido-2-désoxy-β-D-galactopyranosyl)oxy]pentanamido}éthoxy)éthoxy]méthyl}guanylyl-(3'→5')-2'-*O*-{[2-(2-{5-[(2-acétamido-2-désoxy-β-D-galactopyranosyl)oxy]pentanamido}éthoxy)éthoxy]méthyl}adénylyl-(3'→5')-2'-*O*-{[2-(2-{5-[(2-acétamido-2-désoxy-β-D-galactopyranosyl)oxy]pentanamido}éthoxy)éthoxy]méthyl}adénylyl-(3'→5')-2'-*O*-{[2-(2-{5-[(2-acétamido-2-désoxy-β-D-galactopyranosyl)oxy]pentanamido}éthoxy)éthoxy]méthyl}adénylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthylcytidylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthylcytidine

duplex avec acide *tout-P-ambo*-2'-*O*-méthyl-*P*-thioguanylyl-(5'→3')-2'-*O*-méthyl-*P*-thioguanylyl-(5'→3')-2'-*O*-méthyluridylyl-(5'→3')-2'-*O*-méthyl-adénylyl-(5'→3')-2'-désoxy-2'-fluorocytidylyl-(5'→3')-2'-*O*-méthyladénylyl-(5'→3')-2'-désoxy-2'-fluoroadénylyl-(5'→3')-2'-*O*-méthylcytidylyl-(5'→3')-2'-désoxy-2'-fluoroadénylyl-(5'→3')-2'-*O*-méthylguanylyl-(5'→3')-2'-*O*-méthylguanylyl-(5'→3')-2'-*O*-méthyladénylyl-(5'→3')-2'-désoxy-2'-fluoroadénylyl-(5'→3')-2'-désoxy-2'-fluoroadénylyl-(5'→3')-2'-*O*-méthyladénylyl-(5'→3')-2'-désoxy-2'-fluoroadénylyl-(5'→3')-2'-*O*-méthyluridylyl-(5'→3')-2'-désoxy-2'-fluoroadénylyl-(5'→3')-2'-désoxy-2'-fluoro-*P*-thioguanylyl-(5'→3')-2'-désoxy-2'-fluoro-*P*-thioadénylyl-(5'→3')-2'-désoxy-2'-fluoro-*P*-thiocytidylyl-(5'→3')-hydrogéno-2'-*O*-méthyl-5'-oxa-*O*-5'-carba-5'-uridylate de méthyle

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todo-P-ambo-2'-*O*-metil-*P*-tioadenilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-desoxi-2'-fluoroguanilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-desoxi-2'-fluorouridilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-des-oxi-2'-fluoroadenilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-desoxi-2'-fluoro-citidilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metilcitidilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metilcitidilil-(3'→5')-2'-*O*-metilcitidilil-(3'→5')-2'-*O*-{[2-(2-{5-[(2-acetamido-2-desoxi-β-D-galactopiranosil)oxi]-pentanamido}etoxi)etoxi]metil}guanilil-(3'→5')-2'-*O*-{[2-(2-{5-[(2-acetamido-2-desoxi-β-D-galactopiranosil)oxi]pentanamido}etoxi)etoxi]metil}adenilil-(3'→5')-2'-*O*-{[2-(2-{5-[(2-acetamido-2-desoxi-β-D-galactopiranosil)oxi]pentanamido}etoxi)etoxi]metil}adenilil-(3'→5')-2'-*O*-{[2-(2-{5-[(2-acetamido-2-desoxi-β-D-galactopiranosil)oxi]pentanamido}etoxi)etoxi]metil}adenilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metilcitidilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metilcitidina
dúplex con *todo-P-ambo*-2'-*O*-metil-*P*-tioguanilil-(5'→3')-2'-*O*-metil-*P*-tioguanilil-(5'→3')-2'-*O*-metiluridilil-(5'→3')-2'-*O*-metiladenilil-(5'→3')-2'-desoxi-2'-fluorocitidilil-(5'→3')-2'-*O*-metiladenilil-(5'→3')-2'-desoxi-2'-fluoroadenilil-(5'→3')-2'-*O*-metilcitidilil-(5'→3')-2'-desoxi-2'-fluoroadenilil-(5'→3')-2'-*O*-metilguanilil-(5'→3')-2'-*O*-metilguanilil-(5'→3')-2'-*O*-metiladenilil-(5'→3')-2'-desoxi-2'-fluoroadenilil-(5'→3')-2'-desoxi-2'-fluoroadenilil-(5'→3')-2'-*O*-metiladenilil-(5'→3')-2'-desoxi-2'-fluoroadenilil-(5'→3')-2'-*O*-metiluridilil-(5'→3')-2'-desoxi-2'-fluoroadenilil-(5'→3')-2'-desoxi-2'-fluoro-*P*-tioguanilil-(5'→3')-2'-desoxi-2'-fluoro-*P*-tioadenilil-(5'→3')-2'-desoxi-2'-fluoro-*P*-tiocitidilil-(5'→3')-hidrógeno-2'-*O*-metil-5'-oxa-*O*-5'-carba-5'-uridilato de metilo

$C_{662}H_{865}F_{19}N_{231}O_{413}P_{57}S_6$



nemvaleukinum alfa #

nemvaleukin alfa

human interleukin 2 fragment (1-59), variant (Cys^{125}>Ser^{51}), fused via peptidyl linker (^{60}GG^{61}) to human interleukin 2 fragment (62-132), fused via peptidyl linker (^{133}GSGGGS^{138}) to human interleukin 2 receptor α-chain fragment (139-303), produced in Chinese hamster ovary (CHO) cells, glycosylated; human interleukin 2 (IL-2) (75-133)-peptide [$Cys^{125(51)}$>Ser]-mutant (1-59), fused via a G_2 peptide linker (60-61) to human interleukin 2 (IL-2) (4-74)-peptide (62-132) and via a GSG_3S peptide linker (133-138) to human interleukin 2 receptor α-chain (IL2R subunit alpha, IL2Rα, IL2RA) (1-165)-peptide (139-303), produced in Chinese hamster ovary (CHO) cells, glycoform alfa

nemvaleukine alfa

fragment de l'interleukine 2 humaine (1-59), variant (Cys^{125}>Ser^{51}), fusionné via un peptide liant (^{60}GG^{61}) à un fragment de l'interleukine 2 humaine (62-132), fusionné via un peptide liant (^{133}GSGGGS^{138}) au fragment de la chaîne α du récepteur de l'interleukine 2 (139-303), produit dans des cellules ovariennes de hamsters chinois (CHO), glycosylé; peptide 75-133 d'interleukine 2 humaine (IL-2) mutante [$Cys^{125(51)}$>Ser] (1-59), fusionnée via un peptide G_2 (60-61) au peptide 4-74 d'inter-leukine humaine 2 (IL-2) (62-132) et via un peptide GSG_3S (133-138) au peptide 1-165 de la chaîne α du récepteur de l'interleukine 2 humaine (sous-unité alpha de IL2R, IL2Rα, IL2RA) (139-303), produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

nemvaleukina alfa

fragmento de interleukina 2 humana (1-59), variante (Cis^{125}>Ser^{51}), fusionado a través de un conector peptidil (^{60}GG^{61}) al fragmento de interleukina 2 humana (62-132), fusionado a través de un conector peptidil (^{133}GSGGGS^{138}) al fragmento humano de la cadena α del receptor de interleukina 2 (139-303), producido en células ováricas de hámster Chino (CHO), glicosilado;
péptido 75-133 de la interleukina 2 humana (IL-2) mutante [$Cis^{125(51)}$>Ser] (1-59), fusionado a través de un péptido G_2 (60-61) al péptido 4-74 de la interleukina 2 humana (IL-2) (62-132) y a través de un péptido GSG_3S (133-138) al péptido 1-165 de la cadena α del receptor de interleukina 2 humano (subunidad alfa de IL2R, IL2Rα, IL2RA) (139-303), producido en células ováricas de hámster Chino (CHO), glicosilada alfa

Sequence / Séquence / Secuencia

```
SKNFHLRPRD LISNINVIVL ELKGSETTFM CEYADETATI VEFLNRWITF   50
SQSIISTLTG GSSSTKKTQL QLEHLLLDLQ MILNGINNYK NPKLTRMLTF  100
KFYMPKKATE LKHLQCLEEE LKPLEEVLNL AQGSGGGSEL CDDDPPEIPH  150
ATFKAMAYKE GTMLNCECKR GFRRIKSGSL YMLCTGNSSH SSWDNQCQCT  200
SSATRNTTKQ VTPQPEEQKE RKTTEMQSPM QPVDQASLPG HCREPPPWEN  250
EATERIYHFV VGQMVYYQCV QGYRALHRGP AESVCKMTHG KTRWTQPQLI  300
CTG                                                     303
```

Mutation / Mutation / Mutación

C^{51}>S

Post-translational modifications

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

31-116, 141-285, 184-242, 269-301, 166-197 or 166-199, 168-199 or 168-197

Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación

N187, N206, T212

obecabtagenum autoleucelum #

obecabtagene autoleucel

Autologous CD4+ and CD8+ T cells transduced *ex vivo* with a self-inactivating lentiviral vector encoding an anti-CD19 chimeric antigen receptor.
Autologous CD4+ and CD8+ T cells, enriched from peripheral blood mononuclear cells (PBMCs) obtained by apheresis transduced *ex vivo* with a non-replicating, self-inactivating (SIN) lentiviral vector, encoding a chimeric antigen receptor (CAR) consisting of an anti-CD19 specific scFv, a CD8α stalk, transmembrane domain and anchor, a 41BB endodomain and a CD3 zeta endodomain, under the control of a human PGK1 promoter and a modified Woodchuck post transcriptional response element. The vector genome also contains a 5' terminal CMV enhancer/promoter, a Ψ packaging signal, a Rev response element (RRE) and a central polypurine tract (cPPT).

obécabtagène autoleucel

Cellules T CD4+ et CD8+ autologues transduites *ex vivo* avec un vecteur lentiviral auto-inactivable codant pour un récepteur chimérique contre l'antigène CD19.
Cellules T CD4+ et CD8+ autologues, enrichies de cellules mononuclées de sang périphérique (PBMC) et obtenues par aphérèse, transduites *ex vivo* avec un vecteur lentiviral non réplicatif et auto-inactivable (SIN), codant pour un récepteur chimérique d'antigène (CAR) consistant en un scFv spécifique de CD19, un fragment extracellulaire, un domaine transmembranaire et la partie d'ancrage de CD8α, un endo-domaine de 41BB et un endo-domaine de CD3 zêta, sous le contrôle d'un promoteur PGK1 humain et d'un élément de réponse post-transcriptionnel Woodchuck modifié. Le génome du vecteur contient également un promoteur/amplificateur CMV placé en position terminale 5', un signal d'empaquetage Ψ, un élément de réponse Rev (RRE) et un segment central de polypurine (cPPT).

obecabtagén autoleucel

Células T CD4+ y CD8+ autólogas transducidas ex vivo con un vector lentiviral auto-inactivante que codifica para un receptor de antígenos quimérico anti-CD19.
Células T CD4+ y CD8+ autólogas, enriquecidas a partir de células mononucleares de sangre periférica (PBMCs) obtenidas por aféresis, transducidas *ex vivo* con un vector lentiviral no replicativo, auto-inactivante (SIN), que codifica para un receptor de antígenos quimérico (CAR) que consta de scFv específico anti-CD19, un tallo CD8α, un dominio transmembranal y de anclaje, un endodominio 41BB y un endodominio CD3 zeta, bajo el control de un promotor PGK1 humano y un elemento de respuesta post transcripcional de marmota modificado. El genoma del vector también contiene un potenciador (enhancer)/promotor de CMV en 5', una señal de empaquetamiento Ψ, un elemento de respuesta Rev (RRE) y un tramo central de polipurinas (cPPT).

obrindatamabum #

obrindatamab

immunoglobulin G1 scFv-h-CH2-CH3(_scFv)_h-CH2-CH3, anti-[*Homo sapiens* CD276 (B7H3, B7-H3, B7RP-2)] and anti-[*Homo sapiens* CD3E (CD3 epsilon)], monoclonal antibody, bispecific; IG scFv-h-CH2-CH3 single chain, anti-CD276 and anti-CD3E (1-504) [scFv-V-kappa-VH anti-CD276 and anti-CD3E (1-240) [V-KAPPA anti-CD276 (*Homo sapiens* IGKV1D-13*01 (85.1%) -IGHJ2*02 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1-107) -8-mer triglycyl-seryl-tetraglycyl linker (108-115) -VH anti-CD3E (*Mus musculus* IGHV10-1*02 (89.9%) -(IGHD) -GHJ3*01 (93.3%)/*Homo sapiens* IGHV3-72*01 (87.0%) -(IGHD) -IGHJ6*01 (90.9%)) CDR-IMGT [8.10.16] (141-148.166-175.214-229) (116-240)] -linker-E-coil (241-277) [6-mer diglycyl-cysteinyl-triglycyl linker (241-246) -28-mer tetrakis(glutamyl-valyl-dialanyl-leucyl-glutamyl-lysyl) E-coil motif (247-274) -3-mer triglycyl linker (275-277)] -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1, G1v14 CH2 A1.3, A1.2, G1v32 CH3 W22 (knob) (278-504) [hinge 6-15 (278-287), CH2 L1.3>A (291), L1.2>A (292) (288-397), CH3 E12 (413), M14 (415), T22>W (423) (398-502), CHS (503-504)]]; (243-243')-disulfide with the IG scFv single chain, anti-CD3E and anti-CD276 (1'-274') [scFv V-lambda-VH anti-CD3E and anti-CD276 (1'-240') [V-LAMBDA anti-CD3 (*Mus musculus* IGLV1*01 (81.2%) -IGLJ1*01 (100%)/*Homo sapiens* IGLV7-46*01 (77.9%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (26-34.52-54.91-99) (1'-109') -9-mer tetraglycyl-seryl-tetraglycyl linker (110'-118') -VH anti-CD276 (*Homo sapiens* IGHV3-48*02 (91.8%) -(IGHD) -IGHJ4*01 (85.7%)) CDR-IMGT [8.8.15] (144-151.169-176.215-229) (119'-240')] -6-mer diglycyl-cysteinyl-triglycyl linker (241'-246') -28-mer tetrakis(lysyl-valyl-dialanyl-leucyl-lysyl-glutamyl) K-coil motif (247'-274')];
(283-6'':286-9'')-bisdisulfide with the IG h-CH2-CH3 chain, IGHG1*03 nG1m1, G1v14 CH2 A1.3, A1.2, IGHG1v33 CH3 S22, A24, V86 (hole) (1''-227'') [hinge 6-15 (1''-10''), CH2 L1.3>A (14), L1.2>A (15) (11''-120''), CH3 E12 (136), M14 (138), T22>S (146), L24>A (148), Y86>V (187), H115>R (215) (121''-225''), CHS (226''-227'')], produced in Chinese hamster ovary (CHO) cells, glycoform alfa

obrindatamab

immunoglobuline G1 scFv-h-CH2-CH3(_scFv)_h-CH2-CH3, anti-[*Homo sapiens* CD276 (B7H3, B7-H3, B7RP-2)] et anti-[*Homo sapiens* CD3E (CD3 epsilon)], anticorps monoclonal, bispécifique; IG scFv-h-CH2-CH3 chaîne unique, anti-CD276 et anti-CD3E (1-504) [scFv-V-kappa-VH anti-CD276 et anti-CD3E (1-240) [V-KAPPA anti-CD276 (*Homo sapiens* IGKV1D-13*01 (85.1%) -IGHJ2*02 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1-107) -8-mer triglycyl-séryl-tétraglycyl linker (108-115) -VH anti-CD3E (*Mus musculus* IGHV10-1*02 (89.9%) -(IGHD) -GHJ3*01 (93.3%)/*Homo sapiens* IGHV3-72*01 (87.0%) -(IGHD) -IGHJ6*01 (90.9%)) CDR-IMGT [8.10.16] (141-148.166-175.214-229) (116-240)] -linker-E-coil (241-277) [-6-mer diglycyl-cystéinyl-triglycyl linker (241-246) -28-mer tétrakis(glutamyl-valyl-dialanyl-leucyl-glutamyl-lysyl) E-coil motif (247-274) -3-mer triglycyl linker (275-277)] -*Homo sapiens* IGHG1*03 h-CH2-CH3 nG1m1, G1v14 CH2 A1.3, A1.2, G1v32 CH3 W22 (knob) (278-504) [charnière 6-15 (278-287), CH2 L1.3>A (291), L1.2>A (292) (288-397), CH3 E12 (413), M14 (415), T22>W (423) (398-502), CHS (503-504)]; (243-243')-disulfure avec la chaîne unique IG scFv, anti-CD3E et

	anti-CD276 (1'-274') [scFv V-lambda-VH anti-CD3E et anti-CD276 (1'-240') [V-LAMBDA anti-CD3 (*Mus musculus* IGLV1*01 (81.2%) -IGLJ1*01 (100%)/*Homo sapiens* IGLV7-46*01 (77.9%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (26-34.52-54.91-99) (1'-109') -9-mer tétraglycyl-séryl-tétraglycyl linker (110'-118') -VH anti-CD276 (*Homo sapiens* IGHV3-48*02 (91.8%) -(IGHD) -IGHJ4*01 (85.7%)) CDR-IMGT [8.8.15] (144-151.169-176.215-229) (119'-240') -6-mer diglycyl-cystéinyl-triglycyl linker (241'-246') -28-mer tétrakis(lysyl-valyl-dialanyl-leucyl-lysyl-glutamyl) K-coil motif (247'-274')]; (283-6":286-9")-bisdisulfure avec la chaîne IG h-CH2-CH3, IGHG1*03 nG1m1, G1v14 CH2 A1.3, A1.2, IGHG1v33 CH3 S22, A24, V86 (hole) (1"-227") [charnière 6-15 (1"-10"), CH2 L1.3>A (14), L1.2>A (15) (11"-120"), CH3 E12 (136), M14 (138), T22>S (146), L24>A (148), Y86>V (187), H115>R (215) (121"-225"), CHS (226"-227")], produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa
obrindatamab	inmunoglobulina G1 scFv-h-CH2-CH3(_scFv)_h-CH2-CH3, anti-[*Homo sapiens* CD276 (B7H3, B7-H3, B7RP-2)] y anti-[*Homo sapiens* CD3E (CD3 épsilon)], anticuerpo monoclonal, biespecífico; IG scFv-h-CH2-CH3 cadena única, anti-CD276 y anti-CD3E (1-504) [scFv-V-kappa-VH anti-CD276 y anti-CD3E (1-240) [V-KAPPA anti-CD276 (*Homo sapiens* IGKV1D-13*01 (85.1%) -IGHJ2*02 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1-107) -8-mer triglicil-seril-tetraglicil linker (108-115) -VH anti-CD3E (*Mus musculus* IGHV10-1*02 (89.9%) -(IGHD) -GHJ3*01 (93.3%)/*Homo sapiens* IGHV3-72*01 (87.0%) -(IGHD) -IGHJ6*01 (90.9%)) CDR-IMGT [8.10.16] (141-148.166-175.214-229) (116-240)] -linker-E-coil (241-277) [-6-mer diglicil-cisteinil-triglicil linker (241-246) -28-mer tetrakis(glutamil-valil-dialanil-leucil-glutamil-lisil) E-coli motif (247-274) -3-mer triglicil linker (275-277)] -*Homo sapiens* IGHG1*03 h-CH2-CH3 nG1m1, G1v14 CH2 A1.3, A1.2, G1v32 CH3 W22 (knob) (278-504) [bisagra 6-15 (278-287), CH2 L1.3>A (291), L1.2>A (292) (288-397), CH3 E12 (413), M14 (415), T22>W (423) (398-502), CHS (503-504)]; (243-243')-disulfuro con la cadena única IG scFv, anti-CD3E y anti-CD276 (1'-274') [scFv V-lambda-VH anti-CD3E y anti-CD276 (1'-240') [V-LAMBDA anti-CD3 (*Mus musculus* IGLV1*01 (81.2%) -IGLJ1*01 (100%)/*Homo sapiens* IGLV7-46*01 (77.9%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (26-34.52-54.91-99) (1'-109') -9-mer tetraglicil-seril-tetraglicil linker (110'-118') -VH anti-CD276 (*Homo sapiens* IGHV3-48*02 (91.8%) -(IGHD) -IGHJ4*01 (85.7%)) CDR-IMGT [8.8.15] (144-151.169-176.215-229) (119'-240') -6-mer diglicil-cisteinil-triglicil linker (241'-246') -28-mer tetrakis(lisil-valil-dialanil-leucil-lisil-glutamil) K-coli motif (247'-274')]; (283-6":286-9")-bisdisulfuro con la cadena IG h-CH2-CH3, IGHG1*03 nG1m1, G1v14 CH2 A1.3, A1.2, IGHG1v33 CH3 S22, A24, V86 (hole) (1"-227") [bisagra 6-15 (1"-10"), CH2 L1.3>A (14), L1.2>A (15) (11"-120"), CH3 E12 (136), M14 (138), T22>S (146), L24>A (148), Y86>V (187), H115>R (215) (121"-225"), CHS (226"-227")], producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

1. Chain / Chaîne / Cadena: IG scFv h-CH2-CH3 (V-kappa anti-CD276, VH anti-CD3E)

```
DIQLTQSPSF LSASVGDRVT ITCKASQNVD TNVAWYQQKP GKAPKALIYS  50
ASYRYSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ YNNYPFTFGQ 100
GTKLEIKGGG SGGGGEVQLV ESGGGLVQPG GSLRLSCAAS GFTFSTYAMN 150
WVRQAPGKGL EWVGRIRSKY NNYATYYADS VKDRFTISRD DSKNSLYLQM 200
NSLKTEDTAV YYCVRHGNFG NSYVSWFAYW GQGTLVTVSS GGCGGGEVAA 250
LEKEVAALEK EVAALEKEVA ALEKGGGDKT HTCPPCPAPE AAGGPSVFLF 300
PPKPKDTLMI SRTPEVTCVV VDVSHEDPEV KFNWYVDGVE VHNAKTKPRE 350
EQYNSTYRVV SVLTVLHQDW LNGKEYKCKV SNKALPAPIE KTISKAKGQP 400
REPQVYTLPP SREEMTKNQV SLWCLVKGFY PSDIAVEWES NGQPENNYKT 450
TPPVLDSDGS FFLYSKLTVD KSRWQQGNVF SCSVMHEALH NHYTQKSLSL 500
SPGK                                                    504
```

2. Chain / Chaîne / Cadena: IG scFv (V-lambda anti-CD3E, VH anti-CD276)

```
QAVVTQEPSL TVSPGGTVTL TCRSSTGAVT TSNYANWVQQ KPGQAPRGLI  50
GGTNKRAPWT PARFSGSLLG GKAALTITGA QAEDEADYYC ALWYSNLWVF 100
GGGTKLTVLG GGGSGGGGEV QLVESGGGLV QPGGSLRLSC AASGFTFSSF 150
GMHWVRQAPG KGLEWVAYIS SDSSAIYYAD TVKGRFTISR DNAKNSLYLQ 200
MNSLRDEDTA VYYCGRGREN IYYGSRLDYW GQGTTVTVSS GGCGGGKVAA 250
LKEKVAALKE KVAALKEKVA ALKE                              274
```

3. Chain / Chaîne / Cadena: IG h-CH2-CH3

```
DKTHTCPPCP APEAAGGPSV FLFPPKPKDT LMISRTPEVT CVVVDVSHED  50
PEVKFNWYVD GVEVHNAKTK PREEQYNSTY RVVSVLTVLH QDWLNGKEYK 100
CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSREEMTK NQVSLSCAVK 150
GFYPSDIAVE WESNGQPENN YKTTPPVLDS DGSFFLVSKL TVDKSRWQQG 200
NVFSCSVMHE ALHNRYTQKS LSLSPGK                           227
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-chain 1 (C23-C104) 23-88 137-213 318-378 424-482
Intra-chain 2 (C23-C104) 22'-90' 140'-214'
Intra-chain 3 (C23-C104) 41"-101" 147"-205"
Inter-chains 1 - 2 243-243'
Inter-chains 1 - 3 (h 11 -h 11) 283-6"
(h 14 -h 14) 286-9"

N-terminal glutamine cyclization to pyroglutamate (pE, 5-oxoproline)
V-lambda Q1:
1'

Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.
N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
CH2 N84.4:
354, 77"

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
CHS K2:
504, 227"

ociperlimabum #

ociperlimab — immunoglobulin G1-kappa, anti-[*Homo sapiens* TIGIT (T-cell immunoreceptor with Ig domain and ITIM, V-set Ig member 9, VSIG9, V-set and transmembrane member 3, VSTM3)], humanized monoclonal antibody; gamma1 heavy chain humanized (1-449) [VH (*Homo sapiens* IGHV3-66*01 (88.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -*Homo sapiens* IGHG1*01 nG1m1, G1m17 (CH1 K120 (216) (120-217), hinge 1-15 (218-232), CH2 (233-342), CH3 E12 (358), M14 (360) (343-447), CHS (448-449)) (120-449)], (222-214')-disulfide with kappa light chain humanized (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-15*01 (87.4%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')];
dimer (228-228":231-231")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

ociperlimab — immunoglobuline G1-kappa, anti-[*Homo sapiens* TIGIT (immunorécepteur des lymphocytes T avec domaine Ig et ITIM, membre 9 de l'Ig V-set, VSIG9, membre 3 de l'Ig V-set et région transmembrane, VSTM3)], anticorps monoclonal humanisé;

chaîne lourde gamma1 humanisée (1-449) [VH (*Homo sapiens* IGHV3-66*01 (88.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -*Homo sapiens* IGHG1*01 nG1m1, G1m17 (CH1 K120 (216) (120-217), charnière 1-15 (218-232), CH2 (233-342), CH3 E12 (358), M14 (360) (343-447), CHS (448-449)) (120-449)], (222-214')-disulfure avec la chaîne légère kappa humanisée (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-15*01 (87.4%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')];
dimère (228-228":231-231")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

ociperlimab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* TIGIT (inmunoreceptor de los linfocitos T con dominio Ig y ITIM, miembro 9 de la Ig V-set, VSIG9, miembro 3 de la Ig V-set y región transmembrana, VSTM3)], anticuerpo monoclonal humanizado;
cadena pesada gamma1 humanizada (1-449) [VH (*Homo sapiens* IGHV3-66*01 (88.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -*Homo sapiens* IGHG1*01 nG1m1, G1m17 (CH1 K120 (216) (120-217), bisagra 1-15 (218-232), CH2 (233-342), CH3 E12 (358), M14 (360) (343-447), CHS (448-449)) (120-449)], (222-214')-disulfuro con la cadena ligera kappa humanizada (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-15*01 (87.4%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')];
dímero (228-228":231-231")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGGSLRL SCAASGFTFS DYYMYWVRQA PGKGLEWVAY  50
ITKGGGSTYY PDSVKGRFTI SRDNAKNTLY LQMNSLRAED TAVYYCARQT 100
NYDFTMDYWG 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
YTLPPSREEM TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL 400
DSDGSFFLYS KLTVDKSRWQ QGNVFSCSVM HEALHNHYTQ KSLSLSPGK  449
```

Light chain / Chaîne légère / Cadena ligera

```
EIVMTQSPAT LSVSPGERAT LSCKASQDVG TSVAWYQQKP GQAPRLLIYW  50
ASARHTGIPA RFSGSGSGTE FTLTISSLQS EDFAVYYCQQ YSSYPLTFGG 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Post-translational modifications
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"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

C-terminal lysine clipping:
H CHS K2:
449, 449"

omodenbamabum #

omodenbamab	immunoglobulin G3-kappa, anti-[*Staphylococcus aureus* SpA (Staphylococcal protein A)], *Homo sapiens* monoclonal antibody; gamma3 heavy chain *Homo sapiens* (1-502) [VH (*Homo sapiens* IGHV3-23*04 (90.8%) -(IGHD) -IGHJ5*01 (93.3%)) CDR-IMGT [8.8.18] (26-33.51-58.97-114) (1-125) -*Homo sapiens* IGHG3*01, G3m5* (G3m5,10,11,13,14,26,27) (CH1 (126-223), hinge 1-42 (224-285), CH2 (286-395), CH3 S44 (439), M84 (452), Q98 (474), I101 (477), R115 (490), F116 (491) (396-500), CHS (501-502)) (126-502)], (139-214')-disulfide with kappa light chain *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (90.5%) -IGKJ5*01 (91.7%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dimer (236-236'':239-239'':245-245'':251-251'':254-254'':260-260'':266-266'':269-269'':275-275'':281-281'':284-284'')-undecakisdisulfide, produced in Chinese hamster ovary (CHO)-K1SV cells, glycoform alfa
omodenbamab	immunoglobuline G3-kappa, anti-[*Staphylococcus aureus* SpA (protéine A de Staphylocoque)], anticorps monoclonal *Homo sapiens*; chaîne lourde gamma3 *Homo sapiens* (1-502) [VH (*Homo sapiens* IGHV3-23*04 (90.8%) -(IGHD) -IGHJ5*01 (93.3%)) CDR-IMGT [8.8.18] (26-33.51-58.97-114) (1-125) -*Homo sapiens* IGHG3*01, G3m5* (G3m5,10,11,13,14,26,27) (CH1 (126-223), charnière 1-42 (224-285), CH2 (286-395), CH3 S44 (439), M84 (452), Q98 (474), I101 (477), R115 (490), F116 (491) (396-500), CHS (501-502)) (126-502)], (139-214')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (90.5%) -IGKJ5*01 (91.7%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dimère (236-236'':239-239'':245-245'':251-251'':254-254'':260-260'':266-266'':269-269'':275-275'':281-281'':284-284'')-undecakisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO)-K1SV, glycoforme alfa
omodenbamab	inmunoglobulina G3-kappa, anti-[*Staphylococcus aureus* SpA (proteína A de Estafilococo)], anticuerpo monoclonal *Homo sapiens*; cadena pesada gamma3 *Homo sapiens* (1-502) [VH (*Homo sapiens* IGHV3-23*04 (90.8%) -(IGHD) -IGHJ5*01 (93.3%)) CDR-IMGT [8.8.18] (26-33.51-58.97-114) (1-125) -*Homo sapiens* IGHG3*01, G3m5* (G3m5,10,11,13,14,26,27) (CH1 (126-223), bisagra 1-42 (224-285), CH2 (286-395), CH3 S44 (439), M84 (452), Q98 (474), I101 (477), R115 (490), F116 (491) (396-500), CHS (501-502)) (126-502)], (139-214')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (90.5%) -IGKJ5*01 (91.7%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dímero (236-236'':239-239'':245-245'':251-251'':254-254'':260-260'':266-266'':269-269'':275-275'':281-281'':284-284'')-undecakisdisulfuro, producido en las células ováricas de hámster chino (CHO)-K1SV, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGGSLRL SCAASGFTFS TYGMSWVRQA PGKGLEWVSS  50
ITGSGRSTFY ADSVKGRFTI SRDNSTNTLS LQMNSLRAED TAVYYCARSP 100
ADIVTGYYPW WFDLWGQGTL VTVSSASTKG PSVFPLAPCS RSTSGGTAAL 150
GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL SSVVTVPSSS 200
LGTQTYTCNV NHKPSNTKVD KRVELKTPLG DTTHTCPRCP EPKSCDTPPP 250
CPRCPEPKSC DTPPPCPRCP EPKSCDTPPP CPRCPAPELL GGPSVFLFPP 300
KPKDTLMISR TPEVTCVVVD VSHEDPEVQF KWYVDGVEVH NAKTKPREEQ 350
YNSTFRVVSV LTVLHQDWLN GKEYKCKVSN KALPAPIEKT ISKTKGQPRE 400
PQVYTLPPSR EEMTKNQVSL TCLVKGFYPS DIAVEWESSG QPENNYNTTP 450
PMLDSDGSFF LYSKLTVDKS RWQQGNIFSC SVMHEALHNR FTQKSLSLSP 500
GK                                                      502
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS LSASIGDRVT ITCRASQSIN TYLNWYQQKP GKAPRLLIAG  50
ASSLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ ANSFPLTFGQ 100
GTRLEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 152-208 316-376 422-480
22"-96" 152"-208" 316"-376" 422"-480"
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 (h1 13, h1 16, 236-236" 239-239"
h2 5, h2 11, h2 14 245-245" 251-251" 254-254"
h3 5, h3 11, h3 14, 260-260" 266-266" 269-269"
h4 5, h4 11, h4 14) 275-275" 281-281" 284-284"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
352, 352"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

O-glycosylation sites / Sites de O-glycosylation / Posiciones de O-glicosilación
h2 S7 h3 S7 h4 S7
247, 247" 262, 262" 277, 277"
Sialylated glycans regularly present / glycanes sialylés régulièrement présents / glicanos sialilados regularmente presentes

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
502, 502"

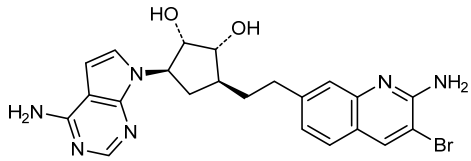
onametostatum

onametostat — (1*S*,2*R*,3*S*,5*R*)-3-[2-(2-amino-3-bromoquinolin-7-yl)ethyl]-5-(4-amino-7*H*-pyrrolo[2,3-*d*]pyrimidin-7-yl)cyclopentane-1,2-diol

onamétostat — (1*S*,2*R*,3*S*,5*R*)-3-[2-(2-amino-3-bromoquinoléin-7-yl)éthyl]-5-(4-amino-7*H*-pyrrolo[2,3-*d*]pyrimidin-7-yl)cyclopentane-1,2-diol

onametostat — (1*S*,2*R*,3*S*,5*R*)-3-[2-(2-amino-3-bromoquinolein-7-il)etil]-5-(4-amino-7*H*-pirrolo[2,3-*d*]pirimidin-7-il)ciclopentano-1,2-diol

$C_{22}H_{23}BrN_6O_2$



ontasameranum #

ontasameran — Messenger RNA encoding transmembrane phosphatase with tensin homology (TPTE).

	Messenger RNA (mRNA), 5'-capped, encoding codon-optimised transmembrane phosphatase with tensin homology (TPTE; cancer/testis antigen 44) expressed as a fusion protein comprising a secretory signal peptide, TPTE, P2P16 tetanus toxoid-derived helper epitopes and a major histocompatibility complex (MHC) class I transmembrane and cytoplasmic domain (MITD), connected by three glycine/serine-rich (GS) linker peptides, flanked by 5' and 3' untranslated regions and a 3' poly(A) tail.
ontasaméran	ARN messager codant pour la phosphatase transmembranaire homologue à la tensine (TPTE). Un ARN messager (ARNm), protégé en 5', codant pour la phosphatase transmembranaire homologue à la tensine (TPTE ; antigène 44 du cancer testiculaire), avec des codons optimisés, exprimé sous la forme d'une protéine de fusion comprenant un peptide signal de sécrétion, TPTE, les épitopes auxiliaires P2P16 dérivés de l'anatoxine tétanique et un domaine transmembranaire et cytoplasmique (MITD) du complexe majeur d'histocompatibilité (CMH) de classe I, reliés par trois peptides de liaison riches en glycine/sérine (GS), flanqués de régions non traduites en 5' et 3' et d'une queue poly(A) en 3'.
ontasamerán	ARN mensajero que codifica para la fosfatasa transmembranal con homología con la tensina (TPTE). ARN mensajero (ARNm), protegido en 5', que codifica para la fosfatasa transmembranal con homología con la tensina (TPTE; antígeno de cáncer/testículo 44), con codones optimizados, expresada como una proteína de fusión que consta de un péptido señal de secreción, TPTE, los epítopos auxiliares P2P16 derivados del toxoide tetánico y un dominio citoplásmico y transmembrana del complejo principal de histocompatibilidad (MHC) de clase I, conectados mediante tres péptidos de enlace ricos en glicina/serina (GS), flanqueado por las regiones 5' y 3' no traducidas y una cola poly(A) en 3'.
oplunofuspum # oplunofusp	*Actinomyces viscosus* L-methionyl sialidase (exo-α-sialidase) catalytic domain fragment (239-631, 2-394 in the current sequence), fused to human amphiregulin heparin binding domain fragment (25-45, 395-415 in the current sequence) anti-(binding to human heparin and cell surface glycosaminoglycans), produced in *Escherichia coli*; L-methionyl (1)-sialidase (exo-α-sialidase, EC:3.2.1.18) (*Actinomyces viscosus*) (239-631)-peptide (containing the sialidase domain) (2-394), fused to human amphiregulin (25-45)-peptide (binding to human heparin and glycosaminoglycans) (395-415), produced in *Escherichia coli*
oplunofusp	L-méthionyl, fragment du domaine catalytique (239-631, 2-394 dans la séquence actuelle) de la sialidase d'*Actinomyces viscosus* (exo-α-sialidase), fusionné à un fragment du domaine liant l'héparine de l'amphiréguline humaine (25-45, 395-415 dans la séquence actuelle) anti-(liant aux glycosaminoglycanes de surface cellulaire et à l'héparine, humains), produit dans *Escherichia coli;*

L-méthionyl (1)-peptide 239-631 de sialidase (exo-α-sialidase, EC:3.2.1.18) (*Actinomyces viscosus*) (contenant le domaine sialidase) (2-394), fusionné au peptide 25-45 de l'amphiréguline humaine (se liant aux glycosaminoglycanes et à l'héparine) (395-415), produit dans *Escherichia coli*

oplunofusp

L-metionil sialidasa(exo-α-sialidasa) *Actinomyces viscosus* fragmento con dominio catalítico (239-631, 2-394 en la secuencia actual), fusionado al fragmento del dominio de unión a la heparina de la anfiregulina humana (25-45, 395-415 en la secuencia actual) anti-(unión a la heparina humana y a los glicosaminoglicanos de superficie celular, humanos), producido in *Escherichia coli*;
L-metionil (1)-péptido 239-631 de sialidasa (exo-α-sialidasa, EC:3.2.1.18) (*Actinomyces viscosus*) (que contiene el dominio de sialidasa) (2-394), fusionado al péptido 25-45 de anfiregulina humana (se une a glicosaminoglicanos y heparina) (395-415), producido en *Escherichia coli*

Sequence / Séquence / Secuencia

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MGDHPQATPA PAPDASTELP ASMSQAQHLA ANTATDNYRI PAITTAPNGD   50
LLISYDERPK DNGNGGSDAP NPNHIVQRRS TDGGKTWSAP TYIHQGTETG  100
KKVGYSDPSY VVDHQTGTIF NFHVKSYDQG WGGSRGGTDP ENRGIIQAEV  150
STSTDNGWTW THRTITADIT KDKPWTARFA ASGQGIQIQH GPHAGRLVQQ  200
YTIRTAGGAV QAVSVYSDDH GKTWQAGTPI GTGMDENKVV ELSDGSLMLN  250
SRASDGSGFR KVAHSTDGGQ TWSEPVSDKN LPDSVDNAQI IRAFPNAAPD  300
DPRAKVLLLS HSPNPRPWSR DRGTISMSCD DGASWTTSKV FHEPFVGYTT  350
IAVQSDGSIG LLSEDAHNGA DYGGIWYRNF TMNWLGEQCG QKPAKRKKKG  400
GKNGKNRRNR KKKNP                                        415
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Post-translational modifications
Disulfide bridge location / Position du pont disulfure / Posición del puente disulfuro
329-389

Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación
none / aucune / ninguna

pacanalotamabum #
pacanalotamab

immunoglobulin scFv-scFv, anti-[*Homo sapiens* TNFRSF17 (TNF receptor superfamily member 17, tumor necrosis factor receptor superfamily, member 17, B cell maturation antigen, BCMA, BCM, TNFRSF13A, CD269)] and anti-[*Homo sapiens* CD3E (CD3 epsilon)], monoclonal antibody single chain, bispecific;
IG scFv-scFv single chain, anti-TNFRSF17 and anti-CD3E (1-504) [scFv-VH-V-kappa anti-TNFRSF17 (1-243) [VH (*Homo sapiens* IGHV1-46*01 (85.7%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -15-mer tris(tetraglycyl-seryl) linker (122-136) -V-KAPPA (*Homo sapiens* IGKV1-33*01 (91.6%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (163-168.186-188.225-233) (137-243)] -6-mer seryl-tetraglycyl-seryl linker (244-249) -scFv-VH-V-lambda anti-CD3E (250-498) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (275-282.300-309.348-363) (250-374) -15-mer tris(tetraglycyl-seryl) linker (375-389) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%) CDR-IMGT [9.3.9 (415-423.441-443.480-488) (390-498)] -hexahistidine (499-504)], non-glycosylated, produced in Chinese hamster ovary (CHO) cells

pacanalotamab

immunoglobuline scFv-scFv, anti-[*Homo sapiens* TNFRSF17 (membre 17 de la superfamille des récepteurs du TNF, membre 17 de la superfamille des récepteurs du facteur de nécrose tumorale, antigène de maturation de cellule B, BCMA, BCM, TNFRSF13A, CD269)] et anti-[*Homo sapiens* CD3E (CD3 epsilon)], anticorps monoclonal à chaîne unique, bispécifique; IG scFv-scFv chaîne unique, anti-TNFRSF17 et anti-CD3E (1-504) [scFv-VH-V-kappa anti-TNFRSF17 (1-243) [VH (*Homo sapiens* IGHV1-46*01 (85.7%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121)-15-mer tris(tétraglycyl-séryl) linker (122-136) -V-KAPPA (*Homo sapiens* IGKV1-33*01 (91.6%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (163-168.186-188.225-233) (137-243)] -6-mer séryl-tétraglycyl-séryl linker (244-249) -scFv-V-lambda anti-CD3E (250-498) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD)-IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (275-282.300-309.348-363) (250-374) -15-mer tris(tétraglycyl-séryl) linker (375-389) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%) CDR-IMGT [9.3.9] (415-423.441-443.480-488) (390-498)] -hexahistidine (499-504)], non-glycosylé, produit dans des cellules ovariennes de hamster chinois (CHO)

pacanalotamab

inmunoglobulina scFv-scFv, anti-[*Homo sapiens* TNFRSF17 (miembro 17 de la superfamilia de los receptores del TNF, miembro 17 de la superfamilia de los receptores del factor de necrosis tumoral, antígeno de maduración de célula B, BCMA, BCM, TNFRSF13A, CD269)] y anti-[*Homo sapiens* CD3E (CD3 épsilon)], anticuerpo monoclonal con cadena única, biespecífico; IG scFv-scFv cadena única, anti-TNFRSF17 y anti-CD3E (1-504) [scFv-VH-V-kappa anti-TNFRSF17 (1-243) [VH (*Homo sapiens* IGHV1-46*01 (85.7%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121)-15-mer tris(tetraglicil-seril) linker (122-136) -V-KAPPA (*Homo sapiens* IGKV1-33*01 (91.6%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (163-168.186-188.225-233) (137-243)] -6-mer seril-tetraglicil-seril linker (244-249) -scFv-V-lambda anti-CD3E (250-498) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD)-IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (275-282.300-309.348-363) (250-374) -15-mer tris(tetraglicil-seril) linker (375-389) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%) CDR-IMGT [9.3.9] (415-423.441-443.480-488) (390-498)] -hexahistidina (499-504)], no glicosilado, producido en las células ováricas de hamster chino (CHO)

Heavy chain / Chaîne lourde / Cadena pesada

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QVQLVQSGAE VKKPGASVKV SCKASGYTFT NHIIHWVRQA PGQGLEWMGY  50
INPYPGYHAY NEKFQGRATM TSDTSTSTVY MELSSLRSED TAVYYCARDG 100
YYRDTDVLDY WGQGTLVTVS SGGGGSGGGG SGGGGSDIQM TQSPSSLSAS 150
VGDRVTITCQ ASQDISNYLN WYQQKPGKAP KLLIYYTSRL HTGVPSRFSG 200
SGSGTDFTFT ISSLEPEDIA TYYCQQGNTL PWTFGQGTKV EIKSGGGGSE 250
VQLVESGGGL VQPGGSLKLS CAASGFTFNK YAMNWVRQAP GKGLEWVARI 300
RSKYNNYATY YADSVKDRFT ISRDDSKNTA YLQMNNLKTE DTAVYYCVRH 350
GNFGNSYISY WAYWGQGTLV TVSSGGGGSG GGGSGGGGSQ TVVTQEPSLT 400
VSPGGTVTLT CGSSTGAVTS GNYPNWVQQK PGQAPRGLIG GTKFLAPGTP 450
ARFSGSLLGG KAALTLSGVQ PEDEAEYYCV LWYSNRWVFG GGTKLTVLHH 500
HHHH                                                    504
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Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-V (C23 C104) 22-96 159-224 271-347 411-479

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
VH Q1: 1

No N-glycosylation sites / pas de sites de N-glycosylation / ningún posición de N-glicosilación
Aglycosylated

pariglasgenum brecaparvovecum #

pariglasgene brecaparvovec	A non-replicating adeno-associated viral vector encoding codon-optimized human glucose-6-phosphatase (G6PC). A recombinant non-replicating adeno-associated viral vector serotype 8 (rAAV8), encoding codon-optimized human glucose-6-phosphatase (G6PC) under the control of the native human G6PC promoter/enhancer and an SV40 polyadenylation sequence, containing a chimeric intron in the 5' UTR between the promoter/enhancer and the transgene, flanked by AAV2 inverted terminal repeats (ITR).
pariglasgène brécaparvovec	Un vecteur adéno-viral non-réplicatif codant pour la glucose-6-phosphatase (G6PC) humaine avec des codons optimisés. Un vecteur recombinant adéno-viral non-réplicatif de sérotype 8 (rAAV8), codant pour la glucose-6-phosphatase (G6PC) humaine avec des codons optimisés, sous le contrôle du promoteur/activateur de la G6PC humaine native et d'une séquence de polyadénylation du SV40, contenant un intron chimérique dans l'UTR 5' entre le promoteur/activateur et le transgène, flanqué de répétitions terminales inversées (ITR) AAV2.
pariglasgén brecaparvovec	Un vector viral adeno-asociado, no replicativo, que codifica para la glucosa-6-fosfatasa (G6PC) humana, con codones optimizados. Un vector viral adeno-asociado recombinante de serotipo 8 (rAAV8) no replicativo, que codifica para la glucosa-6-fosfatasa (G6PC) humana, con codones optimizados, bajo el control del promotor/potenciador (enhancer) nativo de la G6PC humana y una secuencia de poliadenilación del SV40, conteniendo un intron quimérico en la región 5' UTR entre el promotor/potenciador y el transgén, flanqueado por repeticiones invertidas terminales (ITR) del AAV2.

pavurutamabum #

pavurutamab	immunoglobulin scFv-scFv-scFc, anti-[*Homo sapiens* TNFRSF17 (TNF receptor superfamily member 17, tumor necrosis factor receptor superfamily, member 17, B cell maturation antigen, BCMA, BCM, TNFRSF13A, CD269)] and anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], monoclonal antibody single chain (scFv)2-scFc, bispecific; IG single chain scFv-scFv-scFc, anti-TNFRS17 and anti-CD3E (1-986) [scFv-VH-V-kappa anti-TNFRSF17 (1-243) [VH (*Homo sapiens* IGHV1-46*01 G49>C (44) (84.7%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -15-mer tris(tetraglycyl-seryl) linker (122-136)-V-KAPPA (*Homo sapiens* IGKV1-33*01 (91.6%) -IGKJ1*01 Q120>C (236) (91.7%)) CDR-IMGT [6.3.9] (163-168.186-188.225-233) (137-243)] -6 mer seryl-tetraglycyl-seryl linker (244-249) -scFv-VH-V-lambda anti-CD3E (250-498) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (275-282.300-309.348-363) (250-374) -15-mer tris(tetraglycyl-seryl) linker (375-389) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (415-423.441-443.480-488) (390-498)] -4-mer tetraglycyl linker

	(499-502) -scFc (h-CH2-CH3)-(h-CH2-CH3) (503-986) [*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (hinge 6-15 (503-512), CH2 R83>C (574), N84.4>G (579), V85>C (584) (513-622), CH3 E12 (638), M14 (640) (623-727), CHS (728-729)) (503-729) -30-mer hexakis(tetraglycyl-seryl) linker (730-759) -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (hinge 6-15 (760-769), CH2 R83>C (831), N84.4>G (836), V85>C (841) (770-879), CH3 E12 (895), M14 (897) (880-984), CHS (985-986)) (760-986)], non-glycosylated, produced in Chinese hamster ovary (CHO) cells
pavurutamab	immunoglobuline scFv-scFv-scFc, anti-[*Homo sapiens* TNFRSF17 (membre 17 de la superfamille des récepteurs du TNF, membre 17 de la superfamille des récepteurs du facteur de nécrose tumorale, antigène de maturation de cellule B, BCMA, BCM, TNFRSF13A, CD269)] et anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], anticorps monoclonal à chaîne unique (scFv)2-scFc, bispécifique; IG à chaîne unique scFv-scFv-scFc, anti-TNFRSF17 et anti-CD3E (1-986) [scFv-VH-V-kappa anti-TNFRSF17 (1-243) [VH (*Homo sapiens* IGHV1-46*01 G49>C (44) (84.7%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -15-mer tris(tétraglycyl-séryl) linker (122-136)-V-KAPPA (*Homo sapiens* IGKV1-33*01 (91.6%) -IGKJ1*01 Q120>C (236) (91.7%)) CDR-IMGT [6.3.9] (163-168.186-188.225-233) (137-243)] -6-mer séryl-tétraglycyl-séryl linker (244-249) -scFv-VH-V-lambda anti-CD3E (250-498) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (275-282.300-309.348-363) (250-374) -15-mer tris(tétraglycyl-séryl) linker (375-389) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (415-423.441-443.480-488) (390-498)] -4-mer tétraglycyl linker (499-502) -scFc (h-CH2-CH3)-(h-CH2-CH3) (503-986) [*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (503-729) (charnière 6-15 (503-512), CH2 R83>C (574), N84.4>G (579), V85>C (584) (513-622), CH3 E12 (638), M14 (640) (623-727), CHS (728-729)) -30-mer hexakis(tétraglycyl-séryl) linker (730-759) -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (charnière 6-15 (760-769), CH2 R83>C (831), N84.4>G (836), V85>C (841) (770-879), CH3 E12 (895), M14 (897) (880-984), CHS (985-986)) (760-986]], non-glycosylé, produit dans des cellules ovariennes de hamster chinois (CHO)
pavurutamab	inmunoglobulina scFv-scFv-scFc, anti-[*Homo sapiens* TNFRSF17 (miembro 17 de la superfamilia de los receptores del TNF, miembro 17 de la superfamilia de los receptores del factor de necrosis tumoral, antígeno de maduración de célula B, BCMA, BCM, TNFRSF13A, CD269)] y anti-[*Homo sapiens* CD3E (CD3 épsilon, Leu-4)], anticuerpo monoclonal con cadena única (scFv)2-scFc, biespecífico;

IG con cadena única scFv-scFv-scFc, anti-TNFRSF17 y anti-CD3E (1-986) [scFv-VH-V-kappa anti-TNFRSF17 (1-243) [VH (*Homo sapiens* IGHV1-46*01 G49>C (44) (84.7%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -15-mer tris(tetraglicil-seril) linker (122-136)-V-KAPPA (*Homo sapiens* IGKV1-33*01 (91.6%) -IGKJ1*01 Q120>C (236) (91.7%)) CDR-IMGT [6.3.9] (163-168.186-188.225-233) (137-243)] -6-mer seril-tetraglicil-seril linker (244-249) -scFv-VH-V-lambda anti-CD3E (250-498) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (275-282.300-309.348-363) (250-374) -15-mer tris(tetraglicil-seril) linker (375-389) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (415-423.441-443.480-488) (390-498)] -4-mer tetraglicil linker (499-502) -scFc (h-CH2-CH3)-(h-CH2-CH3) (503-986) [*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (503-729) (bisagra 6-15 (503-512), CH2 R83>C (574), N84.4>G (579), V85>C (584) (513-622), CH3 E12 (638), M14 (640) (623-727), CHS (728-729)) -30-mer hexakis(tetraglicil-seril) linker (730-759) -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (bisagra 6-15 (760-769), CH2 R83>C (831), N84.4>G (836), V85>C (841) (770-879), CH3 E12 (895), M14 (897) (880-984), CHS (985-986)) (760-986]], no glicosilado, producido en las células ováricas de hamster chino (CHO)

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGASVKV SCKASGYTFT NHIIHWVRQA PGQCLEWMGY   50
INPYPGYHAY NEKFQGRATM TSDTSTSTVY MELSSLRSED TAVYYCARDG  100
YYRDTDVLDY WGQGTLVTVS SGGGGSGGGG SGGGGSDIQM TQSPSSLSAS  150
VGDRVTITCQ ASQDISNYLN WYQQKPGKAP KLLIYYTSRL HTGVPSRFSG  200
SGSGTDFTFT ISSLEPEDIA TYYCQQGNTL PWTFGCGTKV EIKSGGGGSE  250
VQLVESGGGL VQPGGSLKLS CAASGFTFNK YAMNWVRQAP GKGLEWVARI  300
RSKYNNYATY YADSVKDRFT ISRDDSKNTA YLQMNNLKTE DTAVYYCVRH  350
GNFGNSYISY WAYWGQGTLV TVSSGGGGSG GGGSGGGGSQ TVVTQEPSLT  400
VSPGGTVTLT CGSSTGAVTS GNYPNWVQQK PGQAPRGLIG GTKFLAPGTP  450
ARFSGSLLGG KAALTLSGVQ PEDEAEYYCV LWYSNRWVFG GGTKLTVLGG  500
GGDKTHTCPP CPAPELLGGP SVFLFPPKPK DTLMISRTPE VTCVVVDVSH  550
EDPEVKFNWY VDGVEVHNAK TKPCEEQYGS TYRCVSVLTV LHQDWLNGKE  600
YKCKVSNKAL PAPIEKTISK AKGQPREPQV YTLPPSREEM TKNQVSLTCL  650
VKGFYPSDIA VEWESNGQPE NNYKTTPPVL DSDGSFFLYS KLTVDKSRWQ  700
QGNVFSCSVM HEALHNHYTQ KSLSLSPGKG GGGSGGGGSG GGGSGGGGSG  750
GGGSGGGGSD KTHTCPPCPA PELLGGPSVF LFPPKPKDTL MISRTPEVTC  800
VVVDVSHEDP EVKFNWYVDG VEVHNAKTKP CEEQYGSTYR CVSVLTVLHQ  850
DWLNGKEYKC KVSNKALPAP IEKTISKAKG QPREPQVYTL PPSREEMTKN  900
QVSLTCLVKG FYPSDIAVEW ESNGQPENNY KTTPPVLDSD GSFFLYSKLT  950
VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL SLSPGK               986
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Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-V (C23 C104) 22-96 159-224 271-347 411-479
Intra-C (C23-C104) 543-603 649-707 800-860 906-964
Intra-CH2 (C83-C85) 574-584 831-841
Inter VH-VL (C49-C120) 44-236
Inter h11 (h 11-h 11) 508-765
Inter h14 (h 14-h 14) 511-768

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
VH Q1: 1

No N-glycosylation sites / pas de sites de N-glycosylation / ningún posición de N-glicosilación
H CH2 N84.4>G:
579, 836
Aglycosylated

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
CHS K2:
986

pegtibatinasum #

pegtibatinase

human cystathionine β-synthase fragment (2-413, M[1] cleaved) mutant (C[15]>S), homodimer, produced in *Escherichia coli*, pegylated at *N*[6] of lysine residues with an average of five 5-[α-methylpoly(oxyethylene)-ω-oxy]-5-oxopentanoyl groups per protein monomer;
des-Met[1]-[Cys[15]>Ser] human cystathionine β-synthase (CBS, beta-thionase, serine sulfhydrase, EC:4.2.1.22) (2-413)-peptide, non-covalent dimer, produced in *Escherichia coli*, substituted with approximately five 5-[α-methylpoly(oxyethylene)-ω-oxy]-5-oxopentanoyl groups (20 kDa each) per protein monomer at *N*[6] of lysine residues

pegtibatinase

fragment de la cystathionine β-synthase humaine (2-413, M[1] supprimée) mutant (C[15]>S), homodimère, produit dans *Escherichia coli*, pégylé en *N*[6] des résidus lysine avec une moyenne de cinq groupes 5-[α-méthylpoly(oxyéthylène)-ω-oxy]-5-oxopentanoyle par monomère de protéine;
peptide 2-413 de des-Mét[1]-[Cys[15]>Sér] cystathionine β-synthase humaine (CBS, bêta-thionase, sérine sulfhydrase, EC: 4.2.1.22), dimère non covalent, produit dans *Escherichia coli*, substitué par environ cinq groupes 5-[α-méthylpoly(oxyéthylène)-ω-oxy]-5-oxopentanoyle (~20 kDa chacun) par monomère de protéine au *N*[6] des résidus de lysine

pegtibatinasa

fragmento de la cistationina β-sintasa humana (2-413, M[1] escindido) mutante (C[15]>S), homodímero, producido en *Escherichia coli*, pegilada en *N*[6] residuos de lisina con una medida de cinco grupos 5-[α-metilpoli(oxietileno)-ω-oxi]-5-oxopentanoilo por monómero de proteína;
péptido 2-413 de des-Met[1]-[Cis[15]>Ser] cistationina β-sintasa humana (CBS, beta-tionasa, serina sulfhidrasa, EC: 4.2.1.22), dímero no covalente, producido en *Escherichia coli*, sustituido con aproximadamente cinco grupos 5-[α-metilpoli(oxietilen)-ω-oxi]-5-oxopentanoilo (~20 kDa cada uno) por proteína monomérica en *N*[6] de residuos de lisina

Sequence / Séquence / Secuencia

```
-PSETPQAEV GPTGSPHRSG PHSAKGSLEK GSPEDKEAKE PLWIRPDAPS   50
RCTWQLGRPA SESPHHHTAP AKSPKILPDI LKKIGDTPMV RINKIGKKFG  100
LKCELLAKCE FFNAGGSVKD RISLRMIEDA ERDGTLKPGD TIIEPTSGNT  150
GIGLALAAAV RGYRCIIVMP EKMSSEKVDV LRALGAEIVR TPTNARFDSP  200
ESHVGVAWRL KNEIPNSHIL DQYRNASNPL AHYDTTADEI LQQCDGKLDM  250
LVASVGTGGT ITGIARKLKE KCPGCRIIGV DPEGSILAEP EELNQTEQTT  300
YEVEGIGYDF IPTVLDRTVV DKWFKSNDEE AFTFARMLIA QEGLLCGGSA  350
GSTVAVAVKA AQELQEGQRC VVILPDSVRN YMTKFLSDRW MLQKGFLKEE  400
DLTEKKPWWW HLR                                          415
```

Mutation / Mutation / Mutación

C[15]>S

Post-translational modifications

Removal of Met[1] / Suppression de Met[1] / Eliminación de Met[1]

Disulfide bridges location / Position des ponts disulfure / Posición del puentes disulfuro

272-275, 272'-275' (and further variable potential bridges)

Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación

none / aucune / ninguna

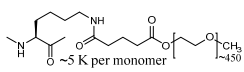
Cofactor binding sites / Sites de liaison des cofacteurs / Sitios de unión de cofactores

N^{6}-pyridoxylidene 5'-phosphate / 5'-phosphate de N^{6}-pyridoxylidène / 5'-fosfato de N^{6}-piridoxilideno K119, K119'

heme B (protoheme IX) / hème b (protohème IX) / hemo B (protohemo IX)

Cys52-S -Fe(II)- N^{1}-His65, Cys52'-S -Fe(II)- N^{1}-His65'

Chemical modification / Modification chimique / Modificación química



pegulicianinum

pegulicianine

N-[6-(1-{2-[3,6-bis(2,3-dihydro-1*H*-indol-1-yl)xanthylium-9-yl]benzene-1-sulfonyl}piperidine-4-carboxamido)hexanoyl]glycylglycyl-L-arginyl-N^6-(6-{2-[(1*E*,3*E*,5*Z*)-5-(1-ethyl-3,3-dimethyl-5-sulfonato-1,3-dihydro-2*H*-indol-2-ylidene)penta-1,3-dien-1-yl]-3,3-dimethyl-5-sulfonato-3*H*-indol-1-ium-1-yl}hexanoyl)-L-lysyl-[2-(2-aminoethoxy)ethoxy]acetyl-*S*-[(3*RS*)-1-{6-[α-methylpoly(oxyethylene)-ω-amino]-6-oxohexyl}-2,5-dioxopyrrolidin-3-yl]-L-cysteinamide

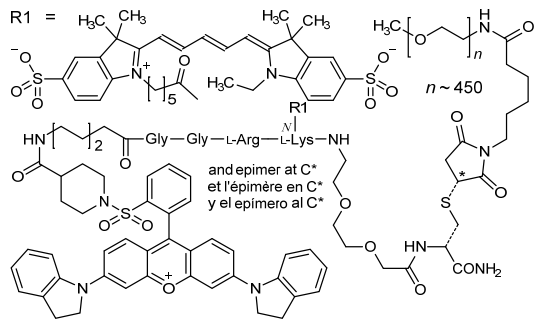
pégulicianine

N-[6-(1-{2-[3,6-bis(2,3-dihydro-1*H*-indol-1-yl)xanthylium-9-yl]benzène-1-sulfonyl}pipéridine-4-carboxamido)hexanoyl]glycylglycyl-L-arginyl-N^6-(6-{2-[(1*E*,3*E*,5*Z*)-5-(1-éthyl-3,3-diméthyl-5-sulfonato-1,3-dihydro-2*H*-indol-2-ylidene)penta-1,3-dién-1-yl]-3,3-diméthyl-5-sulfonato-3*H*-indol-1-ium-1-yl}hexanoyl)-L-lysyl-[2-(2-aminoéthoxy)éthoxy]acétyl-*S*-[(3*RS*)-1-{6-[α-méthylpoly(oxyethylène)-ω-amino]-6-oxohexyl}-2,5-dioxopyrrolidin-3-yl]-L-cystéinamide

pegulicianina

N-[6-(1-{2-[3,6-bis(2,3-dihidro-1*H*-indol-1-il)xantilio-9-il]benceno-1-sulfonil}piperidina-4-carboxamido)hexanoil]glicilglicil-L-arginil-N^6-(6-{2-[(1*E*,3*E*,5*Z*)-5-(1-etil-3,3-dimetil-5-sulfonato-1,3-dihidro-2*H*-indol-2-ilideno)penta-1,3-dien-1-il]-3,3-dimetil-5-sulfonato-3*H*-indol-1-io-1-il}hexanoil)-L-lisil-[2-(2-aminoetoxi)etoxi]acetil-*S*-[(3*RS*)-1-{6-[α-metilpoli(oxietileno)-ω-amino]-6-oxohexil}-2,5-dioxopirrolidin-3-il]-L-cisteinamida

$C_{116}H_{147}N_{19}O_{23}S_4(C_2H_4O)_n$



pelabresibum

pelabresib

2-[(4*S*)-6-(4-chlorophenyl)-1-methyl-4*H*-[1,2]oxazolo[5,4-*d*][2]benzazepin-4-yl]acetamide

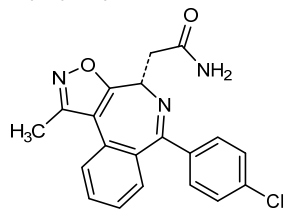
pélabrésib

2-[(4*S*)-6-(4-chlorophényl)-1-méthyl-4*H*-[1,2]oxazolo[5,4-*d*][2]benzazépin-4-yl]acetamide

pelabresib

2-[(4*S*)-6-(4-clorofenil)-1-metil-4*H*-[1,2]oxazolo[5,4-*d*][2]benzazepin-4-il]acetamida

$C_{20}H_{16}ClN_3O_2$



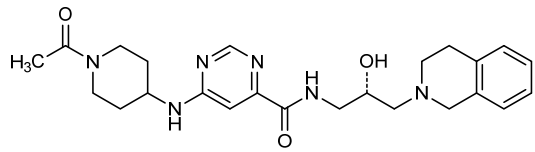
pemrametostatum

pemrametostat — 6-[(1-acetylpiperidin-4-yl)amino]-*N*-[(2*S*)-3-(3,4-dihydroisoquinolin-2(1*H*)-yl)-2-hydroxypropyl]pyrimidine-4-carboxamide

pemramétostat — 6-[(1-acétylpipéridin-4-yl)amino]-*N*-[(2*S*)-3-(3,4-dihydroisoquinoléin-2(1*H*)-yl)-2-hydroxypropyl]pyrimidine-4-carboxamide

pemrametostat — 6-[(1-acetilpiperidin-4-il)amino]-*N*-[(2*S*)-3-(3,4-dihidroisoquinolein-2(1*H*)-il)-2-hidroxipropil]pirimidina-4-carboxamida

$C_{24}H_{32}N_6O_3$



penpulimabum #

penpulimab — immunoglobulin G1-kappa, anti-[*Homo sapiens* PDCD1 (programmed cell death 1, PD-1, PD1, CD279)], monoclonal antibody;
gamma1 heavy chain (1-448) [VH (*Homo sapiens* IGHV3-23*04 (88.7%) -(IGHD) -IGHJ6*01 (90.9%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) - *Homo sapiens* IGHG1*01 G1m17,1, G1v14 CH2 A1.3, A1.2 (CH1 K120 (215) (119-216), hinge 1-15 (217-231), CH2 L1.3>A (235), L1.2>A (236), G1>A (238) (232-341), CH3 D12 (357), L14 (359) (342-446), CHS (447-448)) (119-448)], (221-214')-disulfide with kappa light chain (1'-214') [V-KAPPA (*Mus musculus* IGKV14-111*01 (86.3%) -IGKJ5*01 (100%)/*Homo sapiens* IGKV1-16*01 (80%) -IGKJ2*01 (81.8%) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')];
dimer (227-227'':230-230'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

penpulimab — immunoglobuline G1-kappa, anti-[*Homo sapiens* PDCD1 (protéine 1 de mort cellulaire programmée, PD-1, PD1, CD279)], anticorps monoclonal;

chaîne lourde gamma1 (1-448) [VH (*Homo sapiens* IGHV3-23*04 (88.7%) -(IGHD) -IGHJ6*01 (90.9%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) -*Homo sapiens* IGHG1*01 G1m17,1, G1v14 CH2 A1.3, A1.2 (CH1 K120 (215) (119-216), charnière 1-15 (217-231), CH2 L1.3>A (235), L1.2>A (236), G1>A (238) (232-341), CH3 D12 (357), L14 (359) (342-446), CHS (447-448)) (119-448)], (221-214')-disulfure avec la chaîne légère kappa (1'-214') [V-KAPPA (*Mus musculus* IGKV14-111*01 (86.3%) -IGKJ5*01 (100%)/*Homo sapiens* IGKV1-16*01 (80%) -IGKJ2*01 (81.8%) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')];
dimère (227-227'':230-230'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

penpulimab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* PDCD1 (proteína 1 de muerte celular programada, PD-1, PD1, CD279)], anticuerpo monoclonal;
cadena pesada gamma1 (1-448) [VH (*Homo sapiens* IGHV3-23*04 (88.7%) -(IGHD) -IGHJ6*01 (90.9%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) -*Homo sapiens* IGHG1*01 G1m17,1, G1v14 CH2 A1.3, A1.2 (CH1 K120 (215) (119-216), bisagra 1-15 (217-231), CH2 L1.3>A (235), L1.2>A (236), G1>A (238) (232-341), CH3 D12 (357), L14 (359) (342-446), CHS (447-448)) (119-448)], (221-214')-disulfuro con la cadena ligera kappa (1'-214') [V-KAPPA (*Mus musculus* IGKV14-111*01 (86.3%) -IGKJ5*01 (100%)/*Homo sapiens* IGKV1-16*01 (80%) -IGKJ2*01 (81.8%) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')];
dímero (227-227'':230-230'')-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa



Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGGSLRL SCAASGFAFS SYDMSWVRQA PGKGLDWVAT 050
ISGGGRYTYY PDSVKGRFTI SRDNSKNNLY LQMNSLRAED TALYYCANRY 100
GEAWFAYWGQ GTLVTVSSAS TKGPSVFPLA PSSKSTSGGT AALGCLVKDY 150
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTQTYI 200
CNVNHKPSNT KVDKKVEPKS CDKTHTCPPC PAPEAAGAPS VFLFPPKPKD 250
TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY 350
TLPPSRDELT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD 400
SDGSFFLYSK LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPGK   448
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Light chain / Chaîne légère / Cadena ligera

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DIQMTQSPSS MSASVGDRVT FTCRASQDIN TYLSWFQQKP GKSPKTLIYR 050
ANRLVSGVPS RFSGSGSGQD YTLTISSLQP EDMATYYCLQ YDEFPLTFGA 100
GTKLELKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                       214
```

Post-translational modifications
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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
448, 448"

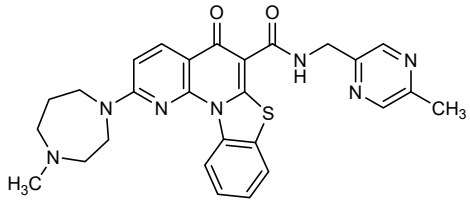
pidnarulexum

pidnarulex — 2-(4-methyl-1,4-diazepan-1-yl)-*N*-[(5-methylpyrazin-2-yl)methyl]-5-oxo-5*H*-[1,3]benzothiazolo[3,2-*a*][1,8]naphthyridine-6-carboxamide

pidnarulex — 2-(4-méthyl-1,4-diazépan-1-yl)-*N*-[(5-méthylpyrazin-2-yl)méthyl]-5-oxo-5*H*-[1,3]benzothiazolo[3,2-*a*][1,8]naphtyridine-6-carboxamide

pidnarulex — 2-(4-metil-1,4-diazepan-1-il)-*N*-[(5-metilpirazin-2-il)metil]-5-oxo-5*H*-[1,3]benzotiazolo[3,2-*a*][1,8]naftiridina-6-carboxamida

$C_{27}H_{27}N_7O_2S$



pimivalimabum #

pimivalimab — immunoglobulin G4-kappa, anti-[*Homo sapiens* PDCD1 (programmed cell death 1, PD-1, PD1, CD279)], *Homo sapiens* monoclonal antibody; gamma4 heavy chain *Homo sapiens* (1-445) [VH (*Homo sapiens* IGHV1-46*01 (96.9%) -(IGHD) - IGHJ5*02 (100%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118)-*Homo sapiens* IGHG4*01 (CH1 (119-216), hinge 1-12 S10>P (226) (217-228), CH2 (229-338), CH3 (339-443), CHS (444-445)) (119-445)], (132-214')-disulfide with kappa light chain *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-5*01 (97.9%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dimer (224-224":227-227")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

pimivalimab — immunoglobuline G4-kappa, anti-[*Homo sapiens* PDCD1 (protéine 1 de mort cellulaire programmée, PD-1, PD1, CD279)], anticorps monoclonal *Homo sapiens*;
chaîne lourde gamma4 *Homo sapiens* (1-445) [VH (*Homo sapiens* IGHV1-46*01 (96.9%) -(IGHD) - IGHJ5*02 (100%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) -*Homo sapiens* IGHG4*01 (CH1 (119-216), charnière 1-12 S10>P (226) (217-228), CH2 (229-338), CH3 (339-443), CHS (444-445)) (119-445)], (132-214')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-5*01 (97.9%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dimère (224-224":227-227")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

pimivalimab

inmunoglobulina G4-kappa, anti-[*Homo sapiens* PDCD1 (proteína 1 de muerte celular programada, PD-1, PD1, CD279)], anticuerpo monoclonal *Homo sapiens*; cadena pesada gamma4 *Homo sapiens* (1-445) [VH (*Homo sapiens* IGHV1-46*01 (96.9%) -(IGHD) -IGHJ5*02 (100%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) -*Homo sapiens* IGHG4*01 (CH1 (119-216), bisagra 1-12 S10>P (226) (217-228), CH2 (229-338), CH3 (339-443), CHS (444-445)) (119-445)], (132-214')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-5*01 (97.9%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dímero (224-224":227-227")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGASVKV SCKASGYTFP SYYMHWVRQA PGQGLEWMGI  50
INPEGGSTAY AQKFQGRVTM TRDTSTSTVY MELSSLRSED TAVYYCARGG 100
TYYDYTYWGQ GTLVTVSSAS TKGPSVFPLA PCSRSTSEST AALGCLVKDY 150
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTKTYT 200
CNVDHKPSNT KVDKRVESKY GPPCPPCPAP EFLGGPSVFL FPPKPKDTLM 250
ISRTPEVTCV VVDVSQEDPE VQFNWYVDGV EVHNAKTKPR EEQFNSTYRV 300
VSVLTVLHQD WLNGKEYKCK VSNKGLPSSI EKTISKAKGQ PREPQVYTLP 350
PSQEEMTKNQ VSLTCLVKGF YPSDIAVEWE SNGQPENNYK TTPPVLDSDG 400
SFFLYSRLTV DKSRWQEGNV FSCSVMHEAL HNHYTQKSLS LSLGK      445
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Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPST LSASVGDRVT ITCRASQSIS SWLAWYQQKP GKAPKLLIYE  50
ASSLESGVPS RFSGSGSGTE FTLTISSLQP DDFATYYCQQ YNSFPPTFGG 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 145-201 259-319 365-423
22"-96" 145"-201" 259"-319" 365"-423"
Intra-L (C23-C104) 23'-88' 134'-194'
23'"-88'" 134'"-194"
Inter-H-L (h 10-CL 126) 132-214' 132"-214'"
Inter-H-H (h 8, h 11) 224-224" 227-227"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"

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.

C-terminal lysine clipping:
H CHS K2:
445, 445"

pirepematum

pirepemat

(3*S*)-3-(2,3-difluorophenyl)-3-methoxypyrrolidine

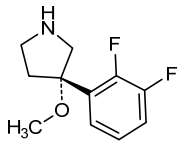
pirépémat

(3*S*)-3-(2,3-difluorophényl)-3-méthoxypyrrolidine

pirepemat

(3*S*)-3-(2,3-difluorofenil)-3-metoxipirrolidina

$C_{11}H_{13}F_2NO$



pomulmeranum #

pomulmeran	Messenger RNA encoding cystic fibrosis transmembrane conductance regulator (CFTR). Messenger RNA (mRNA), 5' capped, encoding codon-optimised human cystic fibrosis transmembrane conductance regulator (CFTR; channel conductance-controlling ATPase, cAMP-dependent chloride channel, ATP-binding cassette sub-family C member 7, ABCC7), flanked by 5' and 3' untranslated regions and a 3' poly(A) tail (200-1000 A).
pomulméran	ARN messager codant pour le régulateur de conductance transmembranaire de la mucoviscidose (CFTR). ARN messager (ARNm), protégé en 5', codant pour le régulateur de conductance transmembranaire de la mucoviscidose humaine avec des codons optimisés (CFTR ; canal ATPase contrôlant la conductance, canal chlorure dépendant de l'AMPc, sous-famille C membre 7, ABCC7), flanqué de régions 5' et 3' non traduites et d'une queue 3' poly(A) (200-1000 A).
pomulmerán	RNA mensajero que codifica para el regulador de la conductancia transmembrana de la fibrosis quística (CFTR). RNA mensajero (RNAm), protegido en 5', que codifica para el regulador de la conductancia transmembrana de la fibrosis quística (CFTR; canal ATPasa controlador de la conductancia, canal de cloro dependiente de AMPc, subfamilia C miembro 7 del casete de unión a ATP, ABCC7) con los codones optimizados, flanqueado por regiones 5' y 3' no traducidas y una cola poly(A) (200-1000 A) en 3'.

posoleucelum

posoleucel	Allogeneic human leukocyte antigen (HLA)-matched virus-specific T cells reactive to cytomegalovirus (CMV), EBV, BK virus, adenovirus and human herpesvirus-6 (HHV-6). The cells are derived from peripheral blood mononuclear cells (PBMCs) from donors seropositive for all five of these viruses. The cells are expanded and co-cultured with 15-mer peptides overlapping by 11 amino acids spanning antigenic proteins from polyomaviruses BK and JC (VP1 and large T), from adenovirus (hexon and penton), from cytomegalovirus (IE1 and pp65), from Epstein-Barr virus (LMP2, EBNA1, BZLF1), and from human herpesvirus-6 (U90, U11 and U14). The cells have specific anti-virus reactivity for each virus above a pre-specified potency threshold, and predominantly express CD3 (generally >95%) with a mixture of CD4+ (average 60%) and CD8+ (average 34%) subsets, including both central (CD45RA-/62L+/CCR7+) and effector (CD45RA-/62L-/CCR7-) memory markers.
posoleucel	Lymphocytes T allogéniques, compatibles pour les antigènes leucocytaires humains (HLA) et spécifiques pour le cytomégalovirus (CMV), l'EBV, le virus BK, l'adénovirus et le virus herpès humain 6 (HHV-6). Les cellules sont dérivées de cellules mononucléaires du sang périphérique (PBMC) provenant de donneurs séropositifs pour ces cinq virus. Les cellules sont amplifiées et cultivées avec des peptides de 15 résidus se chevauchant par 11 acides aminés couvrant les protéines antigéniques du polyomavirus BK et JC (VP1 et grand T), de l'adénovirus (hexon et penton), du cytomégalovirus (IE1 et pp65), du virus d'Epstein-Barr (LMP2, EBNA1, BZLF1), et du virus herpès humain 6 (U90, U11 et U14).

Les cellules ont une réactivité antivirus spécifique pour chacun des virus au-delà d'un seuil prédéfini, et expriment principalement CD3 (généralement >95%) avec un mélange de sous-populations de CD4+ (60% en moyenne) et de CD8+ (34% en moyenne), comprenant des marqueurs des mémoires centrale (CD45RA-/62L+/CCR7+) et effectrice (CD45RA-/62L-/CCR7-).

posoleucel

Células T alogénicas específicas de virus con compatibilidad para el antígeno leucocitario humano (HLA) reactivas frente a citomegalovirus (CMV), EBV, virus BK, adenovirus y herpesvirus humano 6 (HHV-6). Las células se obtienen a partir de células mononucleares de sangre periférica (PBMCs) de donantes seropositivos para estos cinco virus.
Las células tienen una reactividad antivirus específica para cada de estos virus por encima de un umbral de potencia preestablecido, y se expanden y co-cultivan con péptidos de 15 residuos que solapan en 11 amino ácidos cubriendo proteínas antigénicas de poliomavirus BK y JC (VP1 y T grande), de adenovirus (hexón y pentón), de citomegalovirus (IE1 y pp65), de virus de Epstein-Barr (LMP2, EBNA1, BZLF1), y de herpesvirus humano 6 (U90, U11 and U14).
Las células expresan predominantemente CD3 (generalmente >95%) con una mezcla de subtipos CD4+ (60% como media) y CD8+ (34% como media), incluyendo marcadores de memoria central (CD45RA-/62L+/CCR7+) y efectora (CD45RA-/62L-/CCR7-).

radgocitabinum

radgocitabine

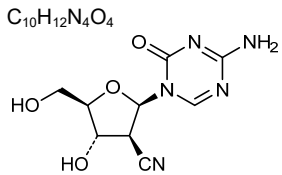
4-amino-1-(2-cyano-2-deoxy-β-D-arabinofuranosyl)pyrimidin-2(1*H*)-one;
2'-cyano-2'-deoxy-D-*arabino*-cytidine

radgocitabine

4-amino-1-(2-cyano-2-désoxy-β-D-arabinofuranosyl)pyrimidin-2(1*H*)-one;
2'-cyano-2'-désoxy-D-*arabino*-cytidine

radgocitabina

4-amino-1-(2-ciano-2-desoxi-β-D-arabinofuranosil)pirimidin-2(1*H*)-ona;
2'-ciano-2'-desoxi-D-*arabino*-citidina



rebonuputemcelum

rebonuputemcel

Allogenic human adult nucleus pulposus cells.
The cells are derived from the central region of intervertebral discs and isolated from the tissue using mechanical and enzymatic (collagenase) procedures. Isolated cells are expanded in culture involving

	adherent and non- adherent conditions until clusters of cells, 100-200 µm in diameter, are generated. Cells comprising the cell substance are dissociated out of these clusters and stored frozen. Cells (on average >95%) express the surface markers CD73, CD90, CD44 and HLA-ABC, and release proteoglycan, collagen and anti-inflammatory cytokines. Cells (on average <3%) lack expression of CD24 (classically associated with native nucleus pulposus cells), CD34, CD45, CD271, Stro-1 or HLA-DR/DP/DQ.
rébonuputemcel	Cellules allogènes du noyau pulpeux humain adulte. Les cellules sont dérivées de la région centrale des disques intervertébraux et isolées du tissu à l'aide de procédures mécaniques et enzymatiques (collagénase). Les cellules isolées sont multipliées en culture dans des conditions adhérentes et non adhérentes jusqu'à ce que des groupes de cellules, de 100 à 200 µm de diamètre, soient générés. Les cellules composant la substance cellulaire sont dissociées de ces amas et conservées congelées. Les cellules (en moyenne> 95%) expriment les marqueurs de surface CD73, CD90, CD44 et HLA-ABC, et libèrent du protéoglycane, du collagène et des cytokines anti-inflammatoires. Les cellules (en moyenne <3%) manquent d'expression de CD24 (classiquement associé aux cellules pulpeuses du noyau natif), CD34, CD45, CD271, Stro-1 ou HLA-DR/DP/DQ.
rebonuputemcel	Células alogénicas del núcleo pulposo adulto humano. Las células son derivadas de la región central de los discos intervertebrales y se aíslan del tejido usando procedimientos mecánicos y enzimáticos (colagenasa). Las células aisladas se expanden en cultivo en condiciones adherentes y no adherentes hasta que se generan grumos de células de 100-200 mm de diámetro. Las células que componen el principio activo se disocian de estos grumos y se almacenan congeladas. >95% de las células expresan los marcadores de superficie CD73, CD90, CD44 y HLA-ABC, y liberan proteoglicano, colágeno y citoquinas anti-inflamatorias. <3% de las células expresan CD24 (asociado clásicamente con células del núcleo pulposo nativo), CD34, CD45, CD271, Stro-1 o HLA-DR/DP/DQ.
recaticimabum # recaticimab	immunoglobulin G1-kappa, anti-[*Homo sapiens* PCSK9 (proprotein convertase subtilisin/kexin type 9, neural apoptosis-regulated convertase 1, NARC1, NARC-1, proprotein convertase 9, PC9)], monoclonal antibody;

	gamma1 heavy chain (1-451) [VH (*Homo sapiens* IGHV1-2*02 (89.8%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -*Homo sapiens* IGHG1*01**,** G1m17,1, G1v21 CH2 Y15.1, T16, E18 (CH1 K120 (218) (122-219), hinge 1-15 (220-234), CH2 M15.1>Y (256), S16>T (258), T18>E (260) (235-344), CH3 D12 (360), L14 (362) (345-449), CHS (450-451)) (122-451)], (224-219')-disulfide with kappa light chain (1'-219') [V-KAPPA (*Mus musculus* IGKV8-21*01 (85%) -IGKJ4*01 (91.7%)/*Homo sapiens* IGKV4-1*01 (76.8%) -IGKJ2*02 (100%)) CDR-IMGT [12.3.8] (27-38.56-58.95-102) (1'-112') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (158), V101 (196) (113-219')]; dimer (230-230":233-233")-bisdisulfide, produced in a Chinese hamster ovary (CHO) cell line (CHOK1SV GS-KO), glycoform alfa
récaticimab	immunoglobuline G1-kappa, anti-[*Homo sapiens* PCSK9 (proprotéine convertase subtilisine/kexine type 9, convertase 1 régulée par l'apoptose neuronale, NARC1, NARC-1, proprotéine convertase 9, PC9)], anticorps monoclonal; chaîne lourde gamma1 (1-451) [VH (*Homo sapiens* IGHV1-2*02 (89.8%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -*Homo sapiens* IGHG1*01**,** G1m17,1, G1v21 CH2 Y15.1, T16, E18 (CH1 K120 (218) (122-219), charnière 1-15 (220-234), CH2 M15.1>Y (256), S16>T (258), T18>E (260) (235-344), CH3 D12 (360), L14 (362) (345-449), CHS (450-451)) (122-451)], (224-219')-disulfure avec la chaîne légère kappa (1'-219') [V-KAPPA (*Mus musculus* IGKV8-21*01 (85%) -IGKJ4*01 (91.7%)/*Homo sapiens* IGKV4-1*01 (76.8%) -IGKJ2*02 (100%)) CDR-IMGT [12.3.8] (27-38.56-58.95-102) (1'-112') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (158), V101 (196) (113-219')]; dimère (230-230":233-233")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHOK1SV GS-KO, glycoforme alfa
recaticimab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* PCSK9 (proproteína convertasa subtilisina/kexina tipo 9, convertasa 1 regulada por la apoptosis neuronal, NARC1, NARC-1, proproteína convertasa 9, PC9)], anticuerpo monoclonal; cadena pesada gamma1 (1-451) [VH (*Homo sapiens* IGHV1-2*02 (89.8%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -*Homo sapiens* IGHG1*01**,** G1m17,1, G1v21 CH2 Y15.1, T16, E18 (CH1 K120 (218) (122-219), bisagra 1-15 (220-234), CH2 M15.1>Y (256), S16>T (258), T18>E (260) (235-344), CH3 D12 (360), L14 (362) (345-449), CHS (450-451)) (122-451)], (224-219')-disulfuro con la cadena ligera kappa (1'-219') [V-KAPPA (*Mus musculus* IGKV8-21*01 (85%) -IGKJ4*01 (91.7%)/*Homo sapiens* IGKV4-1*01 (76.8%) -IGKJ2*02 (100%)) CDR-IMGT [12.3.8] (27-38.56-58.95-102) (1'-112') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (158), V101 (196) (113-219')]; dímero (230-230":233-233")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHOK1SV GS-KO, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

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QVQLVQSGAE VKKPGASVKV SCKASGYTFT DYWMHWVRQA PGQGLEWMGY  50
INPSSGFTKY HQNFKDRVTM TRDTSISTAY MELSRLRSDD TAVYYCARQY 100
DYDEDWYFDV WGQGTTVTVS SASTKGPSVF PLAPSSKSTS GGTAALGCLV 150
KDYFPEPVTV SWNSGALTSG VHTFPAVLQS SGLYSLSSVV TVPSSSLGTQ 200
TYICNVNHKP SNTKVDKKVE PKSCDKTHTC PPCPAPELLG GPSVFLFPPK 250
PKDTLYITRE PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY 300
NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP 350
QVYTLPPSRD ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP 400
VLDSDGSFFL YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG 450
K                                                       451
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Light chain / Chaîne légère / Cadena ligera

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DIVMSQSPSS LSASVGDRVT ITCKSSQSLL NSRTRKNFLA WYQQKPGKSP  50
KLLIYWASTR ESGVPDRFSG SGSGTDFTLT ISSLQPEDFA TYYCKQSFNL 100
FTFGQGTKLE IKRTVAAPSV FIFPPSDEQL KSGTASVVCL LNNFYPREAK 150
VQWKVDNALQ SGNSQESVTE QDSKDSTYSL SSTLTLSKAD YEKHKVYACE 200
VTHQGLSSPV TKSFNRGEC                                    219
```

Post-translational modifications
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'-94' 139'-199'
23'"-94'" 139'"-199'"
Inter-H-L (h 5-CL 126) 224-219' 224"-219'"
Inter-H-H (h 11, h 14) 230-230" 233-233"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"

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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
451, 451"

relmacabtagenum autoleucelum #

relmacabtagene autoleucel

Autologous CD4+ and CD8+ enriched T cells transduced *ex vivo* with a self-inactivating lentivirus vector encoding an anti-CD19 chimeric antigen receptor.
Autologous CD4+ and CD8+ T cells, enriched from peripheral blood mononuclear cells (PBMCs) transduced with a non-replicative self-inactivating (SIN) lentiviral vector encoding a chimeric antigen receptor (CAR) consisting of the human CD19-specific scFv, an IgG4 hinge region, CD28 transmembrane domain, CD137 (4-1BB) co-stimulatory domain and CD3 zeta signalling domain, under the control of a hybrid Elongation Factor 1 alpha (EF1α) and Human T cell Leukemia Virus type 1 (HTLV-1) regulatory element promoter and woodchuck hepatitis virus post-transcriptional regulatory element (WPRE). The vector genome also encodes a truncated human epidermal growth factor receptor (EGFRt) that is co-expressed with the CAR and cleaved from it by the T2A self-cleaving peptide. The vector genome also contains a splice donor, a fragment of *gag*, a Rev response element (RRE), a mutated central polypurine tract (cPPT), and a splice acceptor.

relmacabtagène autoleucel

Cellules T autologues enrichies en CD4+ et CD8+ transduites *ex vivo* avec un vecteur lentiviral auto-inactivant codant pour un récepteur chimérique dirigé contre l'antigène CD19.

Cellules T CD4+ et CD8+ autologues, enrichies de cellules mononucléaires du sang périphérique (PBMC), transduites avec un vecteur lentiviral auto-inactivable et non réplicatif (SIN) codant pour un récepteur chimérique (CAR) constitué du scFv spécifique de l'antigène CD19 humain, d'une région charnière IgG4, d'un domaine transmembranaire CD28, du domaine co-stimulateur de CD137 (4-1BB) et du domaine de signalisation CD3 zeta, sous le contrôle d'un hybride du facteur d'allongement 1 alpha (EF1α) et du promoteur de l'élément régulateur du virus de la leucémie humaine à cellules T de type 1 (HTLV-1), ainsi que de l'élément régulateur post-transcriptionnel du virus de l'hépatite de la marmotte (WPRE). Le génome du vecteur code également pour un récepteur tronqué du facteur de croissance épidermique humain (EGFRt) qui est co-exprimé avec le CAR et en est relâché par le peptide T2A auto-coupant. Le génome du vecteur contient également un donneur d'épissage, un fragment de gag, un élément de réponse Rev (RRE), un segment central polypurine muté (cPPT) et un accepteur d'épissage.

relmacabtagén autoleucel

Células T autólogas enriquecidas en CD4+ y CD8+ transducidas *ex vivo* con un lentivirus auto-inactivante que codifica un receptor de antígenos quiméricos anti-CD19.
Las células T autólogas CD4+ y CD8+, enriquecidas a partir de células mononucleares de sangre periférica (PBMCs), transducidas con un vector lentiviral no replicativo y auto-inactivante (SIN) que codifica para un receptor de antígenos quimérico (CAR) consistente en un scFv específico de CD19 humano, una región bisagra IgG4, un dominio transmembrana CD28, un dominio co-estimulador CD137 (4-1BB) y un domino de señalización CD3 zeta, bajo el control de un promotor híbrido del factor de elongación 1 alfa (EF1α) y el elemento regulador del virus de la leucemia de células T de tipo 1 humano (HTLV-1), y elemento regulador post-transcripcional del virus de la hepatitis de la marmota (WPRE). El genoma del vector también codifica para un receptor del factor de crecimiento epidérmico humano truncado (EGFRt) que se coexpresa con el CAR y luego se escinde de él por el péptido de auto escisión T2A. El genoma del vector también contiene un sitio donante de procesamiento (splicing), un fragmento de *gag*, un elemento de respuesta Rev (RRE), un segmento central de polipurinas (cPPT) y un sitio aceptor de procesamiento (splicing).

resiniferatoxinum

resiniferatoxin

[(2*S*,3a*R*,3b*S*,6a*R*,9a*R*,9b*R*,10*R*,11a*R*)-2-benzyl-6a-hydroxy-8,10-dimethyl-7-oxo-11a-(prop-1-en-2-yl)-3a,3b,6,6a,9a,10,11,11a-octahydro-2*H*,7*H*-2,9b-epoxyazuleno[5,4-*e*][1,3]benzodioxol-5-yl]methyl (4-hydroxy-3-methoxyphenyl)acetate

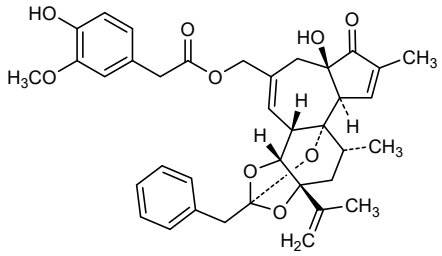
résinifératoxine

(4-hydroxy-3-méthoxyphényl)acétate de [(2*S*,3a*R*,3b*S*,6a*R*,9a*R*,9b*R*,10*R*,11a*R*)-2-benzyl-6a-hydroxy-8,10-diméthyl-7-oxo-11a-(prop-1-én-2-yl)-3a,3b,6,6a,9a,10,11,11a-octahydro-2*H*,7*H*-2,9b-époxyazuléno[5,4-*e*][1,3]benzodioxol-5-yl]méthyle

resiniferatoxina

(4-hidroxi-3-metoxifenil)acetato de [(2*S*,3a*R*,3b*S*,6a*R*,9a*R*,9b*R*,10*R*,11a*R*)-2-bencil-6a-hidroxi-8,10-dimetil-7-oxo-11a-(prop-1-en-2-il)-3a,3b,6,6a,9a,10,11,11a-octahidro-2*H*,7*H*-2,9b-epoxiazuleno[5,4-*e*][1,3]benzodioxol-5-il]metilo

$C_{37}H_{40}O_9$



revakinagenum taroretcelum #

revakinagene taroretcel

Allogeneic human adult retinal pigment epithelial (RPE) cell line stably transfected with a plasmid encoding human ciliary neurotrophic factor (CNTF).
An allogeneic human adult retinal pigment epithelial (RPE) cell line stably transfected with a plasmid encoding human ciliary neurotrophic factor (CNTF) fused in frame to the murine immunoglobulin mu-factor VDJ4C1 signal peptide, under the control of a mouse metallothionein promoter and a human growth hormone polyadenylation signal. The plasmid also contains three eukaryotic expression cassettes for the selectable markers neomycin resistance, mouse DHFR (dihydrofolate reductase) and HSV-TK (thymidine kinase), plus the bacterial components of the pUC18 backbone, including the ampicillin resistance gene (AmpR), origin of replication (ORI) and LacZ gene (alpha fragment of β-galactosidase).

révakinagène taroretcel

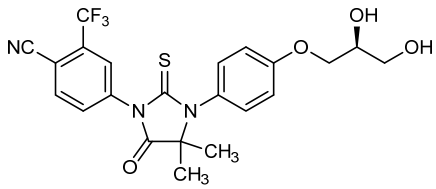
Lignée cellulaire épithéliale allogénique du pigment rétinien humain adulte (EPR) transfectée de façon stable avec un plasmide codant pour le facteur neurotrophique ciliaire humain (CNTF).
Une lignée cellulaire épithéliale allogénique du pigment rétinien humain adulte (RPE) transfectée de manière stable avec un plasmide codant pour le facteur neurotrophique ciliaire humain (CNTF) fusionné dans le cadre de lecture du peptide signal VDJ4C1 du facteur mu d'immunoglobuline murine, sous le contrôle d'un promoteur de la métallothionéine de souris et d'un signal de polyadénylation de l'hormone de croissance humaine. Le plasmide contient également des cassettes d'expression eucaryotes pour trois marqueurs de sélection, à savoir la résistance à la néomycine, la DHFR (réductase du dihydrofolate) et la HSV-TK (kinase de la thymidine) de souris, ainsi que les composants bactériens du plasmide pUC18, dont le gène de résistance à l'ampicilline (AmpR), l'origine de réplication (ORI) et le gène du LacZ (fragment alpha de la β-galactosidase).

revakinagén taroretcel	Línea celular epitelial alogénica de pigmento retiniano adulto (RPE) humano transfectada de forma estable con un plásmido que codifica para el factor neurotrófico ciliar (CNTF) humano. Una línea celular epitelial alogénica de pigmento retiniano adulto (RPE) humano transfectada de forma estable con un plásmido que codifica para el factor neurotrófico ciliar (CNTF) humano fusionado en marco de lectura al péptido señal VDJ4AC1 del factor mu de la inmunoglobulina murina, bajo el control de un promotor de la metalotionina de ratón y una señal de poliadenilación de la hormona de crecimiento humana. El plásmido contiene también tres casetes de expresión eucariotas para los marcadores de selección de resistencia a neomicina, DHFR (dihidrofolato reductasa) de ratón y HSV-TK (timidin quinasa), más los componentes bacterianos del esqueleto de pUC18, incluyendo el gen de resistencia a ampicilina (AmpR), el origin de replicación (ORI) y el gen LacZ (fragmento alfa de la β-galactosidasa).

rezvilutamidum

rezvilutamide	4-(3-{4-[(2*S*)-2,3-dihydroxypropoxy]phenyl}-4,4-dimethyl-5-oxo-2-sulfanylideneimidazolidin-1-yl)-2-(trifluoromethyl)benzonitrile
rezvilutamide	4-(3-{4-[(2*S*)-2,3-dihydroxypropoxy]phényl}-4,4-diméthyl-5-oxo-2-sulfanylidèneimidazolidin-1-yl)-2-(trifluorométhyl)benzonitrile
rezvilutamida	4-(3-{4-[(2*S*)-2,3-dihidroxipropoxi]fenil}-4,4-dimetil-5-oxo-2-sulfanilidenoimidazolidin-1-il)-2-(trifluorometil)benzonitrilo

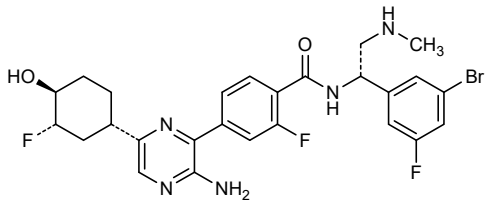
$C_{22}H_{20}F_3N_3O_4S$



rineterkibum

rineterkib	4-{3-amino-6-[(1*S*,3*S*,4*S*)-3-fluoro-4-hydroxycyclohexyl]pyrazin-2-yl}-*N*-[(1*S*)-1-(3-bromo-5-fluorophenyl)-2-(methylamino)ethyl]-2-fluorobenzamide
rinéterkib	4-{3-amino-6-[(1*S*,3*S*,4*S*)-3-fluoro-4-hydroxycyclohexyl]pyrazin-2-yl}-*N*-[(1*S*)-1-(3-bromo-5-fluorophényl)-2-(méthylamino)éthyl]-2-fluorobenzamide
rineterkib	4-{3-amino-6-[(1*S*,3*S*,4*S*)-3-fluoro-4-hidroxiciclohexil]pirazin-2-il}-*N*-[(1*S*)-1-(3-bromo-5-fluorofenil)-2-(metilamino)etil]-2-fluorobenzamida

$C_{26}H_{27}BrF_3N_5O_2$



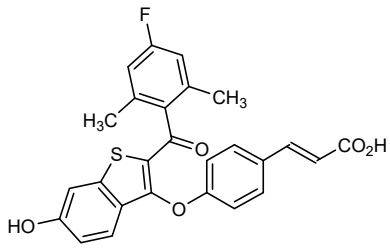
rintodestrantum

rintodestrant — (2*E*)-3-(4-{[2-(4-fluoro-2,6-dimethylbenzoyl)-6-hydroxy-1-benzothiophen-3-yl]oxy}phenyl)prop-2-enoic acid

rintodestrant — acide (2*E*)-3-(4-{[2-(4-fluoro-2,6-diméthylbenzoyl)-6-hydroxy-1-benzothiophén-3-yl]oxy}phényl)prop-2-énoïque

rintodestrant — ácido (2*E*)-3-(4-{[2-(4-fluoro-2,6-dimetilbenzoil)-6-hidroxi-1-benzotiofen-3-il]oxi}fenil)prop-2-enoico

$C_{26}H_{19}FO_5S$



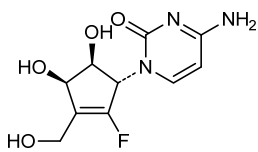
roducitabinum

roducitabine — 4-amino-1-[(1*S*,4*R*,5*S*)-2-fluoro-4,5-dihydroxy-3-(hydroxymethyl)cyclopent-2-en-1-yl]pyrimidin-2(1*H*)-one;
4'a-fluoro-4',4'a-didehydro-4'-*O*-carbacytidine

roducitabine — 4-amino-1-[(1*S*,4*R*,5*S*)-2-fluoro-4,5-dihydroxy-3-(hydroxyméthyl)cyclopent-2-én-1-yl]pyrimidin-2(1*H*)-one;
4'a-fluoro-4',4'a-didéhydro-4'-*O*-carbacytidine

roducitabina — 4-amino-1-[(1*S*,4*R*,5*S*)-2-fluoro-4,5-dihidroxi-3-(hidroximetil)ciclopent-2-en-1-il]pirimidin-2(1*H*)-ona;
4'a-fluoro-4',4'a-didehidro-4'-*O*-carbacitidina

$C_{10}H_{12}FN_3O_4$



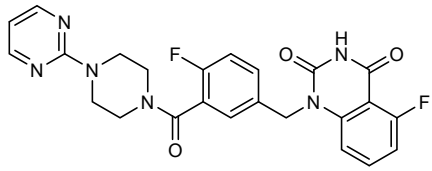
senaparibum

senaparib — 5-fluoro-1-({4-fluoro-3-[4-(pyrimidin-2-yl)piperazine-1-carbonyl]phenyl}methyl)quinazoline-2,4(1*H*,3*H*)-dione

sénaparib — 5-fluoro-1-({4-fluoro-3-[4-(pyrimidin-2-yl)pipérazine-1-carbonyl]phényl}méthyl)quinazoline-2,4(1*H*,3*H*)-dione

senaparib — 5-fluoro-1-({4-fluoro-3-[4-(pirimidin-2-il)piperazina-1-carbonil]fenil}metil)quinazolina-2,4(1*H*,3*H*)-diona

$C_{24}H_{20}F_2N_6O_3$



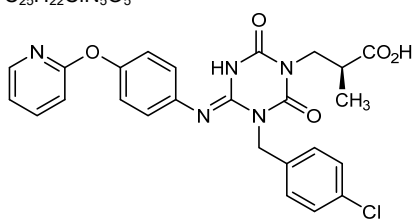
sivopixantum

sivopixant — (2*S*)-3-[(4*E*)-3-[(4-chlorophenyl)methyl]-2,6-dioxo-4-({4-[(pyridin-2-yl)oxy]phenyl}imino)-1,3,5-triazinan-1-yl]-2-methylpropanoic acid

sivopixant — acide (2*S*)-3-[(4*E*)-3-[(4-chlorophényl)méthyl]-2,6-dioxo-4-({4-[(pyridin-2-yl)oxy]phényl}imino)-1,3,5-triazinan-1-yl]-2-méthylpropanoïque

sivopixant — ácido (2*S*)-3-[(4*E*)-3-[(4-clorofenil)metil]-2,6-dioxo-4-({4-[(piridin-2-il)oxi]fenil}imino)-1,3,5-triazinan-1-il)-2-metilpropanoico

$C_{25}H_{22}ClN_5O_5$



sizavaleucelum

sizavaleucel — Allogeneic, HLA-matched CD3+ T-cells, derived from G-CSF mobilized peripheral blood stem cells (PBSC) collected by apheresis. Cells are transplant organ donor-derived, non-cultured and cryopreserved with CD34+ hematopoietic stem cells (HSC) *(firzotemcel (121)(83))* obtained from the same HLA-matched donor. Intended for delivery to a single HLA-matched recipient.

sizavaleucel	Des cellules T CD3+ allogéniques, exprimant des antigènes HLA compatibles, dérivées de cellules souches du sang périphérique (PBSC) mobilisées par le G-CSF et collectées par aphérèse. Les cellules sont dérivées de donneurs d'organes de transplantation, ne sont pas cultivées et sont cryoconservées avec des cellules souches hématopoïétiques (HSC) CD34+ *(firzotemcel (121)(83))* qui proviennent du même donneur compatible pour les antigènes HLA. Destinées à être données à un seul receveur compatible pour les antigènes HLA.
sizavaleucel	Células T CD3+ alogénicas, con HLA compatible, derivadas de células madre de sangre periférica (PBSC) movilizadas con G-CSF y recogidas por aféresis. Las células proceden de donantes de órganos para trasplante, no se cultivan y se criopreservan con células madre hematopoyéticas (HSC) CD34+ *(firzotemcel (121)(83))* obtenidas del mismo donante HLA compatible. Destinadas para administrarse a un sólo receptor HLA compatible.

sotigalimabum #

sotigalimab	immunoglobulin G1-kappa, anti-[*Homo sapiens* CD40 (tumor necrosis factor receptor superfamily member 5, TNFRSF5)], humanized monoclonal antibody; gamma1 heavy chain humanized (1-450) [VH (*Homo sapiens* IGHV3-30*01 (79.8%) -(IGHD) -IGHJ1*01 (90.9%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 G1m17,1 (CH1 K120 (217) (121-218), hinge 1-15 (219-233), CH2 S29>E (270) (234-343), CH3 D12 (359), L14 (361) (344-448), CHS (449-450)) (121-450)], (223-215')-disulfide with kappa light chain humanized (1'-215') [V-KAPPA (*Homo sapiens* IGKV1-27*01 (91%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.13] (27-32.50-52.89-101) (1'-108') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (154), V101 (192) (109'-215')]; dimer (229-229":232-232")-bisdisulfide, produced in Chinese hamster ovary (CHO)-derived cell line, glycoform alfa
sotigalimab	immunoglobuline G1-kappa, anti-[*Homo sapiens* CD40 (membre 5 de la superfamille des récepteurs du TNF, TNFRSF5)], anticorps monoclonal humanisé; chaîne lourde gamma1 humanisée (1-450) [VH (*Homo sapiens* IGHV3-30*01 (79.8%) -(IGHD) -IGHJ1*01 (90.9%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 G1m17,1 (CH1 K120 (217) (121-218), charnière 1-15 (219-233), CH2 S29>E (270) (234-343), CH3 D12 (359), L14 (361) (344-448), CHS (449-450)) (121-450)], (223-215')-disulfure avec la chaîne légère kappa humanisée (1'-215') [V-KAPPA (*Homo sapiens* IGKV1-27*01 (91%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.13] (27-32.50-52.89-101) (1'-108') (1'-108') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (154), V101 (192) (109'-215')]; dimère (229-229":232-232")-bisdisulfure, produite dans une lignée cellulaire dérivée des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

sotigalimab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* CD40 (miembro 5 de la superfamilia de los receptores del TNF, TNFRSF5)], anticuerpo monoclonal humanizado; cadena pesada gamma1 humanizada (1-450) [VH (*Homo sapiens* IGHV3-30*01 (79.8%) -(IGHD) - IGHJ1*01 (90.9%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 G1m17,1 (CH1 K120 (217) (121-218), bisagra 1-15 (219-233), CH2 S29>E (270) (234-343), CH3 D12 (359), L14 (361) (344-448), CHS (449-450)) (121-450)], (223-215')-disulfuro con la cadena ligera kappa humanizada (1'-215') [V-KAPPA (*Homo sapiens* IGKV1-27*01 (91%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.13] (27-32.50-52.89-101) (1'-108') (1'-108') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (154), V101 (192) (109'-215')];
dímero (229-229":232-232")-bisdisulfuro, producido en una línea celular derivada de las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVESGGG VVQPGRSLRL SCAASGFSFS STYVCWVRQA PGKGLEWIAC  50
IYTGDGTNYS ASWAKGRFTI SKDSSKNTVY LQMNSLRAED TAVYFCARPD 100
ITYGFAINFW GPGTLVTVSS ASTKGPSVFP LAPSSKSTSG GTAALGCLVK 150
DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT 200
YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG PSVFLFPPKP 250
KDTLMISRTP EVTCVVVDVE 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

```
DIQMTQSPSS LSASVGDRVT IKCQASQSIS SRLAWYQQKP GKPPKLLIYR  50
ASTLASGVPS RFSGSGSGTD FTLTISSLQP EDVATYYCQC TGYGISWPIG 100
GGTKVEIKRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK 150
VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ 200
GLSSPVTKSF NRGEC                                       215
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 35-50 147-203 264-324 370-428
22"-96" 35"-50" 147"-203" 264"-324" 370"-428"
Intra-L (C23-C104) 23'-88' 135'-195'
23'"-88'" 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-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H VH N65:
58, 58"
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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
450, 450"

sotorasibum

sotorasib

(1*M*)-6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-[4-methyl-2-(propan-2-yl)pyridin-3-yl]-4-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]pyrido[2,3-*d*]pyrimidin-2(1*H*)-one

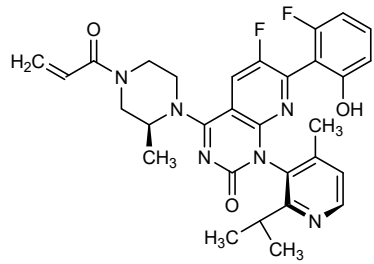
sotorasib

(1*M*)-6-fluoro-7-(2-fluoro-6-hydroxyphényl)-1-[4-méthyl-2-(propan-2-yl)pyridin-3-yl]-4-[(2*S*)-2-méthyl-4-(prop-2-énoyl)pipérazin-1-yl]pyrido[2,3-*d*]pyrimidin-2(1*H*)-one

sotorasib

(1*M*)-6-fluoro-7-(2-fluoro-6-hidroxifenil)-1-[4-metil-2-(propan-2-il)piridin-3-il]-4-[(2*S*)-2-metil-4-(prop-2-enoil)piperazin-1-il]pirido[2,3-*d*]pirimidin-2(1*H*)-ona

$C_{30}H_{30}F_2N_6O_3$



sulanemadlinum

sulanemadlin

C$^{2.11}$,*C*$^{2.4}$-[(4*E*)-undec-4-ene-1,11-diyl](*N*-acetyl-L-leucyl-L-threonyl-L-phenylalanyl-L-alanyl-L-α-glutamyl-L-tyrosyl-L-tryptophyl-L-alanyl-L-glutaminyl-L-leucyl-D-alanyl-L-alanyl-L-alanyl-L-alanyl-L-alanyl-L-alanyl-D-alaninamide)

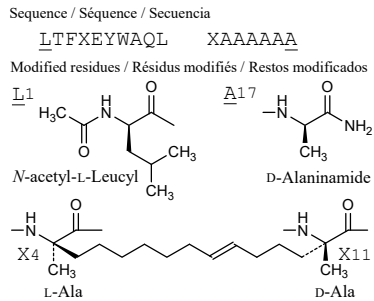
sulanémadline

C$^{2.11}$,*C*$^{2.4}$-[(4*E*)-undéc-4-ène-1,11-diyl](*N*-acétyl-L-leucyl-L-thréonyl-L-phénylalanyl-L-alanyl-L-α-glutamyl-L-tyrosyl-L-tryptophyl-L-alanyl-L-glutaminyl-L-leucyl-D-alanyl-L-alanyl-L-alanyl-L-alanyl-L-alanyl-L-alanyl-D-alaninamide)

sulanemadlina

C$^{2.11}$,*C*$^{2.4}$-[(4*E*)-undec-4-eno-1,11-diil](*N*-acetil-L-leucil-L-treonil-L-fenilalanil-L-alanil-L-α-glutamil-L-tirosil-L-triptofil-L-alanil-L-glutaminil-L-leucil-D-alanil-L-alanil-L-alanil-L-alanil-L-alanil-L-alanil-D-alaninamida)

$C_{95}H_{140}N_{20}O_{23}$



suntinorextonum

suntinorexton

N-[(2*S*,3*S*)-2-[(2,3'-difluoro[1,1'-biphenyl]-3-yl)methyl]-1-(2-hydroxy-2-methylpropanoyl)pyrrolidin-3-yl]ethanesulfonamide

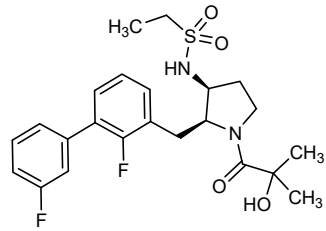
suntinorexton

N-[(2*S*,3*S*)-2-[(2,3'-difluoro[1,1'-biphényl]-3-yl)méthyl]-1-(2-hydroxy-2-méthylpropanoyl)pyrrolidin-3-yl]éthanesulfonamide

suntinorextón

N-[(2*S*,3*S*)-2-[(2,3'-difluoro[1,1'-bifenil]-3-il)metil]-1-(2-hidroxi-2-metilpropanoil)pirrolidin-3-il]etanosulfonamida

$C_{23}H_{28}F_2N_2O_4S$



suratadenoturevum #

suratadenoturev

A replication-competent adenovirus type 5 in which the E1A and E1B genes are under the control of a human telomerase reverse transcriptase (hTERT) and IRES, respectively.
A recombinant replication-competent adenovirus type 5 (Ad-5) in which the E1 gene, including its normal transcriptional regulatory element, has been deleted and replaced by an expression cassette containing an hTERT (human telomerase reverse transcriptase) promoter, the Ad E1A gene, an IRES (internal ribosome entry site) and the Ad E1B gene. E1A expression is controlled by the hTERT promoter; E1B translation is effected by the IRES.

suratadénoturev

Un adénovirus de type 5 réplicatif dans lequel les gènes E1A et E1B sont, respectivement, sous le contrôle de la transcriptase inverse de la télomérase humaine (hTERT) et d'IRES.
Un adénovirus recombinant réplicatif de type 5 (Ad-5) dans lequel le gène E1, y compris son élément normal de régulation de la transcription, a été supprimé et remplacé par une cassette d'expression contenant un promoteur hTERT (transcriptase inverse de la télomérase humaine), le gène Ad E1A, un IRES (site d'entrée interne du ribosome) et le gène Ad E1B. L'expression de E1A est contrôlée par le promoteur hTERT; la traduction de E1B est effectuée par l'IRES.

suratadenoturev

Un adenovirus tipo 5 competente de replicación en el que los genes E1A y E1B están bajo el control de la telomerasa transcriptasa inversa humana (hTERT) e IRES, respectivamente.
Un adenovirus tipo 5 (Ad-5) recombinante competente de replicación en el que el gen E1, incluyendo su elemento de regulación transcripcional normal, ha sido delecionado y reemplazado por un casete de expresión que contiene un promotor de hTERT (telomerasa transcriptasa inversa humana), el gen Ad E1A, un IRES (sitio interno de entrada al ribosoma) y el gen Ad E1B. La expresión de E1A esta controlada por el promotor hTERT; La traducción de E1B se efectúa por el IRES.

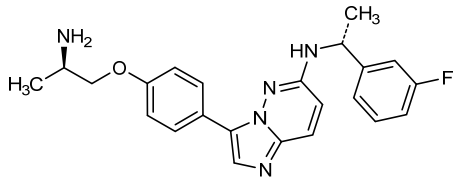
taletrectinibum

taletrectinib — 3-{4-[(2*R*)-2-aminopropoxy]phenyl}-*N*-[(1*R*)-1-(3-fluorophenyl)ethyl]imidazo[1,2-*b*]pyridazin-6-amine

talétrectinib — 3-{4-[(2*R*)-2-aminopropoxy]phényl}-*N*-[(1*R*)-1-(3-fluorophényl)éthyl]imidazo[1,2-*b*]pyridazin-6-amine

taletrectinib — 3-{4-[(2*R*)-2-aminopropoxi]fenil}-*N*-[(1*R*)-1-(3-fluorofenil)etil]imidazo[1,2-*b*]piridazin-6-amina

$C_{23}H_{24}FN_5O$



taniraleucelum

taniraleucel — Allogeneic natural killer (NK) cells derived from CD34+ umbilical cord blood (UCB) hematopoietic stem/progenitor cells.
The cells are expanded and differentiated in the presence of cytokines including thrombopoietin, SCF, Flt3 ligand, IL-7, IL-15 and IL-2 (average population doublings 15) to generate the NK cell population.
Cells (on average >95% of the cells) are CD56+/CD3- and have detectable levels of CD94, NKG2D and CD16.
The cells secrete IFN-γ, perforin and granzyme B, and have cytolytic activity against human tumour cell lines.

taniraleucel — Cellules tueuses naturelles (NK) allogéniques dérivées de cellules souches/progénitrices hématopoïétiques CD34+ du sang de cordon ombilical (UCB).
Les cellules sont amplifiées et différenciées en présence de cytokines, notamment la thrombopoïétine, le SCF, le ligand de Flt3, l'IL-7, l'IL-15 et l'IL-2 (la population double en moyenne 15 fois) pour générer la population de cellules NK.
Les cellules (en moyenne >95% des cellules) sont CD56+/CD3- et ont des niveaux détectables de CD94, NKG2D et CD16. Les cellules sécrètent l'IFN-γ, la perforine et la granzyme B, et ont une activité cytolytique contre les lignées de cellules tumorales humaines.

taniraleucel — Células natural killer (NK) alogénicas derivadas de células madre/progenitoras hematopoyéticas de sangre de cordón umbilical (UCB).
Las células se expanden y diferencian en presencia de citoquinas incluyendo trombopoyetina, SCF, ligando de Flt3, IL-7, IL-15 e IL-2 (la media de duplicaciones de la población es 15 veces) hasta generar la población de células NK. Las células (como media >95% de las células) son CD56+/CD3- y tienen niveles detectables de CD94, NKG2D y CD16. Las células secretan IFN-γ, perforina y granzima B, y tienen actividad citolítica frente a líneas celulares tumorales humanas.

tarlatamabum #

tarlatamab	immunoglobulin scFv-scFv-scFc, anti-[*Homo sapiens* DLL3 (delta-like ligand 3)] and anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], monoclonal antibody single chain (scFv)2-scFc, bispecific; IG single chain scFv-scFv-scFc, anti-DLL3 and anti-CD3E (1-982) [scFv-VH-V-kappa anti-DLL3 (1-241) [VH (*Homo sapiens* IGHV4-59*01 G49>C (44) (96.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.7.12] (26-33.51-57.96-107) (1-118) -15-mer-tris(tetraglycyl-seryl) linker (119-133)-V-KAPPA (*Homo sapiens* IGKV3-20*01 (91.7%) -IGKJ2*01 Q120>C (234) (90.9%)) CDR-IMGT [7.3.9] (160-166.184-186.223-231) (134-241)] -6-mer-seryl-tetraglycyl-seryl linker (242-247) -scFv-VH-V-lambda anti-CD3E (248-496) [VH (*Mus musculus*IGHV10-1*02 (91.9%) -(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87.0%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (273-280.298-307.346-361) (248-372)-15-mer-tris(tetraglycyl-seryl) linker (373-387) – V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (413-421.439-441.478-486) (388-496)] -4-mer-tetraglycyl linker (497-500) - scFc (h-CH2-CH3)-(h-CH2-CH3) (501-982) [*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (hinge 6-15 (501-510), CH2 R83>C (572), N84.4>G (577), V85>C (582) (511-620), CH3 E12 (636), M14 (638) (621-725), CHS>del) (501-725) -30-mer-hexakis(tetraglycyl-seryl) linker (726-755) -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (hinge 6-15 (756-765), CH2 R83>C (827), N84.4>G (832), V85>C (837) (766-875), CH3 E12 (891), M14 (893) (876-980), CHS (981-982)) (756-982)]], non-glycosylated, produced in Chinese hamster ovary (CHO) cells
tarlatamab	immunoglobuline scFv-scFv-scFc, anti-[*Homo sapiens* DLL3 (delta-like ligand 3)] et anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], anticorps monoclonal à chaîne unique (scFv)2-scFc, bispécifique; IG à chaîne unique scFv-scFv-scFc, anti-DLL3 et anti-CD3E (1-982) [scFv-VH-V-kappa anti-DLL3 (1-241) [VH (*Homo sapiens* IGHV4-59*01 G49>C (44) (96.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.7.12] (26-33.51-57.96-107) (1-118) -15-mer-tris(tétraglycyl-séryl) linker (119-133)-V-KAPPA (*Homo sapiens* IGKV3-20*01 (91.7%) -IGKJ2*01 Q120>C (234) (90.9%)) CDR-IMGT [7.3.9] (160-166.184-186.223-231) (134-241)] -6-mer-séryl-tétraglycyl-séryl linker (242-247) -scFv-VH-V-lambda anti-CD3E (248-496) [VH (*Mus musculus*IGHV10-1*02 (91.9%) -(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (273-280.298-307.346-361) (248-372) -15-mer-tris(tétraglycyl-séryl) linker (373-387) – V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (413-421.439-441.478-486) (388-496)] -4-mer-tétraglycyl linker (497-500) - scFc (h-CH2-CH3)-(h-CH2-CH3) (501-982) [*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (charnière 6-15 (501-510), CH2 R83>C (572), N84.4>G (577), V85>C (582) (511-620), CH3 E12 (636), M14 (638) (621-725), CHS>del) (501-725) -30-mer-hexakis(tétraglycyl-séryl) linker (726-755) -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (charnière 6-15 (756-765), CH2 R83>C (827), N84.4>G (832), V85>C (837) (766-875), CH3 E12 (891), M14 (893) (876-980), CHS (981-982)) (756-982)]], non-glycosylé, produit dans des cellules ovariennes de hamster chinois (CHO)

tarlatamab

inmunoglobulina scFv-scFv-scFc, anti-[*Homo sapiens* DLL3 (delta-like ligando 3)] y anti-[*Homo sapiens* CD3E (CD3 épsilon, Leu-4)], anticuerpo monoclonal con cadena única (scFv)2-scFc, biespecífica;
IG con cadena única scFv-scFv-scFc, anti-DLL3 y anti-CD3E (1-982) [scFv-VH-V-kappa anti-DLL3 (1-241) [VH (*Homo sapiens* IGHV4-59*01 G49>C (44) (96.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.7.12] (26-33.51-57.96-107) (1-118) -15-mer-tris(tetraglicil-seril) linker (119-133)-V-KAPPA (*Homo sapiens* IGKV3-20*01 (91.7%) -IGKJ2*01 Q120>C (234) (90.9%)) CDR-IMGT [7.3.9] (160-166.184-186.223-231) (134-241)] -6-mer-seril-tetraglicil-seril linker (242-247) - scFv-VH-V-lambda anti-CD3E (248-496) [VH (*Mus musculus* IGHV10-1*02 (91.9%) -(IGHD) -IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-73*01 (87%) -(IGHD) -IGHJ5*01 (100%)) CDR-IMGT [8.10.16] (273-280.298-307.346-361) (248-372) -15-mer-tris(tetraglicil-seril) linker (373-387) -V-LAMBDA (*Homo sapiens* IGLV7-43*01 (85.1%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.9] (413-421.439-441.478-486) (388-496)] -4-mer-tetraglicil linker (497-500) - scFc (h-CH2-CH3)-(h-CH2-CH3) (501-982) [*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (bisagra 6-15 (501-510), CH2 R83>C (572), N84.4>G (577), V85>C (582) (511-620), CH3 E12 (636), M14 (638) (621-725), CHS>del) (501-725) - 30-mer-hexakis(tetraglicil-seril) linker (726-755) -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (bisagra 6-15 (756-765), CH2 R83>C (827), N84.4>G (832), V85>C (837) (766-875), CH3 E12 (891), M14 (893) (876-980), CHS (981-982)) (756-982)]], no glicosilado, producido en las células ováricas de hámster chino (CHO)

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLQESGPG LVKPSETLSL TCTVSGGSIS SYYWSWIRQP PGKCLEWIGY  50
VYYSGTTNYN PSLKSRVTIS VDTSKNQFSL KLSSVTAADT AVYYCASIAV 100
TGFYFDYWGQ GTLVTVSSGG GGSGGGGSGG GGSEIVLTQS PGTLSLSPGE 150
RVTLSCRASQ RVNNNYLAWY QQRPGQAPRL LIYGASSRAT GIPDRFSGSG 200
SGTDFTLTIS RLEPEDFAVY YCQQYDRSPL TFGCGTKLEI KSGGGGSEVQ 250
LVESGGGLVQ PGGSLKLSCA ASGFTFNKYA MNWVRQAPGK GLEWVARIRS 300
KYNNYATYYA DSVKDRFTIS RDDSKNTAYL QMNNLKTEDT AVYYCVRHGN 350
FGNSYISYWA YWGQGTLVTV SSGGGGSGGG GSGGGGSQTV VTQEPSLTVS 400
PGGTVTLTCG SSTGAVTSGN YPNWVQQKPG QAPRGLIGGT KFLAPGTPAR 450
FSGSLLGGKA ALTLSGVQPE DEAEYYCVLW YSNRWVFGGG TKLTVLGGGG 500
DKTHTCPPCP APELLGGPSV FLFPPKPKDT LMISRTPEVT CVVVDVSHED 550
PEVKFNWYVD GVEVHNAKTK PCEEQYGSTY RCVSVLTVLH QDWLNGKEYK 600
CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSREEMTK NQVSLTCLVK 650
GFYPSDIAVE WESNGQPENN YKTTPPVLDS DGSFFLYSKL TVDKSRWQQG 700
NVFSCSVMHE ALHNHYTQKS LSLSPGGGGS GGGGSGGGGS GGGGSGGGGS 750
GGGGSDKTHT CPPCPAPELL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD 800
VSHEDPEVKF NWYVDGVEVH NAKTKPCEEQ YGSTYRCVSV LTVLHQDWLN 850
GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR EEMTKNQVSL 900
TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDSDGSFF LYSKLTVDKS 950
RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GK                    982
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-V (C23 C104) 22-95 156-222 269-345 409-477
Intra-C (C23-C104) 541-601 647-705 796-856 902-960
Intra-CH2 (C83-C85) 572-582 827-837
Inter-VH-VL (C49-C120) 44-234
Inter-h11 (h 11 - h 11) 506-761
Inter-h14 (h 14 - h 14) 509-764

No N-glycosylation sites / pas de sites de N-glycosylation / ningún posición de N-glicosilación
CH2 N84.4>G:
577, 832
Aglycosylated

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
CHS K2:
982

telpegfilgrastimum #

telpegfilgrastim — human granulocyte colony-stimulating factor (G-CSF, pluripoietin) short isoform, variant (A^1>M), produced in *Escherichia coli*, pegylated with one *N*-{[α-methylpoly(oxyethylene)-ω-oxy]acetyl}-*N*-[α-methylpoly(oxyethylene)-ω-yl]glycyl group at N^2 of M^1 (85-95%) or at N^6 of K^{17} (3-13%) or at N^6 of K^{24}, K^{35} and K^{41} (total not more than 5%);
[1-L-methionine]human granulocyte colony-stimulating factor (G-CSF, pluripoietin) short isoform, produced in *Escherichia coli,* substituted with one *N*-{[α-methylpoly(oxyeth-ylene)-ω-oxy]acetyl}-*N*-[α-methylpoly(oxyethylene)-ω-yl]glycyl group at N^2 of Met^1 (85-95%) or at N^6 of Lys^{17} (3-13 %) or one other lysine residue (total not more than 5%)

telpegfilgrastim — isoforme courte du facteur de stimulation des colonies de granulocytes humain (G-CSF, pluripoiétine), variant (A^1>M), produite dans *Escherichia coli,* pégylé avec un groupe *N*-{[α-méthylpoly(oxyéthylène)-ω-oxy]acétyl}-*N*-[α-méthylpoly(oxyéthylène)-ω-yl]glycyle en N^2 de M^1 (85-95%) ou en
N^6 de K^{17} (3-13%) ou en N^6 de K^{24}, K^{35} et K^{41} (pas plus de 5% au total);
[1-L-méthionine]isoforme courte du facteur de stimulation des colonies de granulocytes humain (G-CSF, pluripoiétine), produite dans *Escherichia coli,* substituée par un groupe *N*-{[α-méthylpoly(oxyéthylène-ω-oxy]acétyl}-*N*-[α-méthylpoly(oxyéthylène)-ω-yl]glycyle en N^2 du $Mét^1$ (85-95 %) ou en N^6 du Lys^{17} (3-13 %) ou d'un autre résidu de lysine (pas plus de 5 % au total)

telpegfilgrastim — factor humano de estimulación de colonias de granulocitos (G-CSF, pluripoyetina) isoforma corta, variante (A^1>M), producido en *Escherichia coli*, pegilado con un grupo *N*-{[α-metilpoli(oxietileno)-ω-oxi]acetil}-*N*-[α-metilpoli(oxietileno)-ω-il]glicilo en N^2 de M^1 (85-95%) o en N^6 de K^{17} (3-13%) o en N^6 de K^{24}, K^{35} y K^{41} (total no más del 5%);
[1-L-metionina]isoforma corta del factor humano de estimulación de colonias de granulocitos (G-CSF, pluripoyetina), producida en *Escherichia coli*, sustituido con un grupo *N*-{[α-metilpoli(oxietileno)-ω-oxi]acetil}-*N*-[α-metilpoli(oxietileno)-ω-il]glicilo en N^2 de la Met^1 (85-95 %) o en N^6 de la Lis^{17} (3-13 %) o un otro residuo de lisina (total no más del 5 %)

$C_{853}H_{1352}N_{224}O_{247}S_9[(C_2H_4O)_{2n}]$ (n ≈ 400-500)

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
```

Mutation / Mutation / Mutación

A^1>**M**

Post-translational modifications

Disulfide bridge location / Position du pont disulfure / Posición del puente disulfuro

37-43, 65-75

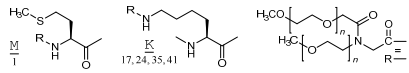
Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación

none / aucune / ninguna

Chemical modification sites / Sites de modification chimique / Posiciones de modificación química

major / principal / mayormente : **M**1, **K**17;

minor / secondaire / inferior : **K**24, **K**35, **K**41



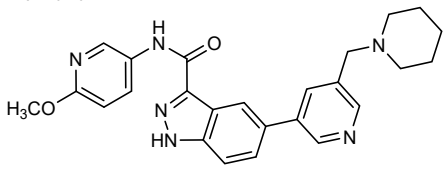
tenvumestrocelum

tenvumestrocel	Allogeneic human mesenchymal stromal cells derived from umbilical cord blood (hUCB-MSCs). The cells are isolated by density-gradient centrifugation and expanded by sub-culturing of the adherent cell population. Cells (on average > 95%) express mesenchymal stromal cell related antigens (CD105 and CD73). The cells are also positive for the CD29 antigen (integrin beta-1), the CD44 antigen (cell adhesion glycoprotein), the CD13 and CD90 antigens, and the HLA-ABC histocompatibility antigen. Cells do not express (on average < 1%) hematopoietic antigens (CD45, CD34 and CD14), histocompatibility antigen (HLA-DR), endothelial cell antigen (CD31), osteoclast antigen (CD51/61), and CD64.
tenvumestrocel	Cellules stromales mésenchymateuses humaines allogéniques dérivées du sang de cordon ombilical (hUCB-MSCs). Les cellules sont isolées par centrifugation à gradient de densité et amplifiées par sous-culture de la population des cellules adhérentes. Les cellules (en moyenne > 95%) expriment des antigènes liés aux cellules stromales mésenchymateuses (CD105 et CD73). Les cellules sont également positives pour l'antigène CD29 (intégrine beta-1), l'antigène CD44 (glycoprotéine d'adhésion cellulaire), les antigènes CD13 et CD90, et l'antigène d'histocompatibilité HLA-ABC. Les cellules n'expriment pas (en moyenne < 1%) les antigènes hématopoïétiques (CD45, CD34 et CD14), l'antigène d'histocompatibilité (HLA-DR), l'antigène des cellules endothéliales (CD31), l'antigène des ostéoclastes (CD51/61), ni l'antigène CD64.
tenvumestrocel	Células estromales mesenquimales humanas alogénicas derivadas de sangre de cordón umbilical (hUCB-MSCs). Las células se aíslan por centrifugación en un gradiente de densidad y se expanden mediante subcultivo de las poblaciones adherentes. Las células (de media >95%) expresan los antígenos relacionados con las células estromales mesenquimales (CD105 y CD73). Las células son también positivas para los antígenos CD29 (integrina beta-1), CD44 (receptor de matriz extracelular), CD13 y CD90, y para el antígeno de histocompatibilidad HLA-ABC. Las células no expresan (de media <1%) antígenos hematopoyéticos (CD45, CD34 y CD14), antígeno de histocomaptiblidad (HLA-DR), antígeno de células endoteliales (CD31), antígeno de osteoclastos (CD51/61), ni CD64.

teplinovivintum

teplinovivint	*N*-(6-methoxypyridin-3-yl)-5-{5-[(piperidin-1-yl)methyl]pyridin-3-yl}-1*H*-indazole-3-carboxamide
téplinovivint	*N*-(6-méthoxypyridin-3-yl)-5-{5-[(pipéridin-1-yl)méthyl]pyridin-3-yl}-1*H*-indazole-3-carboxamide
teplinovivint	*N*-(6-metoxipiridin-3-il)-5-{5-[(piperidin-1-il)metil]piridin-3-il}-1*H*-indazol-3-carboxamida

$C_{25}H_{26}N_6O_2$



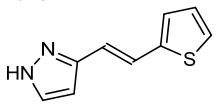
terevalefimum

terevalefim — 3-[(1*E*)-2-(thiophen-2-yl)ethen-1-yl]-1*H*-pyrazole

térévaléfim — 3-[(1*E*)-2-(thiophén-2-yl)éthén-1-yl]-1*H*-pyrazole

terevalefim — 3-[(1*E*)-2-(tiofen-2-il)eten-1-il]-1*H*-pirazol

$C_9H_8N_2S$



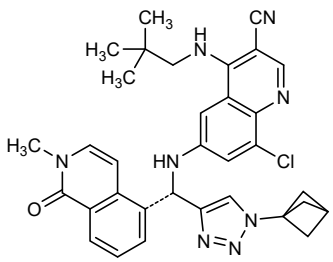
tilpisertibum

tilpisertib — 6-{[(*S*)-[1-(bicyclo[1.1.1]pentan-1-yl)-1*H*-1,2,3-triazol-4-yl](2-methyl-1-oxo-1,2-dihydroisoquinolin-5-yl)methyl]amino}-8-chloro-4-[(2,2-dimethylpropyl)amino]quinoline-3-carbonitrile

tilpisertib — 6-{[(*S*)-[1-(bicyclo[1.1.1]pentan-1-yl)-1*H*-1,2,3-triazol-4-yl](2-méthyl-1-oxo-1,2-dihydroisoquinoléin-5-yl)méthyl]amino}-8-chloro-4-[(2,2-diméthylpropyl)amino]quinoléine-3-carbonitrile

tilpisertib — 6-{[(*S*)-[1-(biciclo[1.1.1]pentan-1-il)-1*H*-1,2,3-triazol-4-il](2-metil-1-oxo-1,2-dihidroisoquinolein-5-il)metil]amino}-8-cloro-4-[(2,2-dimetilpropil)amino]quinoleína-3-carbonitrilo

$C_{33}H_{33}ClN_8O$



tusamitamabum #

tusamitamab — immunoglobulin G1-kappa, anti-[*Homo sapiens* CEACAM5 (carcinoembryonic antigen-related cell adhesion molecule 5, CEA, CD66e)], monoclonal antibody;

	gamma1 heavy chain (1-449) [VH (*Mus musculus* IGHV5-12-1*01 (86.6%) -(IGHD) -IGHJ3*01 (92.9%)/*Homo sapiens* IGHV3-23*01 (77.3%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (217) (121-218), hinge 1-15 (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS K>del (449) (121-449)], (223-214')-disulfide with kappa light chain (1'-214') [V-KAPPA (*Mus musculus* IGKV12-44*01 (87.4%) -IGKJ4*01 (100%)/*Homo sapiens* IGKV1-39*01 (82.1%) -IGKJ2*02 (90.9%)) CDR-IMGT [6.3.9](27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dimer (229-229'':232-232'')-bisdisulfide, produced in Chinese hamster ovary (CHO)-derived cell line, glycoform alfa
tusamitamab	immunoglobuline G1-kappa, anti-[*Homo sapiens* CEACAM5 (molécule d'adhésion cellulaire 5 apparentée à l'antigène carcinoembryonaire, CEA, CD66e)], anticorps monoclonal; chaîne lourde gamma1 (1-449) [VH (*Mus musculus* IGHV5-12-1*01 (86.6%) -(IGHD) -IGHJ3*01 (92.9%)/*Homo sapiens* IGHV3-23*01 (77.3%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (217) (121-218), charnière 1-15 (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS K>del (449) (121-449)], (223-214')-disulfure avec la chaîne légère kappa (1'-214') [V-KAPPA (*Mus musculus* IGKV12-44*01 (87.4%) -IGKJ4*01 (100%)/*Homo sapiens* IGKV1-39*01 (82.1%) -IGKJ2*02 (90.9%)) CDR-IMGT [6.3.9](27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dimère (229-229'':232-232'')-bisdisulfure, produite dans une lignée cellulaire dérivée des cellules ovariennes de hamster chinois (CHO), glycoforme alfa
tusamitamab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* CEACAM5 (molécula de adhesión celular 5 relacionada con el antígeno carcinoembrionario, CEA, CD66e)], anticuerpo monoclonal; cadena pesada gamma1 (1-449) [VH (*Mus musculus* IGHV5-12-1*01 (86.6%) -(IGHD) -IGHJ3*01 (92.9%)/*Homo sapiens* IGHV3-23*01 (77.3%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (217) (121-218), bisagra1-15 (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS K>del (449) (121-449)], (223-214')-disulfuro con la cadena ligera kappa (1'-214') [V-KAPPA (*Mus musculus* IGKV12-44*01 (87.4%) -IGKJ4*01 (100%)/*Homo sapiens* IGKV1-39*01 (82.1%) -IGKJ2*02 (90.9%)) CDR-IMGT [6.3.9](27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dímero (229-229'':232-232'')-bisdisulfuro, producido en una línea celular derivada de las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLQESGPG LVKPGGSLSL SCAASGFVFS SYDMSWVRQT PERGLEWVAY  50
ISSGGGITYA PSTVKGRFTV SRDNAKNTLY LQMNSLTSED TAVYYCAAHY 100
FGSSGPFAYW 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 QKSLSLSPG  449
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Light chain / Chaîne légère / Cadena ligera

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DIQMTQSPAS LSASVGDRVT ITCRASENIF SYLAWYQQKP GKSPKLLVYN  50
TRTLAEGVPS RFSGSGSGTD FSLTISSLQP EDFATYYCQH HYGTPPTFGS 100
GTKLEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                         214
```

Post-translational modifications
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.

tusamitamabum ravtansinum

tusamitamab ravtansine — immunoglobulin G1-kappa, anti-[*Homo sapiens* CEACAM5 (carcinoembryonic antigen-related cell adhesion molecule 5, CEA, CD66e)], monoclonal antibody, conjugated to maytansinoid DM4; gamma1 heavy chain (1-449) [VH (*Mus musculus* IGHV5-12-1*01 (86.6%) -(IGHD) -IGHJ3*01 (92.9%)/*Homo sapiens* IGHV3-23*01 (77.3%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 (100%), G1m17,1 (CH1 K120 (217) (121-218), hinge 1-15 (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS K>del (449) (121-449)], (223-214')-disulfide with kappa light chain (1'-214') [V-KAPPA (*Mus musculus* IGKV12-44*01 (87.4%) -IGKJ4*01 (100%)/*Homo sapiens* IGKV1-39*01 (82.1%) -IGKJ2*02 (90.9%)) CDR-IMGT [6.3.9](27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')];
dimer (229-229":232-232")-bisdisulfide, produced in a Chinese hamster ovary (CHO) cell line derived from CHO-K1SV, glycoform alfa; conjugated, on an average of 3 to 4 lysyl, to maytansinoid DM4 [*N2*'- deacetyl-*N2*'-(4-mercapto-4-methyl-1-oxopentyl)- maytansine] via the reducible SPDB linker [*N*-succinimidyl 4-(2-pyridyldithio)butanoate]
For the *ravtansine* part, please refer to the document "*INN for pharmaceutical substances: Names for radicals, groups and others*"*

tusamitamab ravtansine — immunoglobuline G1-kappa, anti-[*Homo sapiens* CEACAM5 (molécule d'adhésion cellulaire 5 apparentée à l'antigène carcinoembryonaire, CEA, CD66e)], anticorps monoclonal, conjugué au maytansinoïde DM4;
chaîne lourde gamma1 (1-449) [VH (*Mus musculus* IGHV5-12-1*01 (86.6%) -(IGHD) -IGHJ3*01 (92.9%)/*Homo sapiens* IGHV3-23*01 (77.3%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 (100%), G1m17,1 (CH1 K120 (217) (121-218), charnière 1-15 (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS K>del (449) (121-449)], (223-214')-disulfure avec la chaîne légère kappa (1'-214') [V-KAPPA (*Mus musculus* IGKV12-44*01 (87.4%) -IGKJ4*01 (100%)/*Homo sapiens* IGKV1-39*01 (82.1%) -IGKJ2*02 (90.9%)) CDR-IMGT [6.3.9](27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')];

tusamitamab ravtansina

inmunoglobulina G1-kappa, anti-[*Homo sapiens* CEACAM5 (molécula de adhesión celular 5 con el antígeno carcinoembrionario, CEA, CD66e)], anticuerpo monoclonal, conjugado con maitansinoide DM4;
cadena pesada gamma1 (1-449) [VH (*Mus musculus* IGHV5-12-1*01 (86.6%) -(IGHD) -IGHJ3*01 (92.9%)/*Homo sapiens* IGHV3-23*01 (77.3%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 (100%), G1m17,1 (CH1 K120 (217) (121-218), bisagra 1-15 (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS K>del (449) (121-449)], (223-214')-disulfuro con la cadena ligera kappa (1'-214') [V-KAPPA (*Mus musculus* IGKV12-44*01 (87.4%) -IGKJ4*01 (100%)/*Homo sapiens* IGKV1-39*01 (82.1%) -IGKJ2*02 (90.9%)) CDR-IMGT [6.3.9](27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')];
dímero (229-229'':232-232'')-bisdisulfuro, producido en las células ováricas de hámsters chinos (CHO) línea celular derivada de CHO-K1SV, forma glicosilada alfa; conjugado, en 3 a 4 residuos lisil por término medio, con maitansinoide DM4 [*N*2'-deacetil-*N*2'-(4-mercapto-4-metil-1-oxopentil)- maitansina]mediante un conector SPDB reducible [4-(2- piridilditio)butanoato de *N*-succinimidilo]
Para la fracción ravtansina, se ruega referirse al documento "*INN for pharmaceutical substances: Names for radicals, groups and others*"*

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLQESGPG LVKPGGSLSL SCAASGFVFS SYDMSWVRQT PERGLEWVAY  50
ISSGGGITYA PSTVKGRFTV SRDNAKNTLY LQMNSLTSED TAVYYCAAHY 100
FGSSGPFAYW 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 QKSLSLSPG  449
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Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPAS LSASVGDRVT ITCRASENIF SYLAWYQQKP GKSPKLLVYN  50
TRTLAEGVPS RFSGSGSGTD FSLTISSLQP EDFATYYCQH HYGTPFTFGS 100
GTKLEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Post-translational modifications
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, h14) 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.

For the ravtansine part, please refer to the document "INN for pharmaceutical substances: Names for radicals, groups and others"*
Pour la partie ravtansine, veuillez-vous référer au document "INN for pharmaceutical substances: Names for radicals, groups and others"*
Para la fracción ravtansina, se ruega referirse al documento "INN for pharmaceutical substances: Names for radicals, groups and others"*

upifitamabum rilsodotinum

upifitamab rilsodotin

immunoglobulin G1-kappa, anti-[*Homo sapiens* SLC34A2 (solute carrier family 34 sodium phosphate member 2, sodium/phosphate cotransporter 2B, NaPi2b, NaPi3b, NAPI-3B)], monoclonal antibody, conjugated, via a thioether bond, to3 to 5 flexible polymers PHF-BA-EG2-MI-AF-HPA-Ala, each comprising maleimide (MI) bioconjugation linkers and
3 to 4 auristatin F- hydroxypropylamide-L-alanine (AF-HPA-Ala), with a drug ratio of 12:1 to 15:1;

	gamma1 heavy chain (1-449) [VH (*Homo sapiens* IGHV1-46*01 (81.6%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -glycinyl (120) -*Homo sapiens* IGHG1*03 (100%), G1m3, nG1m1 (CH1 R120 (217) (121-218), hinge 1-15 (219-233), CH2 (234-343), CH3 E12 (359), M14 (361) (344-448), CHS K>del (449)) (121-449)], (223-215')-disulfide with kappa light chain (1'-215') [V-KAPPA (*Mus musculus* IGKV10-94*01 (84.2%) -IGKJ5*01 (91.7%)/*Homo sapiens* IGKV1-33*01 (83.2%) -IGKJ2*01 (90.9%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -arginyl (108') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (154), V101 (192) (109''-215')]; dimer (229-229'':232-232'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa; conjugated, via a thioether bond, from 3 to 5 flexible biodegradable polymers, poly(1-hydroxymethylethylene hydroxymethyl-formal) (PHF)-BA-EG2-MI-AF-HPA-Ala, each comprising maleimide (MI) conjugation linkers and 3 to 4 cytotoxic auristatin F- hydroxypropylamide-L-alanine (AF-HPA-Ala), with a drug ratio of 12:1 to 15:1
upifitamab rilsodotine	immunoglobuline G1-kappa, anti-[*Homo sapiens* SLC34A2 (membre 2 de la famille 34 sodium phosphate de transporteurs de solutés, cotransporteur 2B de sodium/phosphate, NaPi2b, NaPi3b, NAPI-3B)], anticorps monoclonal, conjugué, via une liaison thiéther, à 3 à 5 polymères flexibles PHF-BA-EG2-MI-AF-HPA-Ala, comprenant chacun des linkers de bioconjugaison maléimide (MI) et 3 à 4 auristatine F- hydroxypropylamide-alanine (AF-HPA-Ala), dans un rapport produit actif de 12:1 à 15:1; chaîne lourde gamma1 (1-449) [VH (*Homo sapiens* IGHV1-46*01 (81.6%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -glycinyl (120) -*Homo sapiens* IGHG1*03 (100%), G1m3, nG1m1 (CH1 R120 (217) (121-218), charnière 1-15 (219-233), CH2 (234-343), CH3 E12 (359), M14 (361) (344-448), CHS K>del (449)) (121-449)], (223-215')-disulfure avec la chaîne légère kappa (1'-215') [V-KAPPA (*Mus musculus* IGKV10-94*01 (84.2%) -IGKJ5*01 (91.7%)/*Homo sapiens* IGKV1-33*01 (83.2%) -IGKJ2*01 (90.9%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -arginyl (108') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (154), V101 (192) (109'-215')]; dimère (229-229'':232-232'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa; conjugué, via une liaison thiéther, de 3 à 5 polymères flexibles biodégradables poly(1-hydroxyméthyléthylène hydroxyméthyl-formal) (PHF)-BA-EG2-MI-AF-HPA-Ala, comprenant chacun des linkers de conjugaison maléimide (MI) et 3 à 4 auristatine F- hydroxypropylamide-L-alanine (AF-HPA-Ala) cytotoxiques, dans un rapport produit actif de 12:1 à 15:1
upifitamab rilsodotina	inmunoglobulina G1-kappa, anti-[*Homo sapiens* SLC34A2 (miembro 2 de la familia 34 sodio fosfato de transportadores de solutos, cotransportador 2B de sodio/fosfato, NaPi2b, NaPi3b, NAPI-3B)], anticuerpo monoclonal, conjugado, a través de un enlace tioéter, de 3 a 5 polímeros flexibles PHF-BA-EG2-MI-AF-HPA-Ala, que comprende cada uno de los enlaces de bioconjugación maleimida (MI) y 3 a 4 auristatina F- hidroxipropilamida-L-alanina (AF-HPA-Ala), en una relación de principio activo de 12:1 a 15:1;

cadena pesada gamma1 (1-449) [VH (*Homo sapiens* IGHV1-46*01 (81.6%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -glicinil (120) -*Homo sapiens* IGHG1*03 (100%), G1m3, nG1m1 (CH1 R120 (217) (121-218), bisagra 1-15 (219-233), CH2 (234-343), CH3 E12 (359), M14 (361) (344-448), CHS K>del (449)) (121-449)], (223-215')-disulfuro con la cadena ligera kappa (1'-215') [V-KAPPA (*Mus musculus* IGKV10-94*01 (84.2%) -IGKJ5*01 (91.7%)/*Homo sapiens* IGKV1-33*01 (83.2%) -IGKJ2*01 (90.9%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -arginil (108') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (154), V101 (192) (109'-215')];
dímero (229-229":232-232")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa; conjugado, a través de un enlace tioéter, a 3 a 5 polímeros flexibles biodegradables poli(1-hidroximetiletileno hidroximetil-formal) (PHF)-BA-EG2-MI-AF-HPA-Ala, que comprende cada unos de los enlaces de conjugación maleimida (MI) y
3 a 4 auristatina F- hidroxipropilamida-L-alanina (AF-HPA-Ala) citotóxicos, en una relación de principio activo de 12:1 a 15:1

Heavy chain / Chaîne lourde / Cadena pesada

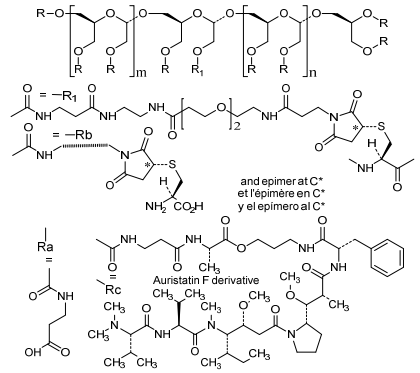
```
QVQLVQSGAE VVKPGASVKM SCKASGYTFT GYNIHWVKQA PGQGLEWIGA  50
IYPGNGDTSY KQKFRGRATL TADTSTSTVY MELSSLRSED SAVYYCARGE 100
TARATFAYWG QGTLVTVSSG ASTKGPSVFP LAPSSKSTSG GTAALGCLVK 150
DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT 200
YICNVNHKPS NTKVDKRVEP KSCDKTHTCP PCPAPELLGG PSVFLFPPKP 250
KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ 350
VYTLPPSREE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPG  449
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Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS LSASVGDRVT ITCSASQDIG NFLNWYQQKP GKTVKVLIYY  50
TSSLYSGVPS RFSGSGSGTD YTLTISSLQP EDFATYYCQQ YSKLPLTFGQ 100
GTKLELKRRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK 150
VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ 200
GLSSPVTKSF NRGEC                                       215
```

Post-translational modifications
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' 135'-195'
23'"-88'" 135'"-195'"
Inter-H-L (h 5-CL 126)* 223-215' 223"-215'"
Inter-H-H (h 11, h 14)* 229-229" 232-232"
*Two or three of the inter-chain disulfide bridges are not present, 3 to 5 cysteinyl being conjugated each via a thioether bond to one maleimide linker of one flexible polymer comprising 3 to 4 drug units.
*Deux ou trois des ponts disulfures inter-chaînes ne sont pas présents, 3 to 5 cystéinyl étant chacun conjugué via une liaison thioéther à un linker-maléimide d'un polymère flexible comprenant 3 à 4 unités de principe actif.
*Faltan dos o tres puentes disulfuro inter-catenarios, 3 a 5 cisteinil está conjugada a conectores de un polimero flexible que contiene 3 a 4 unidades de principio activo.

Modified residues / résidus modifiés / restos modificados:



m + n ~ 35-75 ; R = H , Ra , Rb or Rc ; ratio H : Ra : Rb : Rc ~ 70 : 20 : 2 : 8

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
L VH Q1:
1, 1"

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.

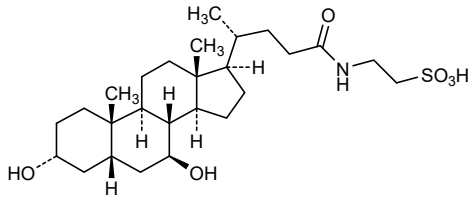
ursodoxicoltaurinum

ursodoxicoltaurine — 2-(3α,7β-dihydroxy-5β-cholan-24-amido)ethane-1-sulfonic acid

ursodoxicoltaurine — acide 2-(3α,7β-dihydroxy-5β-cholan-24-amido)éthane-1-sulfonique

ursodoxicoltaurina — ácido 2-(3α,7β-dihidroxi-5β-colan-24-amido)etano-1-sulfónico

$C_{26}H_{45}NO_6S$



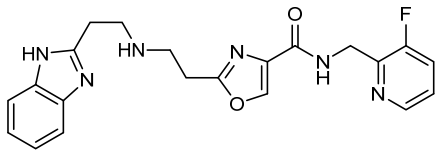
vamifeportum

vamifeport — 2-(2-{[2-(1*H*-benzimidazol-2-yl)ethyl]amino}ethyl)-*N*-[(3-fluoropyridin-2-yl)methyl]-1,3-oxazole-4-carboxamide

vamiféport — 2-(2-{[2-(1*H*-benzimidazol-2-yl)éthyl]amino}éthyl)-*N*-[(3-fluoropyridin-2-yl)méthyl]-1,3-oxazole-4-carboxamide

vamifeport — 2-(2-{[2-(1*H*-benzimidazol-2-il)etil]amino}etil)-*N*-[(3-fluoropiridin-2-il)metil]-1,3-oxazol-4-carboxamida

$C_{21}H_{21}FN_6O_2$



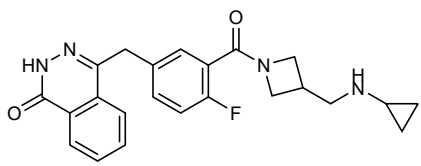
venadaparibum

venadaparib — 3^4-fluoro-7-aza-1(1)-phthalazina-5(1,3)-azetidina-3(1,3)-benzena-8(1)-cyclopropanaoctaphane-1^4(1^3*H*),4-dione

vénadaparib — 3^4-fluoro-7-aza-1(1)-phthalazina-5(1,3)-azétidina-3(1,3)-benzèna-8(1)-cyclopropanaoctaphane-1^4(1^3*H*),4-dione

venadaparib — 3^4-fluoro-7-aza-1(1)-ftalazina-5(1,3)-azetidina-3(1,3)-bencena-8(1)-ciclopropanaoctafano-1^4(1^3*H*),4-diona

$C_{23}H_{23}FN_4O_2$



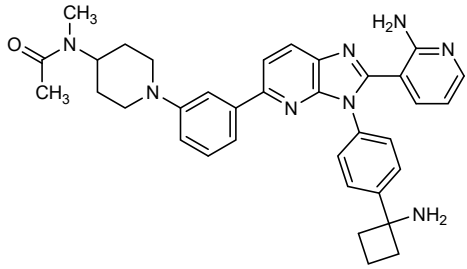
vevorisertibum

vevorisertib — *N*-[1-(3-{3-[4-(1-aminocyclobutyl)phenyl]-2-(2-aminopyridin-3-yl)-3*H*-imidazo[4,5-*b*]pyridin-5-yl}phenyl)piperidin-4-yl]-*N*-methylacetamide

vévorisertib — *N*-[1-(3-{3-[4-(1-aminocyclobutyl)phényl]-2-(2-aminopyridin-3-yl)-3*H*-imidazo[4,5-*b*]pyridin-5-yl}phényl)pipéridin-4-yl]-*N*-méthylacétamide

vevorisertib — *N*-[1-(3-{3-[4-(1-aminociclobutil)fenil]-2-(2-aminopiridin-3-il)-3*H*-imidazo[4,5-*b*]piridin-5-il}fenil)piperidin-4-il]-*N*-metilacetamida

$C_{35}H_{38}N_8O$



vibapapogenum autoleucelum #

vibapapogene autoleucel — Autologous peripheral blood mononuclear cells (PBMCs) expressing human papillomavirus types 16 and 18 antigens.
Autologous peripheral blood mononuclear cells (PBMCs), specifically B lymphocytes and monocytes that are T-cell depleted, transfected *ex vivo* with a non-replicating adenoviral vector that expresses a codon-optimised fusion of tumour-associated antigens (TAAs) E6 and E7 derived from human papillomavirus (HPV) types 16 and 18 (HPV-16/18 E6/E7). The antigen coding region is preceded by a tPA signal sequence and transcription is under the control of the cytomegalovirus (CMV)-tetracycline 10 promoter and the SV40 poly(A) termination sequence. The vector genome is flanked by inverted terminal repeats and contains an encapsidation signal and a K35 knob.

vibapapogène autoleucel — Cellules mononucléaires du sang périphérique autologues exprimant les antigènes de papillomavirus humains de type 16 et 18.
Cellules mononucléaires du sang périphérique autologues, spécifiquement les lymphocytes B et les monocytes qui sont déplétées en lymphocytes T, transfectées *ex vivo* avec une forme non réplicative du vecteur adénoviral exprimant un codon optimisé, fusion des antigènes associés à des tumeurs E6 et E7 dérivés du virus humain du papillome (HPV) types 16 et 18 (HPV-16/18 E6/E7). La région codant l'antigène est précédée d'une séquence signal tPA et la transcription est sous le contrôle du promoteur tétracycline 10 du cytomégalovirus et de la séquence de terminaison poly(A) SV40. Le génome du vecteur est flanqué de répétitions inverses et contient un signal d'encapsidation et un domaine globulaire distal (knob) K35.

vibapapogén autoleucel	Células monucleares de sangre periférica (PBMCs) autólogas que expresan antígenos del papilomavirus humano de tipo 16 y 18. Células monucleares de sangre periférica (PBMCs) autólogas, específicamente linfocitos B y monocitos que están deplecionadas de células T, transfectadas *ex vivo* con un vector adenoviral no replicative que expresa una fusion de los antígenos asociados a tumor (TAAs) E6 y E7 derivados del papillomavirus humano (HPV) de tipo 16 y 18 (HPV-16/18 E6/E7), con codones optimizados. La region codificadora de antigen está precedidad por una secuencia señal tPA y la transcripción está bajo el control del promotor de la tetraciclina 10 del cytomegalovirus (CMV) y la secuencia poly(A) de terminación del SV50. El genoma del vector está flanqueado por repeticiones invertidas terminales y contiene una señal de encapsidación y un dominio globular distal (knob) K35.

vibosameranum #

vibosameran	Messenger RNA encoding tyrosinase. Messenger RNA (mRNA), 5'-capped, encoding codon-optimised tyrosinase (monophenol monooxygenase, tumour rejection antigen AB), expressed as a fusion protein comprising tyrosinase, P2P16 tetanus toxoid-derived helper epitopes and a major histocompatibility complex (MHC) class I transmembrane and cytoplasmic domain, connected by two glycine/serine-rich (GS) linker peptides, flanked by 5' and 3' untranslated regions and a 3' poly(A) tail.
vibosaméran	ARN messager codant pour la tyrosinase. ARN messager (ARNm), protégé en 5', codant pour la tyrosinase (monophénol monooxygénase, antigène de rejet de tumeur AB), avec des codons optimisés, exprimé sous la forme d'une protéine de fusion comprenant la tyrosinase, les épitopes auxiliaires P2P16 dérivés de l'anatoxine tétanique et un domaine transmembranaire et cytoplasmique du complexe majeur d'histocompatibilité (CMH) de classe I, reliés par deux peptides de liaison riches en glycine/sérine (GS), flanqués de régions non traduites en 5' et 3' et d'une queue poly(A) en 3'.
vibosamerán	ARN mensajero que codifica para tirosinasa. ARN mensajero (ARNm), protegido en 5' que codifica para tirosinasa (monofenol monooxigenasa, antígeno de rechazo tumoral AB), con codones optimizados, expresada como una proteína de fusión que consta de la tirosinasa, los epítopos auxiliares P2P16 derivados del toxoide tetánico y un dominio citoplásmico y transmembrana del complejo principal de histocompatibilidad (MHC) de clase I, conectados mediante dos péptidos de enlace ricos en glicina/serina (GS), flanqueado por las regiones 5' y 3' no traducidas y una cola poly(A) en 3'.

vidutolimodum

vidutolimod — immunostimulatory CG-rich palindromic oligodeoxyribonucleotide, flanked by 3'-dG_{10} and 5'-dG_{10} decanucleotides:
deca[2'-deoxyguanylyl-(3'→5')]-2'-deoxyguanylyl-(3'→5')-2'-deoxyadenylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-2'-deoxyguanylyl-(3'→5')-2'-deoxyadenylyl-(3'→5')-thymidylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-2'-deoxyguanylyl-(3'→5')-thymidylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-nona[2'-deoxyguanylyl-(3'→5')]-2'-deoxyguanosine

vidutolimod — oligodésoxyribonucléotide palindromique immunostimulateur riche en CG, flanqué de décanucléotides 3'-dG_{10} et 5'-dG_{10}:
déca[2'-désoxyguanylyl-(3'→5')]-2'-désoxyguanylyl-(3'→5')-2'-désoxyadénylyl-(3'→5')-2'-désoxycytidylyl-(3'→5')-2'-désoxyguanylyl-(3'→5')-2'-désoxyadénylyl-(3'→5')-thymidylyl-(3'→5')-2'-désoxycytidylyl-(3'→5')-2'-désoxyguanylyl-(3'→5')-thymidylyl-(3'→5')-2'-désoxycytidylyl-(3'→5')-nona[2'-désoxyguanylyl-(3'→5')]-2'-désoxyguanosine

vidutolimod — oligodesoxirribonucleótido palindrómico inmunoestimulador rico en CG, flanqueado por decanucleótidos 3'-dG_{10} y 5'-dG_{10}:
deca[2'-desoxiguanilil-(3'→5')]-2'-desoxiguanilil-(3'→5')-2'-desoxiadenilil-(3'→5')-2'-desoxicitidilil-(3'→5')-2'-desoxiguanilil-(3'→5')-2'-desoxiadenilil-(3'→5')-timidilil-(3'→5')-2'-desoxicitidilil-(3'→5')-2'-desoxiguanilil-(3'→5')-timidilil-(3'→5')-2'-desoxicitidilil-(3'→5')-nona[2'-desoxiguanilil-(3'→5')]-2'-desoxiguanosina

$C_{297}H_{363}N_{138}O_{178}P_{29}$

Sequence / Séquence / Secuencia

(3'→5') d(GGGGGGGGGG **GACGATCGTC** GGGGGGGGGG)

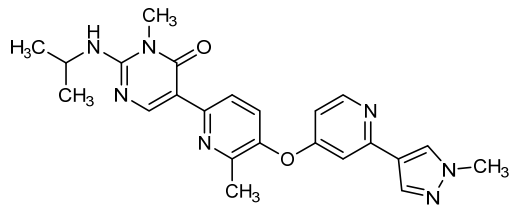
vimseltinibum

vimseltinib — 3-methyl-5-(6-methyl-5-{[2-(1-methyl-1*H*-pyrazol-4-yl)pyridin-4-yl]oxy}pyridin-2-yl)-2-[(propan-2-yl)amino]pyrimidin-4(3*H*)-one

vimseltinib — 3-méthyl-5-(6-méthyl-5-{[2-(1-méthyl-1*H*-pyrazol-4-yl)pyridin-4-yl]oxy}pyridin-2-yl)-2-[(propan-2-yl)amino]pyrimidin-4(3*H*)-one

vimseltinib — 3-metil-5-(6-metil-5-{[2-(1-metil-1*H*-pirazol-4-il)piridin-4-il]oxi}piridin-2-il)-2-[(propan-2-il)amino]pirimidin-4(3*H*)-ona

$C_{23}H_{25}N_7O_2$



vixarelimabum #

vixarelimab	immunoglobulin G4-G1-lambda2, anti-[*Homo sapiens* OSMR (oncostatin M receptor, OSMRB, OSMRbeta)], *Homo sapiens* monoclonal antibody; gamma4-gamma1 heavy chain *Homo sapiens* (1-452) [VH (*Homo sapiens* IGHV1-8*01 (95.9%) -(IGHD) -IGHJ6*01 (95.0%)) CDR-IMGT [8.8.19] (26-33.51-58.97-115) (1-126)-*Homo sapiens* IGHG4*01 CH1-h-CH2, G4v5 h P10, G4v36 CH2 Q84.4 (CH1 (127-224), hinge 1-12 S10>P (234) (225-236), CH2 N84.4>Q (303) (237-346)) -IGHG1*01 CH3-CHS, G1m1 (CH3 D12 (362), L14 (364) (347-451), CHS K>del (452)) (127-452)], (140-215')-disulfide with lambda2 light chain *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV1-44*01 (90.8%) -IGLJ2*01 (100%)) CDR-IMGT [8.3.11] (26-33.51-53.90-100) (1'-110') -*Homo sapiens* IGLC2*01 (100%) (111'-216')]; dimer (232-232":235-235")-bisdisulfide, non-glycosylated, produced in Chinese hamster ovary (CHO)-DG44i cell line
vixarélimab	immunoglobuline G4-G1-lambda2, anti-[*Homo sapiens* OSMR (récepteur de l'oncostatine M, OSMRB, OSMRbeta)], anticorps monoclonal *Homo sapiens*; chaîne lourde gamma4-gamma1 *Homo sapiens*(1-452) [VH (*Homo sapiens* IGHV1-8*01 (95.9%) -(IGHD) -IGHJ6*01 (95.0%)) CDR-IMGT [8.8.19] (26-33.51-58.97-115) (1-126)-*Homo sapiens* IGHG4*01 CH1-h-CH2, G4v5 h P10, G4v36 CH2 Q84.4 (CH1 (127-224), charnière 1-12 S10>P (234) (225-236), CH2 N84.4>Q (303) (237-346)) (127-346) -IGHG1*01 CH3-CHS, G1m1 (CH3 D12 (362), L14 (364) (347-451), CHS K>del (452)) (347-452)], (140-215')-disulfure avec la chaîne légère lambda2 *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV1-44*01 (90.8%) -IGLJ2*01 (100%)) CDR-IMGT [8.3.11] (26-33.51-53.90-100) (1'-110') -*Homo sapiens* IGLC2*01 (100%) (111'-216')]; dimère (232-232":235-235")-bisdisulfure, non-glycosylé, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-DG44i
vixarelimab	inmunoglobulina G4-G1-lambda2, anti-[*Homo sapiens* OSMR (receptor de la oncostatina M, OSMRB, OSMRbeta)], anticuerpo monoclonal *Homo sapiens*; cadena pesada gamma4-gamma1 *Homo sapiens*(1-452) [VH (*Homo sapiens* IGHV1-8*01 (95.9%) -(IGHD) -IGHJ6*01 (95.0%)) CDR-IMGT [8.8.19] (26-33.51-58.97-115) (1-126)-*Homo sapiens* IGHG4*01 CH1-h-CH2, G4v5 h P10, G4v36 CH2 Q84.4 (CH1 (127-224), bisagra 1-12 S10>P (234) (225-236), CH2 N84.4>Q (303) (237-346)) (127-346) -IGHG1*01 CH3-CHS, G1m1 (CH3 D12 (362), L14 (364) (347-451), CHS K>del (452)) (347-452)], (140-215')-disulfuro con la cadena ligera lambda2 *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV1-44*01 (90.8%) -IGLJ2*01 (100%)) CDR-IMGT [8.3.11] (26-33.51-53.90-100) (1'-110') -*Homo sapiens* IGLC2*01 (100%) (111'-216')]; dímero (232-232":235-235")-bisdisulfuro, no glicosilado, producido en las células ováricas de hámster chino (CHO) línea celular CHO-DG44i

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGASVKV SCKASGYTFT SYEINWVRQA TGQGLEWMGW  50
MNPNSGYTGY AQKFQGRVTM TRDTSISTAY MEMSSLRSED TAVYYCARDI 100
VAANTDYYFY YGMDVWGQGT TVTVSSASTK GPSVFPLAPC SRSTSESTAA 150
LGCLVKDYFP EPVTVSWNSG ALTSGVHTFP AVLQSSGLYS LSSVVTVPSS 200
SLGTKTYTCN VDHKPSNTKV DKRVESKYGP PCPPCPAPEF LGGPSVFLFP 250
PKPKDTLMIS RTPEVTCVVV DVSQEDPEVQ FNWYVDGVEV HNAKTKPREE 300
QFQSTYRVVS VLTVLHQDWL NGKEYKCKVS NKGLPSSIEK TISKAKGQPR 350
EPQVYTLPPS RDELTKNQVS LTCLVKGFYP SDIAVEWESN GQPENNYKTT 400
PPVLDSDGSF FLYSKLTVDK SRWQQGNVFS CSVMHEALHN HYTQKSLSLS 450
PG                                                      452
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Light chain / Chaîne légère / Cadena ligera

```
QSVLTQPPSA SGTPGQRVTI SCSGSNSNIG SNTVNWYHQL PGTAPKLLIY  50
NINKRPSGVP DRFSGSKSGS SASLAISGLQ SEDEADYYCS TWDDSLDGVV 100
FGGGTKLTVL GQPKAAPSVT LFPPSSEELQ ANKATLVCLI SDFYPGAVTV 150
AWKADSSPVK AGVETTTPSK QSNNKYAASS YLSLTPEQWK SHRSYSCQVT 200
HEGSTVEKTV APTECS                                      216
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 153-209 267-327 373-431
22"-96" 153"-209" 267"-327" 373"-431"
Intra-L (C23-C104) 22'-89' 138'-197'
22"'-89"' 138"'-197"'
Inter-H-L (CH1 10-CL 126) 140-215' 140"-215"'
Inter-H-H (h 8, h 11) 232-232" 235-235"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"
L VL Q1:
1', 1"'

No N-glycosylation sites / pas de sites de N-glycosylation / ningùn posición de N-glycosilación
H CH2 N84.4>Q (303)
Aglycosylated

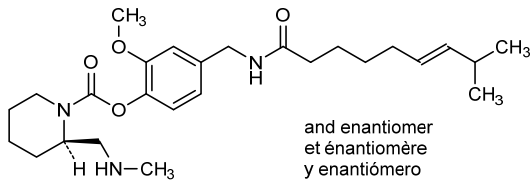
vocacapsaicinum

vocacapsaicin — *rac*-2-methoxy-4-{[(6*E*)-8-methylnon-6-enamido]methyl}phenyl (2*R*)-2-[(methylamino)methyl]piperidine-1-carboxylate

vocacapsaïcine — *rac*-(2*R*)-2-[(méthylamino)méthyl]pipéridine-1-carboxylate de 2-méthoxy-4-{[(6*E*)-8-méthylnon-6-énamido]méthyl}phényle

vocacapsaícina — *rac*-(2*R*)-2-[(metilamino)metil]piperidina-1-carboxilato de 4-{[(6*E*)-8-metilnon-6-enamido]metil}-2-metoxifenilo

$C_{26}H_{41}N_3O_4$



and enantiomer
et énantiomère
y enantiómero

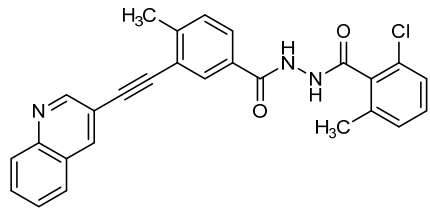
vodobatinibum

vodobatinib — 2-chloro-6-methyl-*N*′-{4-methyl-3-[(quinolin-3-yl)ethynyl]benzoyl}benzohydrazide

vodobatinib — 2-chloro-6-méthyl-*N*′-{4-méthyl-3-[(quinoléin-3-yl)éthynyl]benzoyl}benzohydrazide

vodobatinib — 2-cloro-6-metil-*N*′-{4-metil-3-[(quinolein-3-il)etinil]benzoil}benzohidrazida

$C_{27}H_{20}ClN_3O_2$



vudalimabum #

vudalimab — immunoglobulin half-IG G1-kappa/scFv-h-CH2-CH3, anti-[*Homo sapiens* CTLA4 (cytotoxic T-lymphocyte-associated protein 4, CD152)] and anti-[*Homo sapiens* PDCD1 (programmed cell death 1, PD-1, PD1, CD279)], monoclonal antibody, bispecific;
gamma1 heavy chain anti-CTLA4 (1-447) [VH (*Homo sapiens* IGHV3-48*03 (90.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107)(1-118) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 N114>D (209) R120>K (215) (119-216), hinge 1-15 (217-231), CH2 E1.4,L1.3>P (234), L1.2>V (235), G1.1>A (236), S29>K (267), Q84.2>E (295) (232-340), CH3 E12 (356), M14 (358), L24>D (368), K26>S (370), N44>D (384), Q97>E (418), N100>D (421), M107>L (428), N114>S (434) (341-445), CHS (446-447)) (119-447)], (221-215')-disulfide with kappa light chain anti-CTLA4, *Homo sapiens* (1'-215') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (99.0%) -IGKJ1*01 (100%)) CDR-IMGT [7.3.9] (27-33.51-53.90-98) (1'-108') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (154), V101 (192) (109'-215')];
IG scFv-h-CH2-CH3 single chain, anti-PDCD1 (1''-480'') [scFv V-kappa-VH anti-PDCD1 (1''-249'') [V-KAPPA (*Homo sapiens*IGKV3-15*01 (80.0%)-IGHJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1''-107'') -20-mer tetrakis(glycyl-lysyl-prolyl-glycyl-seryl) linker (108''-127'') -VH (*Mus musculus* IGHV6-6*02 (87.0%) -(IGHD) -IGHJ1*03 (86.7%)/*Homo sapiens* IGHV3-15*07 (81.8%) -(IGHD) -IGHJ2*01 (93.3%)) CDR-IMGT [8.10.13] (153-160.178-187.226-238) (128''-249'')] -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (250''-480'') [hinge 1-15 C5>S (254) (250-264) -CH2 E1.4,L1.3>P (267), L1.2>V (268), G1.1>A (269), S29>K (300) (265-373),CH3 E12 (389), E13>Q (390), M14 (391), S20>K (397), M107>L (461), N114>S (467) (374-478), CHS (479-480)]];
dimer (227-260'':230-263'')-bisdisulfide, produced in Chinese hamster ovary (CHO)-S cell line, glycoform alfa

vudalimab — immunoglobuline demi-IG G1-kappa/scFv-h-CH2-CH3, anti-[*Homo sapiens* CTLA4 (protéine 4 associée aux lymphocytes T cytotoxiques, CD152)] et anti-[*Homo sapiens* PDCD1 (protéine 1 de mort cellulaire programmée, PD-1, PD1, CD279)], anticorps monoclonal, bispécifique;

	chaîne lourde gamma1 anti-CTLA4, (1-447) [VH (*Homo sapiens* IGHV3-48*03 (90.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 N114>D (209) R120>K (215) (119-216), charnière 1-15 (217-231), CH2 E1.4,L1.3>P (234), L1.2>V (235), G1.1>A (236), S29>K (267), Q84.2>E (295) (232-340), CH3 E12 (356), M14 (358), L24>D (368), K26>S (370), N44>D (384), Q97>E (418), N100>D (421), M107>L (428), N114>S (434) (341-445), CHS (446-447)) (119-447)], (221-215')-disulfure avec la chaîne légère kappa anti-CTLA4,*Homo sapiens* (1'-215') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (99.0%) -IGKJ1*01 (100%)) CDR-IMGT [7.3.9] (27-33.51-53.90-98) (1'-108') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (154), V101 (192) (109'-215')]; IG scFv-h-CH2-CH3 chaîne unique, anti-PDCD1 (1''-480'') [scFv V-kappa-VH anti-PDCD1 (1''-249'') [V-KAPPA (*Homo sapiens*IGKV3-15*01 (80.0%)-IGHJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1''-107'') -20-mer tétrakis(glycyl-lysyl-prolyl-glycyl-séryl) linker (108''-127'') -VH (*Mus musculus* IGHV6-6*02 (87.0%) -(IGHD) -IGHJ1*03 (86.7%)/*Homo sapiens* IGHV3-15*07 (81.8%) -(IGHD) -IGHJ2*01 (93.3%)) CDR-IMGT [8.10.13] (153-160.178-187.226-238) (128''-249'')] -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (250''-480'') [charnière 1-15 C5>S (254) (250-264) -CH2 E1.4,L1.3>P (267), L1.2>V (268), G1.1>A (269), S29>K (300) (265-373),CH3 E12 (389), E13>Q (390), M14 (391), S20>K (397), M107>L (461), N114>S (467) (374-478), CHS (479-480)]]; dimère (227-260'':230-263'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-S, glycoforme alfa
vudalimab	inmunoglobulina demi-IG G1-kappa/scFv-h-CH2-CH3, anti-[*Homo sapiens* CTLA4 (proteína 4 asociada a los linfocitos T citotóxicos, CD152)] y anti-[*Homo sapiens* PDCD1 (proteína 1 de muerte celular programada, PD-1, PD1, CD279)], anticuerpo monoclonal, biespecífico; cadena pesada gamma1 anti-CTLA4 (1-447) [VH (*Homo sapiens* IGHV3-48*03 (90.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 N114>D (209) R120>K (215) (119-216), bisagra 1-15 (217-231), CH2 E1.4,L1.3>P (234), L1.2>V (235), G1.1>A (236), S29>K (267), Q84.2>E (295) (232-340), CH3 E12 (356), M14 (358), L24>D (368), K26>S (370), N44>D (384), Q97>E (418), N100>D (421), M107>L (428), N114>S (434) (341-445), CHS (446-447)) (119-447)], (221-215')-disulfuro con la cadena ligera kappa anti-CTLA4,*Homo sapiens* (1'-215') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (99.0%) -IGKJ1*01 (100%)) CDR-IMGT [7.3.9] (27-33.51-53.90-98) (1'-108') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (154), V101 (192) (109'-215')]; IG scFv-h-CH2-CH3 cadena única, anti-PDCD1 (1''-480'') [scFv V-kappa-VH anti-PDCD1 (1''-249'') [V-KAPPA (*Homo sapiens*IGKV3-15*01 (80.0%)-IGHJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1''-107'') -20-mer tetrakis(glicil-lisil-prolil-glicil-seril) linker (108''-127'') -VH (*Mus musculus* IGHV6-6*02 (87.0%) -(IGHD) -IGHJ1*03 (86.7%)/*Homo sapiens* IGHV3-15*07 (81.8%) -(IGHD) -IGHJ2*01 (93.3%)) CDR-IMGT [8.10.13] (153-160.178-187.226-238) (128''-249'')] -*Homo sapiens* IGHG1*03 h-CH2-CH3, nG1m1 (250''-480'') [bisagra 1-15 C5>S (254) (250-264) -CH2 E1.4,L1.3>P (267), L1.2>V (268), G1.1>A (269), S29>K (300) (265-373),CH3 E12 (389), E13>Q (390), M14 (391), S20>K (397), M107>L (461), N114>S (467) (374-478), CHS (479-480)]]; dímero (227-260'':230-263'')-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-S, forma glicosilada alfa

1.Heavy chain / Chaîne lourde / Cadena pesada (anti-CTLA4)

```
EVQLVESGGG LVKPGGSLRL SCAASGFTFS SYTMHWVRQA PGKGLEWVSF  50
ISYDGNNKYY ADSVKGRFTI SRDNAKNSLY LQMNSLRAED TAVYYCARTG 100
WLGPFDYWGQ GTLVTVSSAS TKGPSVFPLA PSSKSTSGGT AALGCLVKDY 150
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTQTYI 200
CNVNHKPSDT KVDKKVEPKS CDKTHTCPPC PAPPVAGPSV FLFPPKPKDT 250
LMISRTPEVT CVVVDVKHED PEVKFNWYVD GVEVHNAKTK PREEEYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT 350
LPPSREEMTK NQVSLTCDVS GFYPSDIAVE WESDGQPENN YKTTPPVLDS 400
DGSFFLYSKL TVDKSRWEQG DVFSCSVLHE ALHSHYTQKS LSLSPGK    447
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2. Light chain / Chaîne légère / Cadena ligera (anti-CTLA4)

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

3. Chain / Chaîne / Cadena IG scFv-h-CH2-CH3 (anti-PDCD1)

```
EIVLTQSPAT LSASPGERVT LTCRASQSVG NDVAWYQQKP GQAPRLLINY  50
ASHRYTGVPD RFTGSGYGTE FTLTISSVQS EDFGVYYCQQ DFSSPRTFGG 100
GTKVEIKGKP GSGKPGSGKP GSGKPGSEVQ LVESGGGLVK PGGSLRLSCV 150
ASGFTFSNYW MNWVRQAPGK GLEWVAEIRL YSNNYATHYA ESVKGRFTIS 200
RDDSKSTLYL QMNNLKTEDT GVYYCTRYYG NYGGYFDVWG RGTLVTVSSE 250
PKSSDKTHTC PPCPAPPVAG PSVFLFPPKP KDTLMISRTP EVTCVVVDVK 300
HEDPEVKFNW YVDGVEVHNA KTKPREEQYN STYRVVSVLT VLHQDWLNGK 350
EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ VYTLPPSREQ MTKNQVKLTC 400
LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW 450
QQGNVFSCSV LHEALHSHYT QKSLSLSPGK                       480
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H (C23-C104)	22-96 145-201 261-321 367-425
Intra-L (C23-C104)	23'-89' 135'-195'
Intra-chain 3	23"-88" 149"-225" 294"-354" 400"-458"
Inter-H-L (h 5-CL 126)	221-215'
Inter-H-chain 3 (h 11, h 14)	227-260" 230-263"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
297, 330"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
447, 480"

zalsenertantum tetraxetanum

zalsenertant tetraxetan

18^4,18^7,18^{10}-tris(carboxymethyl)-4^5-(2,6-dimethoxyphenyl)-7,11,15-trimethyl-3,6,16-trioxo-5^2-(propan-2-yl)-2,7,11,15-tetraaza-18(1)-(1,4,7,10-tetraazacyclododecana)-4(3,1)-pyrazola-1(2)-adamantana-5(1,4)-benzenaoctadecaphane-1^2-carboxylic acid

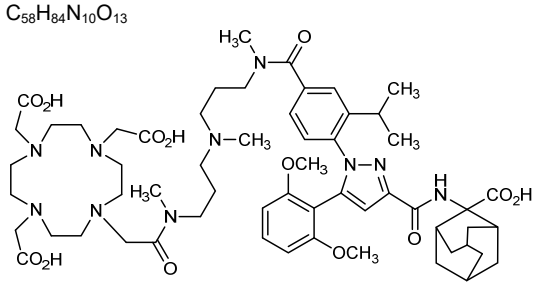
zalsénertant tétraxetan

acide 18^4,18^7,18^{10}-tris(carboxyméthyl)-4^5-(2,6-diméthoxyphényl)-7,11,15-triméthyl-3,6,16-trioxo-5^2-(propan-2-yl)-2,7,11,15-tétraaza-18(1)-(1,4,7,10-tétraazacyclododécana)-4(3,1)-pyrazola-1(2)-adamantana-5(1,4)-benzénaoctadécaphane-1^2-carboxylique

zalsenertant tetraxetán

ácido 18^4,18^7,18^{10}-tris(carboximetil)-4^5-(2,6-dimetoxifenil)-7,11,15-trimetil-3,6,16-trioxo-5^2-(propan-2-il)-2,7,11,15-tetraaza-18(1)-(1,4,7,10-tetraazaciclododecana)-4(3,1)-pirazola-1(2)-adamantana-5(1,4)-bencenaoctadecafano-1^2-carboxílico

$C_{58}H_{84}N_{10}O_{13}$



zanidatamabum zovodotinum #

zanidatamab zovodotin

immunoglobulin half-IG G1-kappa/scFv-h-CH2-CH3, anti-[*Homo sapiens* ERBB2 (epidermal growth factor receptor 2, receptor tyrosine protein kinase erbB-2, EGFR2, HER2, HER-2, p185c-erbB2, NEU, CD340)], humanized monoclonal antibody, biparatopic (targeting two different non-overlapping epitopes on ERBB2, on extracellular domains 2 (ECD2) and 4 (ECD4), respectively), conjugated to auristatin E;
gamma1 heavy chain, anti-ERBB2 extracellular domain 2 (ECD2), humanized (1-449) [VH humanized (*Homo sapiens* IGHV3-66*01 (78.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT[8.8.12] (27-34.52-59.98-109) (1-120) -*Homo sapiens* IGHG1*01 G1m17,1 (CH1 K120 (217) (121-218), hinge 1-15 (219-233), CH2 (234-343), CH3 T6>V (353), L7>Y (354), D12 (359), L14 (361), F85.1>A (408), Y86>V (410) (344-448), CHS K2>del (449)) (121-449)], (223- 215')-disulfide with kappa light chain, anti ERBB2 ECD2, humanized (1'-215') [V-KAPPA humanized (*Homo sapiens* IGKV1-16*01 (84.2%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (28-33.51-53.90-98) (1'-108') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (154), V101 (192) (109'-215')];
IG scFv-h-CH2-CH3 single chain, anti-ERBB2 extracellular domain 4 (ECD4), humanized (1"-481") [scFv V-kappa-VH anti-ERBB2 ECD4 (1'-248') [V-KAPPA humanized (*Homo sapiens* IGKV1-39*01 (86.3%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (28-33.51-53.90-98) (1'-108') -20-mer pentakis(diglycyl-seryl-glycyl) linker (109"-128") -VH humanized (*Homo sapiens* IGHV3-66*01 (81.6%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (154-161.179-186.225-237) (129"-248")] -dialanyl linker (249"-250") -*Homo sapiens* IGHG1*01 h-CH2-CH3, G1m1 (251"-481") [hinge 1-15, C5>S (255) (251-265), CH2 (266-375), CH3 T6>V (385), D12 (391), L14 (393), T22>L (401), K79>L (427), T81>W (429) (376-480), CHS K2>del (481)]];
dimer (229-261":232-264")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa, conjugated, on an average of 2 to 3 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzylcarbonyl (mc-val-cit-PABC) type linker

zanidatamab zovodotine

immunoglobuline G1-kappa, anti-[*Homo sapiens* ERBB2 (récepteur 2 du facteur de croissance épidermique, récepteur tyrosine-protéine kinase erbB-2, EGFR2, HER2, HER-2, p185c-erbB2, NEU, CD340)], anticorps monoclonal humanisé, biparatopique (ciblant deux épitopes différents non chevauchants sur ERBB2, respectivement sur les domaines extracellulaires 2 (ECD2) et 4 (ECD4)), conjugué à l'auristatine E;
chaîne lourde gamma1 anti-ERBB2 domaine extracellulaire 2 (ECD2), humanisée (1-449) [VH humanisé (*Homo sapiens* IGHV3-66*01 (78.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.12] (27-34.52-59.98-109) (1-120) -*Homo sapiens* IGHG1*01 G1m17,1 (CH1 K120 (217) (121-218), charnière 1-15 (219-233), CH2 (234- 343), CH3 T6>V (353), L7>Y (354), D12 (359), L14 (361), F85.1>A (408), Y86>V (410) (344-448), CHS K2>del (449)) (121-449)], (223-215')-disulfure avec la chaîne légère kappa, anti ERBB2 ECD2, humanisée (1'-215') [V-KAPPA humanisé (*Homo sapiens* IGKV1-16*01 (84.2%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (28-33.51-53.90-98) (1'-108') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (154), V101 (192) (109'-215')];

	IG scFv-h-CH2-CH3 chaîne unique, anti-ERBB2 domaine extracellulaire 4 (ECD4), humanisée (1"-481") [scFv V-kappa-VH anti-ERBB2 ECD4 (1'-248') [V-KAPPA humanisé (*Homo sapiens* IGKV1-39*01 (86.3%) - IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (28-33.51-53.90-98) (1'-108') -20-mer pentakis(diglycyl-seryl-glycyl) linker (109"- 128") -VH humanisé (*Homo sapiens* IGHV3-66*01 (81.6%) -(IGHD) - IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (154-161.179-186.225-237) (129"-248")] -dialanyl linker (249"-250") -*Homo sapiens* IGHG1*01 h-CH2-CH3, G1m1 (251"-481") [charnière 1-15 C5>S (255) (251- 265), CH2 (266-375), CH3 T6>V (385), D12 (391), L14 (393), T22>L (401), K79>L (427), T81>W (429) (376-480), CHS K2>del (481)]]; dimère (229-261":232- 264")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa; conjugué, sur 2 à 3 cystéinyl en moyenne, au monométhylauristatine E (MMAE), via un linker clivable de type maléimidécaproyl-valyl-citrullinyl-*p*-aminobenzylcarbonyl (mc-val-cit-PABC).
zanidatamab zovodotina	inmunoglobulina G1-kappa, anti-[*Homo sapiens* ERBB2 (receptor 2 del factor de crecimiento epidérmico, receptor tirosina-proteína kinasa erbB-2, EGFR2, HER2, HER-2, p185c-erbB2, NEU, CD340)], anticuerpo monoclonal humanizado, biparatópico (dirigiendo dos epítopos diferentes no superpuestos sobre ERBB2, respectivamente sobre los dominios extracelulares 2 (ECD2) y 4 (ECD4)), conjugado con la auristatina E; cadena pesada gamma1 anti-ERBB2 dominio extracelular 2 (ECD2), humanizada (1-449) [VH humanizado (*Homo sapiens* IGHV3-66*01 (78.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.12] (27-34.52-59.98-109) (1-120) -*Homo sapiens* IGHG1*01 G1m17,1 (CH1 K120 (217) (121-218), bisagra 1-15 (219-233), CH2 (234- 343), CH3 T6>V (353), L7>Y (354), D12 (359), L14 (361), F85.1>A (408), Y86>V (410) (344-448), CHS K2>del (449)) (121-449)], (223-215')-disulfuro con la cadena ligera kappa, anti ERBB2 ECD2, humanizada (1'-215') [V-KAPPA humanizado (*Homo sapiens* IGKV1-16*01 (84.2%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (28-33.51-53.90-98) (1'-108') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (154), V101 (192) (109'-215')]; IG scFv-h-CH2-CH3 cadena única, anti-ERBB2 dominio extracelular 4 (ECD4), humanizada (1"-481") [scFv V-kappa-VH anti-ERBB2 ECD4 (1'-248') [V-KAPPA humanizado (*Homo sapiens* IGKV1-39*01 (86.3%) - IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (28-33.51-53.90-98) (1'-108') -20-mer pentakis(diglicil-seril-glicil) linker (109"- 128") -VH humanizado (*Homo sapiens* IGHV3-66*01 (81.6%) -(IGHD) - IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (154-161.179-186.225-237) (129"-248")] -dialanil linker (249"-250") -*Homo sapiens* IGHG1*01 h-CH2-CH3, G1m1 (251"-481") [bisagra 1-15 C5>S (255) (251- 265), CH2 (266-375), CH3 T6>V (385), D12 (391), L14 (393), T22>L (401), K79>L (427), T81>W (429) (376-480), CHS K2>del (481)]]; dímero (229-261":232- 264")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa; conjugado, sobre 2 a 3 restos cisteinil en término medio, con monometilauristatina E (MMAE), mediante un conector escindible de tipo maleimidecaproil-valil-citrulinil-*p*-aminobenzilcarbonil (mc-val-cit-PABC).

1.Heavy chain / Chaîne lourde / Cadena pesada (anti-ERBB2 ECD2)

```
GEVQLVESGG GLVQPGGSLR LSCAASGFTF ADYTMDWVRQ APGKGLEWVG  50
DVNPNSGGSI YNQRFKGRFT FSVDRSKNTL YLQMNSLRAE DTAVYYCARN 100
LGPSFYFDYW 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
VYVYPPSRDE LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFALV SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPG  449
```

2. Light chain / Chaîne légère / Cadena ligera (anti-ERBB2 ECD2)

```
GDIQMTQSPS SLSASVGDRV TITCKASQDV SIGVAWYQQK PGKAPKLLIY  50
SASYRYTGVP SRFSGSGSGT DFTLTISSLQ PEDFATYYCQ QYYIYPATFG 100
QGTKVEIKRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK 150
VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ 200
GLSSPVTKSF NRGEC                                      215
```

3. Chain / Chaîne / Cadena: IG scFv-h-CH2-CH3 (anti-ERBB2 ECD4)

```
GDIQMTQSPS SLSASVGDRV TITCRASQDV NTAVAWYQQK PGKAPKLLIY  50
SASFLYSGVP SRFSGSRSGT DFTLTISSLQ PEDFATYYCQ QHYTTPPTFG 100
QGTKVEIKGG SGGGSGGGSG GGSGGGSGEV QLVESGGGLV QPGGSLRLSC 150
AASGFNIKDT YIHWVRQAPG KGLEWVARIY PTNGYTRYAD SVKGRFTISA 200
DTSKNTAYLQ MNSLRAEDTA VYYCSRWGGD GFYAMDYWGQ GTLVTVSSAA 250
EPKSSDKTHT CPPCPAPELL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD 300
VSHEDPEVKF NWYVDGVEVH NAKTKPREEQ YNSTYRVVSV LTVLHQDWLN 350
GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYVLPPSR DELTKNQVSL 400
LCLVKGFYPS DIAVEWESNG QPENNYLTWP PVLDSDGSFF LYSKLTVDKS 450
RWQQGNVFSC SVMHEALHNH YTQKSLSLSP G                     481
```

Post-translational modifications

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

Intra-H (C23-C104) 23-97 147-203 264-324 370-428

Intra-L (C23-C104) 24'-89' 135'-195'

Intra-chain 3 24"-89" 150"-224" 296"-356" 402"-460"

Inter-H-L (h 5-CL 126)* 223-215'

Inter-H-chain 3 (h 11, h 14)* 229-261" 232-264"

*At least two of the three inter-chain disulfide bridges are not present, an average of 2 to 3 cysteinyl being conjugated each via a thioether bond to a drug linker.

*Au moins deux des trois ponts disulfures inter-chaînes ne sont pas présents, 2 à 3 cystéinyl en moyenne étant chacun conjugué via une liaison thioéther à un linker-principe actif.

*Al menos dos de los tres puentes disulfuro inter-catenarios no estan presentes, una media de 2 a 3 cisteinil está conjugada a conectores de principio activo.

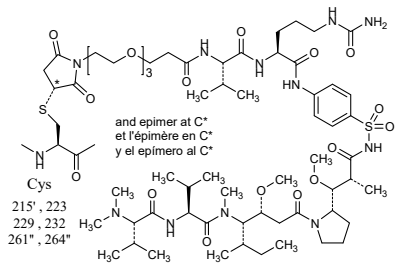
N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación

H CH2 N84.4:

300, 332"

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

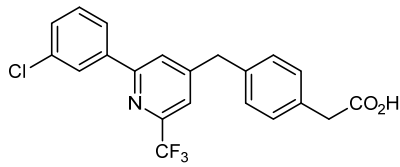
Modified residues / résidus modifiés / restos modificados:



zatolmilastum

zatolmilast	(4-{[2-(3-chlorophenyl)-6-(trifluoromethyl)pyridin-4-yl]methyl}phenyl)acetic acid
zatolmilast	acide (4-{[2-(3-chlorophényl)-6-(trifluorométhyl)pyridin-4-yl]méthyl}phényl)acétique
zatolmilast	ácido (4-{[2-(3-clorofenil)-6-(trifluorometil)piridin-4-il]metil}fenil)acético

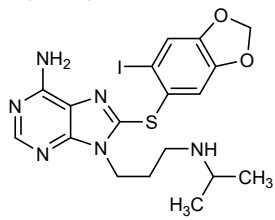
$C_{21}H_{15}ClF_3NO_2$



zelavespibum

zelavespib	8-[(6-iodo-2*H*-1,3-benzodioxol-5-yl)sulfanyl]-9-{3-[(propan-2-yl)amino]propyl}-9*H*-purin-6-amine
zélavespib	8-[(6-iodo-2*H*-1,3-benzodioxol-5-yl)sulfanyl]-9-{3-[(propan-2-yl)amino]propyl}-9*H*-purin-6-amine
zelavespib	8-[(6-iodo-2*H*-1,3-benzodioxol-5-il)sulfanil]-9-{3-[(propan-2-il)amino]propil}-9*H*-purin-6-amina

$C_{18}H_{21}IN_6O_2S$



zimberelimabum #

zimberelimab	immunoglobulin G4-lambda, anti-[*Homo sapiens* PDCD1 (programmed cell death 1, PD-1, PD1, CD279)], *Homo sapiens* monoclonal antibody; gamma4 heavy chain *Homo sapiens* (1-450) [VH (*Homo sapiens* IGHV4-39*01 (87.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [10.7.15] (26-35.53-59.98-112) (1-123)-*Homo sapiens* IGHG4*01 (CH1 (124-221), hinge 1-12 S10>P (231) (222-233), CH2 (234-343), CH3 (344-448), CHS (449-450) (124-450)], (137-215')-disulfide with lambda light chain *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV2-14*01 (94.9%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.10] (26-34.52-54.91-100) (1'-110') -*Homo sapiens* IGLC2*01 (100%) (111'-216')]; dimer (229-229":232-232")-bisdisulfide, produced in Chinese hamster ovary (CHO)-K1 cell line, glycoform alfa
zimbérélimab	immunoglobuline G4-lambda, anti-[*Homo sapiens* PDCD1 (protéine 1 de mort cellulaire programmée, PD-1, PD1, CD279], anticorps monoclonal *Homo sapiens*; chaîne lourde gamma4 *Homo sapiens* (1-450) [VH (*Homo sapiens* IGHV4-39*01 (87.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [10.7.15] (26-35.53-59.98-112) (1-123)-*Homo sapiens* IGHG4*01 (CH1 (124-221), charnière 1-12 S10>P (231) (222-233), CH2 (234-343), CH3 (344-448), CHS (449-450) (124-450)], (137-215')-disulfure avec la chaîne légère

lambda *Homo sapiens*(1'-216') [V-LAMBDA (*Homo sapiens* IGLV2-14*01 (94.9%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.10] (26-34.52-54.91-100) (1'-110') -*Homo sapiens* IGLC2*01 (100%) (111'-216')]; dímero (229-229":232-232")-bisdisulfuro, producido en células ováricas de hámster chino (CHO) línea celular CHO-K1, glicosilada alfa

zimberelimab

inmunoglobulina G4-lambda, anti-[*Homo sapiens* PDCD1 (proteína 1 de muerte celular programada PD-1, PD1, CD279], anticuerpo monoclonal *Homo sapiens*;
cadena pesada gamma4 *Homo sapiens* (1-450) [VH (*Homo sapiens* IGHV4-39*01 (87.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [10.7.15] (26-35.53-59.98-112) (1-123)-*Homo sapiens* IGHG4*01 (CH1 (124-221), bisagra 1-12 S10>P (231) (222-233), CH2 (234-343), CH3 (344-448), CHS (449-450) (124-450)], (137-215')-disulfuro con la cadena ligera lambda *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV2-14*01 (94.9%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.10] (26-34.52-54.91-100) (1'-110') -*Homo sapiens* IGLC2*01 (100%) (111'-216')]; dímero (229-229":232-232")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-K1, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QLQLQESGPG LVKPSETLTL TCTVSADSIS STTYYWVWIR QPPGKGLEWI  50
GSISYSGSTY YNPSLKSRVT VSVDTSKNQF SLKLNSVAAT DTALYYCARH 100
LGYNGRYLPF DYWGQGTLVT VSSASTKGPS VFPLAPCSRS TSESTAALGC 150
LVKDYFPEPV TVSWNSGALT SGVHTFPAVL QSSGLYSLSS VVTVPSSSLG 200
TKTYTCNVDH KPSNTKVDKR VESKYGPPCP PCPAPEFLGG PSVFLFPPKP 250
KDTLMISRTP EVTCVVVDVS QEDPEVQFNW YVDGVEVHNA KTKPREEQFN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKG LPSSIEKTIS KAKGQPREPQ 350
VYTLPPSQEE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFFLY SRLTVDKSRW QEGNVFSCSV MHEALHNHYT QKSLSLSLGK 450
```

Light chain / Chaîne légère / Cadena ligera

```
QSALTQPASV SGSPGQSITI SCTGTSSDVG FYNYVSWYQQ HPGKAPELMI  50
YDVSNRPSGV SDRFSGSKSG NTASLTISGL QAEDEADYYC SSYTSISTWV 100
FGGGTKLTVL GQPKAAPSVT LFPPSSEELQ ANKATLVCLI SDFYPGAVTV 150
AWKADSSPVK AGVETTTPSK QSNNKYAASS YLSLTPEQWK SHRSYSCQVT 200
HEGSTVEKTV APTECS                                      216
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-97 150-206 264-324 370-428
22"-97" 150"-206" 264"-324" 370"-428"
Intra-L (C23-C104) 22'-90' 138'-197'
22'"-90'" 138'"-197'"
Inter-H-L (CH1 10-CL 126) 137-215' 137"-215'"
Inter-H-H (h 8, h 11) 229-229" 232-232"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
L VH Q1:
1, 1"
L VL Q1:
1', 1'"

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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
450, 450"

Please find below the names from proposed **INN List 124 – COVID-19 (special edition)** that have reached the status of recommended INN.
Veuillez trouver ci-dessous les noms de la **Liste 124 des DCI proposées – COVID-19 (édition spéciale)** ayant atteint le statut de DCI recommandées.
Por favor, abajo se encuentran los nombres de la **Lista 124 de DCI propuestas – COVID-19 (edición especial)** que han alcanzado el estatus de DCI recomendadas.

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*

abdavomeranum #

abdavomeran	messenger RNA (mRNA), 5'-capped, encoding the codon-optimised receptor binding domain (RBD) of the SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2, GenBank: MN908947.3) spike (S) glycoprotein, expressed as a fusion protein 5' with an extended S glycoprotein signal peptide and connected 3' by a glycine/serine (GS)-rich linker peptide with a T4 fibritin trimerization domain, flanked by 5' and 3' untranslated regions and a 3' poly(A) tail; contains N1-methylpseudouridine instead of uridine (*all*-U>$m^1\Psi$).
abdavoméran	ARN messager (ARNm), protégé en 5', codant pour le domaine de liaison au récepteur (RBD) de la glycoprotéine spike (S) du SARS-CoV-2 (coronavirus 2 du syndrome respiratoire aigu sévère, GenBank: MN908947.3) avec des codons optimisés, exprimé comme une protéine de fusion 5'-avec un peptide signal de la glycoprotéine S allongé et lié en 3' par un peptide de liaison riche en glycine / sérine (GS) avec un domaine de trimérisation de la fibritine de T4, flanqué par des régions 5' et 3' non traduites et une queue poly(A); contient de la N1-méthylpseudouridine au lieu de l'uridine (*tout*-U>$m^1\Psi$).
abdavomerán	RNA mensajero (mRNA), protegido en 5', que codifica para el dominio de unión al receptor (RBD) de la glicoproteína de la espícula (S) de SRAS-CoV-2 (coronavirus 2 del síndrome respiratorio agudo severo, GenBank: MN908947.3) con codones optimizados, expresado como una proteína de fusión en 5' con un péptido señal de glicoproteína S extendido y conectado en 3' mediante un péptido enlazador (linker) rico en glicina/serina (GS) con un dominio fibritina de trimerización de T4, flanqueado por regiones 5' y 3' no traducidas y una cola poly(A); contiene N1-metilpseudouridina en lugar de uridina (*all*-U>$m^1\Psi$).

alunacedasum alfa #

alunacedase alfa	human angiotensin-converting enzyme 2 extracellular soluble domain (18-740, 1-723 in the current sequence), dimer, glycosylated, produced in Chinese hamster ovary (CHO) cells; human angiotensin-converting enzyme 2 (ACE2, angiotensin-converting enzyme homolog, ACEH, ACE-related carboxypeptidase, metalloprotease MPROT15, EC:3.4.17.23), soluble extracellular (18-740)-domain of the proprotein, non-covalent dimer, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

alunacédase alfa

domaine extracellulaire soluble de l'enzyme de conversion de l'angiotensine de type 2 humaine (18-740, 1-723 dans la séquence actuelle), dimère, glycosylé, produit dans des cellules ovariennes de hamster chinois (CHO);enzyme de conversion de l'angiotensine de type 2 humaine (ECA2, enzyme de conversion homologue de l'angiotensine, HECA, carboxypeptidase liée à l'ECA, métalloprotéase MPROT15, EC: 3.4.17.23), domaine protéique extracellulaire soluble (18-740), dimère non covalent, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

alunacedasa alfa

enzima humana convertidora de la angiotensina 2 dominio extracelular soluble (18-740, 1-723 en la secuencia actual) dímero, glicosilado, producido en células ováricas de hámster Chino (CHO);
enzima humana convertidora de la angiotensina 2 (ECA2, homológo enzima covertidora de angiotensina, HECA, ECA-carboxipeptidasa relacionada, metaloproteasa MPROT15, EC:3.4.17.23), soluble extracelular (18-740)-dominio de la proproteína, dímero no covalente, producido en células ováricas de hámster Chino (CHO), glicoforma alfa

Sequence / Séquence / Secuencia

```
QSTIEEQAKT FLDKFNHEAE DLFYQSSLAS WNYNTNITEE NVQNMNNAGD   50
KWSAFLKEQS TLAQMYPLQE IQNLTVKLQL QALQQNGSSV LSEDKSKRLN  100
TILNTMSTIY STGKVCNPDN PQECLLLEPG LNEIMANSLD YNERLWAWES  150
WRSEVGKQLR PLYEEYVVLK NEMARANHYE DYGDYWRGDY EVNGVDGYDY  200
SRGQLIEDVE HTFEEIKPLY EHLHAYVRAK LMNAYPSYIS PIGCLPAHLL  250
GDMWGRFWTN LYSLTVPFGQ KPNIDVTDAM VDQAWDAQRI FKEAEKFFVS  300
VGLPNMTQGF WENSMLTDPG NVQKAVCHPT AWDLGKGDFR ILMCTKVTMD  350
DFLTAHHEMG HIQYDMAYAA QPFLLRNGAN EGFHEAVGEI MSLSAATPKH  400
LKSIGLLSPD FQEDNETEIN FLLKQALTIV GTLPFTYMLE KWRWMVFKGE  450
IPKDQWMKKW WEMKREIVGV VEPVPHDETY CDPASLFHVS NDYSFIRYYT  500
RTLYQFQFQE ALCQAAKHEG PLHKCDISNS TEAGQKLFNM LRLGKSEPWT  550
LALENVVGAK NMNVRPLLNY FEPLFTWLKD QNKNSFVGWS TDWSPYADQS  600
IKVRISLKSA LGDKAYEWND NEMYLFRSSV AYAMRQYFLK VKNQMILFGE  650
EDVRVANLKP RISFNFFVTA PKNVSDIIPR TEVEKAIRMS RSRINDAFRL  700
NDNSLEFLGI QPTLGPPNQP PVS                                723
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
116-124, 327-344, 513-525 116'-124', 327'-344', 513'-525'
Cys-SH: 244, 481, 244', 481'

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
N36, N73, N86, N305, N415, N529, N36', N73', N86', N305', N415', N529' (97-100% each)
N673, N673' (4% each)

O-glycosylation sites / Sites de O-glycosylation / Posiciones de O-glicosilación
S704, S704' or T713, T713' or S723, S723'

Other modifications: Q1, Q1' >Glp (pyroGlu);
S723, S723': partially clipped (~4%)

atibuclimabum #

atibuclimab

immunoglobulin G4-kappa, anti-[*Homo sapiens* CD14, membrane (mCD14) and soluble (sCD14)], chimeric monoclonal antibody; gamma4 heavy chain chimeric (1-442) [VH *Mus musculus* (Musmus IGHV3-2*02 (95.9%) -(IGHD) -Musmus IGHJ3*01 (92.9%) A128>S (115)) CDR-IMGT [9.7.8] (26-34.52-58.97-104) (1-115) -*Homo sapiens* IGHG4*01 (100%), CH1 (116-213),hinge 1-12 (214-225), CH2 (226-335), CH3 (336-440), CHS (441-442)) (116-442)], (129-218')-disulfide with kappa light chain chimeric (1'-218') [V-KAPPA *Mus musculus* (Musmus IGKV3-5*01 (97.0%) -IGKJ2*01 (100%)) CDR-IMGT [10.3.9] (27-36.54-56.93-101) (1'-111') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (157), V101 (195) (112'-218')]; dimer (221-221":224-224")-bisdisulfide, produced in a Chinese hamster ovary (CHO)-DG44 cell line, glycoform alfa

atibuclimab

immunoglobuline G4-kappa anti-[*Homo sapiens* CD14, membrane (mCD14) et soluble (sCD14)], anticorps monoclonal chimérique; chaîne lourde gamma4 chimérique (1-442) [VH *Mus musculus* (Musmus IGHV3-2*02 (95.9%) -(IGHD) -Musmus IGHJ3*01 (92.9%) A128>S (115)) CDR-IMGT [9.7.8] (26-34.52-58.97-104) (1-115) - *Homo sapiens* IGHG4*01 (100%), CH1 (116-213), charnière 1-12 (214-225), CH2 (226-335), CH3 (336-440), CHS (441-442)) (116-442)], (129-218')-disulfure avec la chaîne légère kappa chimérique (1'-218') [V-KAPPA *Mus musculus* (Musmus IGKV3-5*01 (97.0%) - IGKJ2*01 (100%)) CDR-IMGT [10.3.9] (27-36.54-56.93-101) (1'-111') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (157), V101 (195) (112'-218')]; dimère (221-221":224-224")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-DG44, glycoforme alfa

atibuclimab

inmunoglobulina G4-kappa anti-[*Homo sapiens* CD14, membrana (mCD14) y soluble (sCD14)], anticuerpo monoclonal quimérico; cadena pesada gamma4 quimérico (1-442) [VH *Mus musculus* (Musmus IGHV3-2*02 (95.9%) -(IGHD) -Musmus IGHJ3*01 (92.9%) A128>S (115)) CDR-IMGT [9.7.8] (26-34.52-58.97-104) (1-115) - *Homo sapiens* IGHG4*01 (100%), CH1 (116-213), bisagra 1-12 (214-225), CH2 (226-335), CH3 (336-440), CHS (441-442)) (116-442)], (129-218')-disulfuro con la cadena ligera kappa quimérica (1'-218') [V-KAPPA *Mus musculus* (Musmus IGKV3-5*01 (97.0%) - IGKJ2*01 (100%)) CDR-IMGT [10.3.9] (27-36.54-56.93-101) (1'-111') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (157), V101 (195) (112'-218')]; dímero (221-221":224-224")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-DG44, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
DVQLQQSGPG LVKPSQSLSL TCTVTGYSIT SDSAWNWIRQ FPGNRLEWMG   50
YISYSGSTSY NPSLKSRISI TRDTSKNQFF LQLNSVTTED TATYYCVRGL  100
RFAYWGQGTL VTVSSASTKG PSVFPLAPCS RSTSESTAAL GCLVKDYFPE  150
PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL SSVVTVPSSS LGTKTYTCNV  200
DHKPSNTKVD KRVESKYGPP CPSCPAPEFL GGPSVFLFPP KPKDTLMISR  250
TPEVTCVVVD VSQEDPEVQF NWYVDGVEVH NAKTKPREEQ FNSTYRVVSV  300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ  350
EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDSDGSFF  400
LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL GK          442
```

Light chain / Chaîne légère / Cadena ligera

```
DIVLTQSPAS LAVSLGQRAT ISCRASESVD SYVNSFLHWY QQKPGQPPKL   50
LIYRASNLQS GIPARFSGSG SRTDFTLTIN PVEADDVATY YCQQSNEDPY  100
TFGGGTKLEI KRTVAAPSVF IFPPSDEQLK SGTASVVCLL NNFYPREAKV  150
QWKVDNALQS GNSQESVTEQ DSKDSTYSLS STLTLSKADY EKHKVYACEV  200
THQGLSSPVT KSFNRGEC                                     218
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 142-198 256-316 362-420
22"-96" 142"-198" 256"-316" 362"-420"
Intra-L (C104) 23'-92' 138'-198'
23'"-92'" 138'"-198'"
Inter-H-L (CH1 10-CL 126) 129-218' 129"-218'"
Inter-H-H (h 8, h 11) 221-221" 224-224"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
292, 292"
Fucosylated complex bi-antennary CHO-type glycans (G0F predominant) / glycanes de type CHO bi-antennaires complexes fucosylés (G0F prédominant) / glicanos de tipo CHO biantenarios complejos fucosilados (G0F predominante).

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
442, 442"

bamlanivimabum #

bamlanivimab	immunoglobulin G1-kappa, anti-[*Homo sapiens* severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike (S) protein], *Homo sapiens* monoclonal antibody; gamma1 heavy chain *Homo sapiens* (1-455) [VH (*Homo sapiens* IGHV1-69*04 (99.0%) -(IGHD) -IGHJ6*01 (90.9%) T123>A (120)) CDR-IMGT [8.8.18] (26-33.51-58.97-114) (1-125) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (222) (126-223), hinge 1-15 (224-238), CH2 (239-348), CH3 E12 (364), M14 (366) (349-453), CHS (454-455)) (126-454)], (228-214')-disulfide with kappa light chain *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (97.9%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dimer (234-234":237-237")-bisdisulfide, produced in a Chinese hamster ovary (CHO) cell line derived from CHO-K1SV, lacking the glutamine synthetase (GS) gene, glycoform alfa
bamlanivimab	immunoglobuline G1-kappa anti-[*Homo sapiens* protéine spike (S) du coronavirus 2 du syndrome respiratoire aigu sévère (SARS-CoV-2)], anticorps monoclonal *Homo sapiens*; chaîne lourde gamma1 *Homo sapiens* (1-455) [VH (*Homo sapiens* IGHV1-69*04 (99%) -(IGHD) -IGHJ6*01 (90.9%) T123>A (120)) CDR-IMGT [8.8.18] (26-33.51-58.97-114) (1-125) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (222) (126-223), charnière 1-15 (224-238), CH2 (239-348), CH3 E12 (364), M14 (366) (349-453), CHS (454-455)) (126-454)], (228-214')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (97.9%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dimère (234-234":237-237")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) dérivant de la lignée cellulaire CHO-K1SV, ne présentant pas le gène de la glutamine synthétase, glycoforme alfa
bamlanivimab	inmunoglobulina G1-kappa anti-[*Homo sapiens* proteína espícula (S) del coronavirus 2 del síndrome respiratorio agudo severo (SRAS-CoV-2)], anticuerpo monoclonal *Homo sapiens*; cadena pesada gamma1 *Homo sapiens* (1-455) [VH (*Homo sapiens* IGHV1-69*04 (99%) -(IGHD) -IGHJ6*01 (90.9%) T123>A (120)) CDR-IMGT [8.8.18] (26-33.51-58.97-114) (1-125) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (222) (126-223), bisagra 1-15 (224-238), CH2 (239-348), CH3 E12 (364), M14 (366) (349-453), CHS (454-455)) (126-454)], (228-214')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (97.9%) -IGKJ1*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dímero (234-234":237-237")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular derivada de CHO-K1SV, en ausencia del gen glutamina sintetasa (GS), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGSSVKV SCKASGGTFS NYAISWVRQA PGQGLEWMGR  50
IIPILGIANY AQKFQGRVTI TADKSTSTAY MELSSLRSED TAVYYCARGY 100
YEARHYYYYY AMDVWGQGTA VTVSSASTKG PSVFPLAPSS KSTSGGTAAL 150
GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL SSVVTVPSSS 200
LGTQTYICNV NHKPSNTKVD KRVEPKSCDK THTCPPCPAP ELLGGPSVFL 250
FPPKPKDTLM ISRTPEVTCV VVDVSHEDPE VKFNWYVDGV EVHNAKTKPR 300
EEQYNSTYRV VSVLTVLHQD WLNGKEYKCK VSNKALPAPI EKTISKAKGQ 350
PREPQVYTLP PSREEMTKNQ VSLTCLVKGF YPSDIAVEWE SNGQPENNYK 400
TTPPVLDSDG SFFLYSKLTV DKSRWQQGNV FSCSVMHEAL HNHYTQKSLS 450
LSPGK                                                   455
```

Light chain / Chaîne légère / Cadena ligera

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DIQMTQSPSS LSASVGDRVT ITCRASQSIS SYLSWYQQKP GKAPKLLIYA  50
ASSLQSGVPS RFSGSGSGTD FTLTITSLQP EDFATYYCQQ SYSTPRTFGQ 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                         214
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 152-208 269-329 375-433
22"-96" 152"-208" 269"-329" 375"-433"
Intra-L (C23-C104) 23'-88' 134'-194'
23'"-88'" 134'"-194'"
Inter-H-L (h 5-CL 126) 228-214' 228"-214'"
Inter-H-H (h 11, h 14) 234-234" 237-237"

N-terminal glutamine cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
305, 305"
Fucosylated complex bi-antennary CHO-type glycans (G0F predominant) / glycanes de type CHO bi-antennaires complexes fucosylés (G0F prédominant) / glicanos de tipo CHO biantenarios complejos fucosilados (G0F predominante).

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
455, 455"

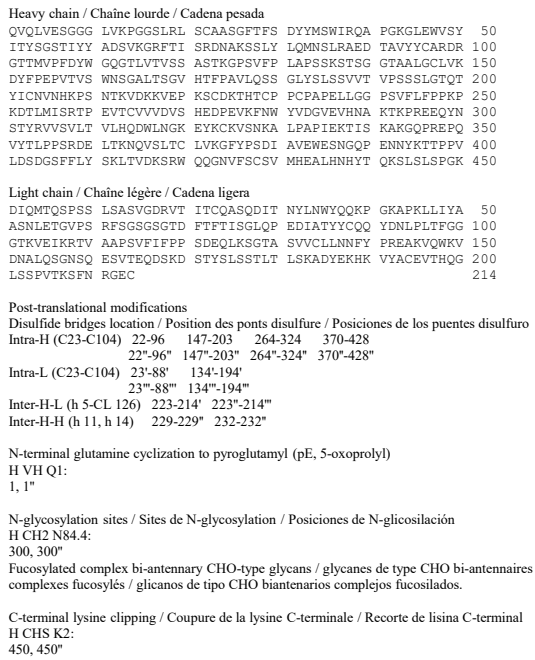
casirivimabum #

casirivimab	immunoglobulin G1-kappa, anti-[*Homo sapiens* severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike (S) protein, receptor binding domain (RBD)], *Homo sapiens* monoclonal antibody; gamma1 heavy chain *Homo sapiens* (1-450) [VH (*Homo sapiens* IGHV3-11*01 (96.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (217) (121-218),hinge 1-15 (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS (449-450)) (121-450)], (223-214')-disulfide with kappa light chain *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-33*01 (96.8%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dimer (229-229":232-232")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa
casirivimab	immunoglobuline G1-kappa anti-[*Homo sapiens* protéine spike (S) du coronavirus 2 du syndrome respiratoire aigu sévère (SARS-CoV-2), domaine de liaison au récepteur (RBD)], anticorps monoclonal *Homo sapiens*;

chaîne lourde gamma1 *Homo sapiens* (1-450) [VH (*Homo sapiens* IGHV3-11*01 (96.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (217) (121-218), charnière 1-15 (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS (449-450)) (121-450)], (223-214')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-33*01 (96.8%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dimère (229-229":232-232")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

casirivimab

inmunoglobulina G1-kappa anti-[*Homo sapiens* proteína espícula (S) del coronavirus 2 del síndrome respiratorio agudo severo (SRAS-CoV-2), dominio de unión al receptor (RBD)], anticuerpo monoclonal *Homo sapiens*;
cadena pesada gamma1 *Homo sapiens* (1-450) [VH (*Homo sapiens* IGHV3-11*01 (96.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (217) (121-218), bisagra 1-15 (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS (449-450)) (121-450)], (223-214')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-33*01 (96.8%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dímero (229-229":232-232")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa



Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVESGGG LVKPGGSLRL SCAASGFTFS DYYMSWIRQA PGKGLEWVSY  50
ITYSGSTIYY ADSVKGRFTI SRDNAKSSLY LQMNSLRAED TAVYYCARDR 100
GTTMVPFDYW 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

```
DIQMTQSPSS LSASVGDRVT ITCQASQDIT NYLNWYQQKP GKAPKLLIYA  50
ASNLETGVPS RFSGSGSGTD FTFTISGLQP EDIATYYCQQ YDNLPLTFGG 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Post-translational modifications
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-terminal glutamine cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"

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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
450, 450"

cilgavimabum #

cilgavimab	immunoglobulin G1-kappa, anti-[*Homo sapiens* severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike (S) protein, receptor binding domain (RBD)], *Homo sapiens* monoclonal antibody; gamma1 heavy chain *Homo sapiens* (1-461) [VH (*Homo sapiens* IGHV3-15*01 (96.0%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.10.22] (26-33.51-60.99-120) (1-131) -*Homo sapiens* IGHG1*03 G1m3, nG1m1, G1v21 CH2 Y15.1, T16, E18, G1v39 CH2 F1.3, E1.2, S116 (CH1 R120 (228) (132-229),hinge 1-15 (230-244), CH2 L1.3>F (248), L1.2>E (249), M15.1>Y (266), S16>T (268), T18>E (270), P116>S (345) (245-354), CH3 E12 (370), M14 (372) (355-459), CHS (460-461)) (132-461)], (234-219')-disulfide with kappa light chain *Homo sapiens* (1'-219') [V-KAPPA (*Homo sapiens* IGKV4-1*01 (96.0%) -IGKJ4*01 (100%)) CDR-IMGT [12.3.8] (27-38.56-58.95-102) (1'-112') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (158), V101 (196) (113'-219')]; dimer (240-240":243-243")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa
cilgavimab	immunoglobuline G1-kappa anti-[*Homo sapiens* protéine spike (S) du coronavirus 2 du syndrome respiratoire aigu sévère (SARS-CoV-2), domaine de liaison au récepteur (RBD)], anticorps monoclonal *Homo sapiens*; chaîne lourde gamma1 *Homo sapiens* (1-461) [VH (*Homo sapiens* IGHV3-15*01 (96.0%) -(IGHD) - IGHJ4*01 (100%)) CDR-IMGT [8.10.22] (26-33.51-60.99-120) (1-131) -Homo sapiens IGHG1*03 G1m3, nG1m1, G1v21 CH2 Y15.1, T16, E18, G1v39 CH2 F1.3, E1.2, S116 (CH1 R120 (228) (132-229), charnière 1-15 (230-244), CH2 L1.3>F (248), L1.2>E (249), M15.1>Y (266), S16>T (268), T18>E (270), P116>S (345) (245-354), CH3 E12 (370), M14 (372) (355-459), CHS (460-461)) (132-461)], (234-219')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-219') [V-KAPPA (*Homo sapiens* IGKV4-1*01 (96.0%) -IGKJ4*01 (100%)) CDR-IMGT [12.3.8] (27-38.56-58.95-102) (1'-112') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (158), V101 (196) (113'-219')]; dimère (240-240":243-243")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa
cilgavimab	inmunoglobulina G1-kappa anti-[*Homo sapiens* proteína espícula (S) del coronavirus 2 del síndrome respiratorio agudo severo (SRAS-CoV-2), dominio de unión al receptor (RBD)], anticuerpo monoclonal *Homo sapiens*; cadena pesada gamma1 *Homo sapiens* (1-461) [VH (*Homo sapiens* IGHV3-15*01 (96.0%) -(IGHD) - IGHJ4*01 (100%)) CDR-IMGT [8.10.22] (26-33.51-60.99-120) (1-131) -*Homo sapiens* IGHG1*03 G1m3, nG1m1, G1v21 CH2 Y15.1, T16, E18, G1v39 CH2 F1.3, E1.2, S116 (CH1 R120 (228) (132-229), bisagra 1-15 (230-244), CH2 L1.3>F (248), L1.2>E (249), M15.1>Y (266), S16>T (268), T18>E (270), P116>S (345) (245-354), CH3 E12 (370), M14 (372) (355-459), CHS (460-461)) (132-461)], (234-219')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-219') [V-KAPPA (*Homo sapiens* IGKV4-1*01 (96.0%) -IGKJ4*01 (100%)) CDR-IMGT [12.3.8] (27-38.56-58.95-102) (1'-112') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (158), V101 (196) (113'-219')]; dímero (240-240":243-243")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVKPGGSLRL SCAASGFTFR DVWMSWVRQA PGKGLEWVGR  50
IKSKIDGGTT DYAAPVKGRF TISRDDSKNT LYLQMNSLKT EDTAVYYCTT 100
AGSYYYDTVG PGLPEGKFDY WGQGTLVTVS SASTKGPSVF PLAPSSKSTS 150
GGTAALGCLV KDYFPEPVTV SWNSGALTSG VHTFPAVLQS SGLYSLSSVV 200
TVPSSSLGTQ TYICNVNHKP SNTKVDKRVE PKSCDKTHTC PPCPAPEFEG 250
GPSVFLFPPK PKDTLYITRE PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN 300
AKTKPREEQY NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK ALPASIEKTI 350
SKAKGQPREP QVYTLPPSRE EMTKNQVSLT CLVKGFYPSD IAVEWESNGQ 400
PENNYKTTPP VLDSDGSFFL YSKLTVDKSR WQQGNVFSCS VMHEALHNHY 450
TQKSLSLSPG K                                          461
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Light chain / Chaîne légère / Cadena ligera

```
DIVMTQSPDS LAVSLGERAT INCKSSQSVL YSSNNKNYLA WYQQKPGQPP  50
KLLMYWASTR ESGVPDRFSG SGSGAEFTLT ISSLQAEDVA IYYCQQYYST 100
LTFGGGTKVE IKRTVAAPSV FIFPPSDEQL KSGTASVVCL LNNFYPREAK 150
VQWKVDNALQ SGNSQESVTE QDSKDSTYSL SSTLTLSKAD YEKHKVYACE 200
VTHQGLSSPV TKSFNRGEC                                  219
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-98 158-214 275-335 381-439
22"-98" 158"-214" 275"-335" 381"-439"
Intra-L (C23-C104) 23'-94' 139'-199'
23'"-94'" 139'"-199'"
Inter-H-L (h 5-CL 126) 234-219' 234"-219'"
Inter-H-H (h 11, h 14) 240-240" 243-243"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
311, 311"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
461, 461"

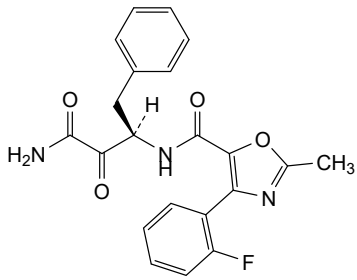
dazcapistatum

dazcapistat — *rac*-*N*-[(2*R*)-4-amino-3,4-dioxo-1-phenylbutan-2-yl]-4-(2-fluorophenyl)-2-methyl-1,3-oxazole-5-carboxamide

dazcapistat — *rac*-*N*-[(2*R*)-4-amino-3,4-dioxo-1-phénylbutan-2-yl]-4-(2-fluorophényl)-2-méthyl-1,3-oxazole-5-carboxamide

dazcapistat — *rac*-*N*-[(2*R*)-4-amino-3,4-dioxo-1-fenilbutan-2-il]-4-(2-fluorofenil)-2-metil-1,3-oxazol-5-carboxamida

$C_{21}H_{18}FN_3O_4$



and enantiomer
et énantiomère
y enantiómero

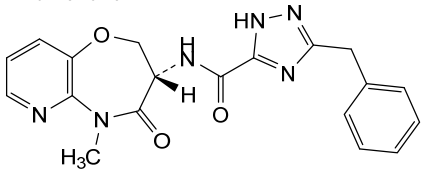
eclitasertibum

eclitasertib — 5-benzyl-*N*-[(3*S*)-5-methyl-4-oxo-2,3,4,5-tetrahydropyrido[3,2-*b*][1,4]oxazepin-3-yl]-1*H*-1,2,4-triazole-3-carboxamide

éclitasertib — 5-benzyl-*N*-[(3*S*)-5-méthyl-4-oxo-2,3,4,5-tétrahydropyrido[3,2-*b*][1,4]oxazépin-3-yl]-1*H*-1,2,4-triazole-3-carboxamide

eclitasertib — 5-bencil-*N*-[(3*S*)-5-metil-4-oxo-2,3,4,5-tetrahidropirido[3,2-*b*][1,4]oxazepin-3-il]-1*H*-1,2,4-triazol-3-carboxamida

$C_{19}H_{18}N_6O_3$



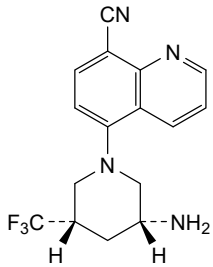
enpatoranum

enpatoran — 5-[(3*R*,5*S*)-3-amino-5-(trifluoromethyl)piperidin-1-yl]quinoline-8-carbonitrile

enpatoran — 5-[(3*R*,5*S*)-3-amino-5-(trifluorométhyl)pipéridin-1-yl]quinoléine-8-carbonitrile

enpatorán — 5-[(3*R*,5*S*)-3-amino-5-(trifluorometil)piperidin-1-il]quinoleína-8-carbonitrilo

$C_{16}H_{15}F_3N_4$



etesevimabum

etesevimab — immunoglobulin G1-kappa, anti-[*Homo sapiens* severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike (S) protein, receptor binding domain (RBD)], *Homo sapiens* monoclonal antibody; gamma1 heavy chain *Homo sapiens* (1-449) [VH (*Homo sapiens* IGHV3-66*01 (96.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.7.13] (26-33.51-57.96-108) (1-119) -*Homo sapiens* IGHG1*03 G1m3, nG1m1, G1v14 A1.3, A1.2 (CH1 R120 (216) (120-217), hinge 1-15 (218-232), CH2 L1.3>A (236), L1.2>A (237), (233-342), CH3 E12 (358), M14 (360) (343-447), CHS (448-449)) (120-449)], (222-216')-disulfide with kappa light chain *Homo sapiens* (1'-216') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (97.9%) -IGKJ2*01 (100%)) CDR-IMGT [6.3.11] (27-32.50-52.89-99) (1'-109') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (155), V101 (193) (110'-216')]; dimer (228-228":231-231")-bisdisulfide, produced in a Chinese hamster ovary (CHO) cell line derived from CHO-K1SV, lacking the glutamine synthetase (GS) gene, glycoform alfa

étésévimab

immunoglobuline G1-kappa anti-[*Homo sapiens* protéine spike (S) du coronavirus 2 du syndrome respiratoire aigu sévère (SARS-CoV-2), domaine de liaison au récepteur (RBD)], anticorps monoclonal *Homo sapiens*;
chaîne lourde gamma1 *Homo sapiens* (1-449) [VH (*Homo sapiens* IGHV3-66*01 (96.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.7.13] (26-33.51-57.96-108) (1-119) -*Homo sapiens* IGHG1*03 G1m3, nG1m1, G1v14 A1.3, A1.2 (CH1 R120 (216) (120-217), charnière 1-15 (218-232), CH2 L1.3>A (236), L1.2>A (237), (233-342), CH3 E12 (358), M14 (360) (343-447), CHS (448-449)) (120-449)], (222-216')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-216') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (97.9%) -IGKJ2*01 (100%)) CDR-IMGT [6.3.11] (27-32.50-52.89-99) (1'-109') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (155), V101 (193) (110'-216')]; dimère (228-228":231-231")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) dérivant de la lignée cellulaire CHO-K1SV, ne présentant pas le gène de la glutamine synthétase, glycoforme alfa

etesevimab

inmunoglobulina G1-kappa anti-[*Homo sapiens* proteína espícula (S) del coronavirus 2 del síndrome respiratorio agudo severo (SRAS-CoV-2), dominio de unión al receptor (RBD)], anticuerpo monoclonal *Homo sapiens*; cadena pesada gamma1 *Homo sapiens* (1-449) [VH (*Homo sapiens* IGHV3-66*01 (96.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.7.13] (26-33.51-57.96-108) (1-119) -*Homo sapiens* IGHG1*03 G1m3, nG1m1, G1v14 A1.3, A1.2 (CH1 R120 (216) (120-217), bisagra 1-15 (218-232), CH2 L1.3>A (236), L1.2>A (237), (233-342), CH3 E12 (358), M14 (360) (343-447), CHS (448-449)) (120-449)], (222-216')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-216') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (97.9%) -IGKJ2*01 (100%)) CDR-IMGT [6.3.11] (27-32.50-52.89-99) (1'-109') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (155), V101 (193) (110'-216')]; dímero (228-228":231-231")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular derivada de CHO-K1SV, en ausencia del gen Glutamina Sintetasa (GS), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGGSLRL SCAASGFTVS SNYMSWVRQA PGKGLEWVSV  50
IYSGGSTFYA DSVKGRFTIS RDNSMNTLFL QMNSLRAEDT AVYYCARVLP 100
MYGDYLDYWG QGTLVTVSSA STKGPSVFPL APSSKSTSGG TAALGCLVKD 150
YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY 200
ICNVNHKPSN TKVDKRVEPK SCDKTHTCPP CPAPEAAGGP 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

```
DIVMTQSPSS LSASVGDRVT ITCRASQSIS RYLNWYQQKP GKAPKLLIYA  50
ASSLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ SYSTPPEYTF 100
GQGTKLEIKR TVAAPSVFIF PPSDEQLKSG TASVVCLLNN FYPREAKVQW 150
KVDNALQSGN SQESVTEQDS KDSTYSLSST LTLSKADYEK HKVYACEVTH 200
QGLSSPVTKS FNRGEC                                      216
```

Post-translational modifications

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

Intra-H (C23-C104) 22-95 146-202 263-323 369-427
22"-95" 146"-202" 263"-323" 369"-427"
Intra-L (C23-C104) 23'-88' 136'-196'
23'"-88'" 136'"-196'"
Inter-H-L (h 5-CL 126) 222-216' 222"-216'"
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"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal

H CHS K2:
449, 449"

ganulameranum #

ganulameran

messenger RNA (mRNA), 5'-capped, encoding the codon-optimised receptor binding domain (RBD) of the SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2, GenBank: MN908947.3) spike (S) glycoprotein expressed as a fusion protein, 5' with an extended S glycoprotein signal peptide, and 3' with a T4 fibritin trimerization domain and the S glycoprotein transmembrane domain (TM) connected by two glycine/serine-rich (GS) linker peptides, flanked by 5' and 3' untranslated regions and a 3' poly(A) tail; contains N1-methylpseudouridine instead of uridine (*all*-U>$m^1\Psi$).

ganulaméran

ARN messager (ARNm), protégé en 5', codant pour le domaine de liaison au récepteur (RBD) de la glycoprotéine spike (S) du SARS-CoV-2 (coronavirus 2 du syndrome respiratoire aigu sévère, GenBank: MN908947.3) avec des codons optimisés, exprimés sous forme de protéine de fusion, 5' avec un peptide signal de la glycoprotéine S allongé et 3' avec un domaine de trimérisation de la fibritine de T4 et le domaine transmembranaire (TM) de la glycoprotéine S, liés au moyen de deux peptides de liaison (linker) riches en glycine / sérine (GS), flanqués de régions 5' et 3' non traduites et d'une queue poly(A); contient de la N1-méthylpseudouridine au lieu de l'uridine (*tout*-U>$m^1\Psi$).

ganulamerán

RNA mensajero (mRNA), protegido en 5', que codifica para el dominio de unión al receptor (RBD) de la glicoproteína de la espícula (S) de SRAS-CoV-2 (coronavirus 2 del síndrome respiratorio agudo severo, GenBank: MN908947.3) con codones optimizados, expresado como una proteína de fusión, en 5' con un péptido señal de glicoproteína S extendido y en 3' con un dominio fibritina de trimerización de T4 y el dominio transmembrana (TM) de la glicoproteína S, conectado mediante dos péptidos enlazadores (linker) ricos en glicina/serina (GS), flanqueado por regiones 5' y 3' no traducidas y una cola poly(A); contiene N1-metilpseudouridina en lugar de uridina (*all*-U>$m^1\Psi$).

goflikiceptum #

goflikicept

human interleukin-1 receptor accessory protein fragment (21-358, 1-338 in the current sequence) fused via peptidyl linker ^{339}GSGGG^{343} to a human immunoglobulin G1 Fc fragment (344-570, C-terminal Lys clipped) variant (S>C^{477}, T>W^{489}, K>A^{532}), covalent dimer with human interleukin-1 receptor type 1 fragment (21-333, 1-313 in the current sequence) fused via peptidyl linker ^{314}GSGG^{318} to a human immunoglobulin G1 Fc fragment (319-545, C-terminal Lys clipped) variant (Y>C^{447}, T>S^{464}, L>A^{466}, F>K^{503}, Y>V^{505}), glycosylated, produced in Chinese hamster ovary (CHO) cells;
fusion protein comprising the (1-338)-fragment of the human interleukin 1 receptor accessory protein (IL1RAP, IL-1RAcP, interleukin-1 receptor 3, IL1R3), a GSGGG linker (339-343), and the (S>C^{477}, T>W^{489}, K>A^{532}) variant of the C-terminal 227-peptide (Fc fragment) of human immunoglobulin G1 (344-570), (349-324':352-327':477-447')-trisdisulfide with a fusion protein comprising the (21-333)-fragment of the precursor of human interleukin 1 receptor type 1 (IL1R1, IL1Rα, IL1R type I, p80, CD121a) (1-313), a GSGGG linker (314-318), and the (Y>C^{447}, T>S^{464}, L>A^{466}, F>K^{503}, Y>V^{505}) variant of the C-terminal 227-peptide (Fc fragment) of human immunoglobulin G1 (319-545), produced in Chinese hamster ovary (CHO) cells, glycoform alfa

goflikicept	fragment de la protéine accessoire du récepteur de l'interleukine 1 humaine (21-358, 1-338 dans la séquence actuelle) fusionné via un peptide liant ^{339}GSGGG^{343} au fragment Fc de l'immunoglobuline humaine G1 (344-570, C-terminal attaché Lys) variant (S>C^{477}, T>W^{489}, K>A^{532}), dimère covalent avec fragment de récepteur de l'interleukine-1 humaine de type 1 (21-333, 1-313 dans la séquence actuelle) fusionné via un peptide liant ^{314}GSGG^{318} à un fragment Fc d'immunoglobuline humaine G1 (319-545, attaché au variant C-terminal Lys) (Y>C^{447}, T>S^{464}, L>A^{466}, F>K^{503}, Y>V^{505}), glycosylé, produit dans des cellules ovariennes de hamster chinois (CHO); une protéine de fusion comprenant le fragment (1-338) de la protéine accessoire du récepteur de l'interleukine 1 humaine (IL1RAP, IL-1RAcP, récepteur 3 de l'interleukine-1, IL1R3), un linker GSGGG (339-343), et le variant (S>C^{477}, T>W^{489}, K>A^{532}) du peptide C-terminal-227 (fragment Fc) de l'immunoglobuline humaine G1 (344-570), (349-324': 352-327': 477-447') -trisdisulfure avec une protéine de fusion comprenant le fragment- (21-333) du précurseur du récepteur de l'interleukine humaine de type 1 (IL1R1, IL1Rα, IL1R type I, p80, CD121a) (1-313), une liaison GSGGG (314-318) et le variant (Y>C^{447}, T>S^{464,} L>A^{466}, F>K^{503}, Y>V^{505}) du peptide C-terminal-227 (fragment Fc) de l'immunoglobuline humaine G1 (319-545), produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa
goflikicept	receptor de la interleukina-1 humana fragmento de la proteína complemento (21-358, 1-338 en la secuencia actual) fusionado a través de un enlace peptidil ^{339}GSGGG^{343} a la inmunoglobulina humana G1 Fc fragmento (344-570, fijado al C-terminal Lis) variante (S>C^{477}, T>W^{489}, K>A^{532}), dímero covalente con receptor de interleukina-1 humana fragmento tipo 1 (21-333, 1-313 en la secuencia actual) fusionado a través del enlace peptidil ^{314}GSGG^{318} a una inmunoglobulina humana G1 Fc fragmento (319-545, fijado al C-terminal Lis) variante (Y>C^{447}, T>S^{464}, L>A^{466}, F>K^{503}, Y>V^{505}), glicosilado, producido en células ováricas de hámster Chino (CHO). una proteína de fusión que comprende el fragmento-(1-338) del receptor humano de la interleukina 1 proteína accesorio (IL1RAP, IL-1RAcP, interleukina-1 receptor 3, IL1R3), un enlace GSGGG (339-343), y la variante (S>C^{477}, T>W^{489}, K>A^{532}) del termina-C péptido-227 (Fc fragmento) de la inmunoglobulina humana G1 (344-570), (349-324':352-327':477-447')-trisdisulfuro con una proteína de fusión que comprende el fragmento-(21-333) del precursor del receptor tipo 1 de la interleukina humana (IL1R1, IL1Rα, IL1R tipo I, p80, CD121a) (1-313), un enlace GSGGG (314-318), y la (Y>C^{447}, T>S^{464}, L>A^{466}, F>K^{503}, Y>V^{505}) variante del terminal-C péptido-227 (Fc fragmento) de inmunoglobulina humana G1 (319-545), producido en células ováricas de hámster Chino (CHO), glicoforma alfa

Sequence / Séquence / Secuencia

IL1RAP-GSG$_3$-Fc

```
SERCDDWGLD TMRQIQVFED EPARIKCPLF EHFLKFNYST AHSAGLTLIW   50
YWTRQDRDLE EPINFRLPEN RISKEKDVLW FRPTLLNDTG NYTCMLRNTT  100
YCSKVAFPLE VVQKDSCFNS PMKLPVHKLY IEYGIQRITC PNVDGYFPSS  150
VKPTITWYMG CYKIQNFNNV IPEGMNLSFL IALISNNGNY TCVVTYPENG  200
RTFHLTRTLT VKVVGSPKNA VPPVIHSPND HVVYEKEPGE ELLIPCTVYF  250
SFLMDSRNEV WWTIDGKKPD DITIDVTINE SISHSRTEDE TRTQILSIKK  300
VTSEDLKRSY VCHARSAKGE VAKAAKVKQK VPAPRYTVGS GGGDKTHTCP  350
PCPAPELLGG PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW  400
YVDGVEVHNA KTKPREEQYN STYRVVSVLT VLHQDWLNGK EYKCKVSNKA  450
LPAPIEKTIS KAKGQPREPQ VYTLPPCRDE LTKNQVSLWC LVKGFYPSDI  500
AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SALTVDKSRW QQGNVFSCSV  550
MHEALHNHYT QKSLSLSPGK                                   570
```

IL1R1-GSG$_3$-Fc

```
DKCKEREEKI ILVSSANEID VRPCPLNPNE HKGTITWYKD DSKTPVSTEQ   50
ASRIHQHKEK LWFVPAKVED SGHYYCVVRN SSYCLRIKIS AKFVENEPNL  100
CYNAQAIFKQ KLPVAGDGGL VCPYMEFFKN ENNELPKLQW YKDCKPLLLD  150
NIHFSGVKDR LIVMNVAEKH RGNYTCHASY TYLGKQYPIT RVIEFITLEE  200
NKPTRPVIVS PANETMEVDL GSQIQLICNV TGQLSDIAYW KWNGSVIDED  250
DPVLGEDYYS VENPANKRRS TLITVLNISE IESRFYKHPF TCFAKNTHGI  300
DAAYIQLIYP VTNGSGGGDK THTCPPCPAP ELLGGPSVFL FPPKPKDTLM  350
ISRTPEVTCV VVDVSHEDPE VKFNWYVDGV EVHNAKTKPR EEQYNSTYRV  400
VSVLTVLHQD WLNGKEYKCK VSNKALPAPI EKTISKAKGQ PREPQVCTLP  450
PSRDELTKNQ VSLSCAVKGF YPSDIAVEWE SNGQPENNYK TTPPVLDSDG  500
SFKLVSKLTV DKSRWQQGNV FSCSVMHEAL HNHYTQKSLS LSPGK       545
```

Mutations / Mutations / Mutaciones

S^{477}>C, T^{489}>W, K^{532}>A
Y^{447}>C, $T^{464'}$>S, $L^{466'}$>A, $F^{503'}$>K, $Y^{505'}$>V

Post-translational modifications

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

Inter-chain: 349-324' 352-327' 477-447'

Intra-chain IL1RAP-GSG3-Fc : 4-102 27-94 117-161 140-192 246-312 384-444 490-548

Intra-chain IL1R1-GSG3-Fc : 3'-84' 24'-76' 101'-144' 122'-176' 228'-292' 359'-419' 465'-523'

Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación

N37, N87, N91, N98, N176, N189, N279, N420;
N80', N173', N213', N229', N243', N277', N313', N395'

Other modifications: K570, K545' clipped

imdevimabum #

imdevimab	immunoglobulin G1-lambda, anti-[*Homo sapiens* severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike (S) protein, receptor binding domain (RBD)], *Homo sapiens* monoclonal antibody; gamma1 heavy chain *Homo sapiens* (1-450) [VH (*Homo sapiens* IGHV3-30*01 (96.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (217) (121-218),hinge 1-15 (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS (449-450)) (121-450)], (223-215')-disulfide with lambda light chain *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV2-14*01 (93.9%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.10] (26-34.52-54.91-100) (1'-110') -*Homo sapiens* IGLC2*01 (100%) (111'-216')]; dimer (229-229":232-232")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa
imdévimab	immunoglobuline G1-lambda anti-[*Homo sapiens* protéine spike (S) du coronavirus 2 du syndrome respiratoire aigu sévère (SARS-CoV-2), domaine de liaison au récepteur (RBD)], anticorps monoclonal *Homo sapiens*;

chaîne lourde gamma1 *Homo sapiens* (1-450) [VH (*Homo sapiens* IGHV3-30*01 (96.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (217) (121-218), charnière 1-15 (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS (449-450)) (121-450)], (223-215')-disulfure avec la chaîne légère lambda *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV2-14*01 (93.9%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.10] (26-34.52-54.91-100) (1'-110') -*Homo sapiens* IGLC2*01 (100%) (111'-216')]; dimère (229-229":232-232")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

imdevimab

inmunoglobulina G1-lambda anti-[*Homo sapiens* proteína espícula (S) del coronavirus 2 del síndrome respiratorio agudo severo (SRAS-CoV-2), dominio de unión al receptor (RBD)], anticuerpo monoclonal *Homo sapiens*;
cadena pesada gamma1 *Homo sapiens* (1-450) [VH (*Homo sapiens* IGHV3-30*01 (96.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (217) (121-218), bisagra 1-15 (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS (449-450)) (121-450)], (223-215')-disulfuro con la cadena ligera lambda *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV2-14*01 (93.9%) -IGLJ3*02 (100%)) CDR-IMGT [9.3.10] (26-34.52-54.91-100) (1'-110') -*Homo sapiens* IGLC2*01 (100%) (111'-216')]; dímero (229-229":232-232")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVESGGG VVQPGRSLRL SCAASGFTFS NYAMYWVRQA PGKGLEWVAV  50
ISYDGSNKYY ADSVKGRFTI SRDNSKNTLY LQMNSLRTED TAVYYCASGS 100
DYGDYLLVYW 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
YDVSKRPSGV SNRFSGSKSG NTASLTISGL QSEDEADYYC NSLTSISTWV 100
FGGGTKLTVL GQPKAAPSVT LFPPSSEELQ ANKATLVCLI SDFYPGAVTV 150
AWKADSSPVK AGVETTTPSK QSNNKYAASS YLSLTPEQWK SHRSYSCQVT 200
HEGSTVEKTV APTECS                                      216
```

Post-translational modifications
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-terminal glutamine cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"
L VL Q1:
1', 1'"

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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
450, 450"

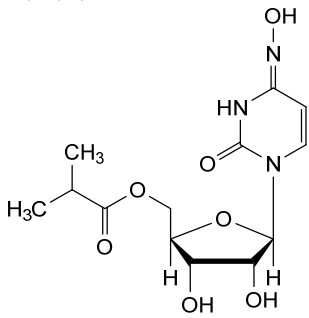
molnupiravirum

molnupiravir — N^4-hydroxycytidine 5'-(2-methylpropanoate)

molnupiravir — 5'-(2-méthylpropanoate) de N^4-hydroxycytidine

molnupiravir — 5'-(2-metilpropanoato) de N^4-hidroxicitidina

$C_{13}H_{19}N_3O_7$



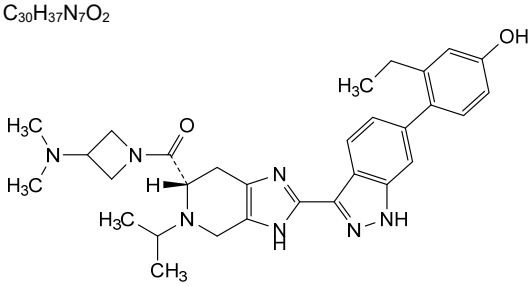
nezulcitinibum

nezulcitinib — [3-(dimethylamino)azetidin-1-yl]{(6*S*)-2-[6-(2-ethyl-4-hydroxyphenyl)-1*H*-indazol-3-yl]-5-(propan-2-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-6-yl}methanone

nézulcitinib — [3-(diméthylamino)azétidin-1-yl]{(6*S*)-2-[6-(2-éthyl-4-hydroxyphényl)-1*H*-indazol-3-yl]-5-(propan-2-yl)-4,5,6,7-tétrahydro-1*H*-imidazo[4,5-*c*]pyridin-6-yl}méthanone

nezulcitinib — [3-(dimetilamino)azetidin-1-il]{(6*S*)-2-[6-(2-etil-4-hidroxifenil)-1*H*-indazol-3-il]-5-(propan-2-il)-4,5,6,7-tetrahidro-1*H*-imidazo[4,5-*c*]piridin-6-il}metanona

$C_{30}H_{37}N_7O_2$



pemziviptadilum #

pemziviptadil — human L-methionyl vasoactive intestinal peptide (2-29) fused to 121 repeats of different elastin-derived pentapeptides (VPGVG, VPGGG, VPGAG, VPGWP) (30-634), produced in *Escherichia coli;*
fusion protein comprising L-methionyl (1)-vasoactive intestinal polypeptide (human VIP) (2-29) and an elastin-like artificial polymer (30-629) of 120 alternating pentapeptides of three types VPGVG, VPGGG, and VPGAG, and a C-terminal pentapeptide VPGWP (630-634), produced in *Escherichia coli*

pemziviptadil

L-méthionyl peptide vasoactif intestinal humain (2-29) fusionné à 121 répétitions de différents pentapeptides dérivés de l'élastine (VPGVG, VPGGG, VPGAG, VPGWP) (30-634), produits dans *Escherichia coli* ;
protéine de fusion comprenant le polypeptide intestinal vasoactif L-méthionyl (1) (VIP humain) (2-29) et un polymère artificiel de type élastine (30-629) de 120 pentapeptides alternés de trois types VPGVG, VPGGG et VPGAG, et un pentapeptide C-terminal VPGWP (630-634), produit dans *Escherichia coli*

pemziviptadil

péptido humano L-metionil vasoactivo intestinal (2-29) fusionado a 121 repeticiones de pentapéptidos derivados de elastina diferentes (VPGVG, VPGGG, VPGAG, VPGWP) (30-634), producido en *Escherichia coli;*
proteína de fusión que comprende polipéptido intestinal vasoactivo L-metionil (1) (humano VIP) (2-29) y un polímero artificial parecido a la elastina (30-629) de 120 pentapéptidos alternos de tres tipos VPGVG, VPGGG, y VPGAG, y un pentapéptido C-terminal VPGWP (630-634), producido en *Escherichia coli*

Sequence / Séquence / Secuencia

```
MHSDAVFTDN YTRLRKQMAV KKYLNSILNV PGVGVPGVGV PGGGVPGAGV   50
PGVGVPGVGV PGVGVPGGGV PGAGVPGGGV PGVGVPGVGV PGGGVPGAGV  100
PGVGVPGVGV PGVGVPGGGV PGAGVPGGGV PGVGVPGVGV PGGGVPGAGV  150
PGVGVPGVGV PGVGVPGGGV PGAGVPGGGV PGVGVPGVGV PGGGVPGAGV  200
PGVGVPGVGV PGVGVPGGGV PGAGVPGGGV PGVGVPGVGV PGGGVPGAGV  250
PGVGVPGVGV PGVGVPGGGV PGAGVPGGGV PGVGVPGVGV PGGGVPGAGV  300
PGVGVPGVGV PGVGVPGGGV PGAGVPGGGV PGVGVPGVGV PGGGVPGAGV  350
PGVGVPGVGV PGVGVPGGGV PGAGVPGGGV PGVGVPGVGV PGGGVPGAGV  400
PGVGVPGVGV PGVGVPGGGV PGAGVPGGGV PGVGVPGVGV PGGGVPGAGV  450
PGVGVPGVGV PGVGVPGGGV PGAGVPGGGV PGVGVPGVGV PGGGVPGAGV  500
PGVGVPGVGV PGVGVPGGGV PGAGVPGGGV PGVGVPGVGV PGGGVPGAGV  550
PGVGVPGVGV PGVGVPGGGV PGAGVPGGGV PGVGVPGVGV PGGGVPGAGV  600
PGVGVPGVGV PGVGVPGGGV PGAGVPGGGV PGWP                   634
```

positions 30-634: 12 × pattern AABCAAABCB of 10 pentapeptides of three types A = **VPGVG**, B = **VPGGG,** and C = **VPGAG** plus a C-terminal pentapeptide **VPGWP**

pidacmeranum #

pidacmeran

self-replicating messenger RNA (mRNA), 5'-capped, encoding *Venezuelan equine encephalitis virus* (VEEV) RNA-dependent RNA polymerase (VEEV proteins nsP1, nsP2, nsP3 and nsP4) and a full-length codon-optimised pre-fusion stabilised conformation variant (K986P and V987P) of the SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2, GenBank: MN908947.3) spike (S) glycoprotein, flanked by 5' and 3' untranslated regions and a 3' poly(A) tail; replication of the RNA is under control of a VEEV subgenomic promoter.

pidacméran

ARN messager (ARNm) auto-répliquant, protégé en 5', codant pour l'ARN polymérase ARN-dépendante du *virus de l'encéphalite équine vénézuélienne* (protéines VEEV nsP1, nsP2, nsP3 et nsP4) et une variante complète de pré-fusion de conformation stabilisée (K986P et V987P) de la glycoprotéine spike (S) du SARS-CoV-2 (coronavirus 2 du syndrome respiratoire aigu sévère, GenBank: MN908947.3) avec des codons optimisés, flanqués de régions 5 'et 3' non traduites une queue poly(A) 3'; la réplication de l'ARN est sous le contrôle du promoteur sous-génomique de VEEV.

pidacmerán	RNA mensajero auto replicativo (mRNA), protegido en 5', que codifica para la RNA polimerasa dependiente de RNA del *virus de la encefalitis equina venezolana* (proteínas VEEV nsP1, nsP2, nsP3 y nsP4) y una variante pre-fusión completa de conformación estabilizada (K986P and V987P) de la glicoproteína de la espícula (S) del SRAS-CoV-2 (coronavirus 2 del síndrome respiratorio agudo severo, GenBank: MN908947.3) con codones optimizados, flanqueada por regiones 5' y 3' no traducidas y una cola poly(A) en 3'; la replicación del ARN está bajo el control del promotor subgenómico de VEEV.
regdanvimabum #	
regdanvimab	immunoglobulin G1-lambda, anti-[*Homo sapiens* severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike (S) protein, receptor binding domain (RBD)], humanized and *Homo sapiens* monoclonal antibody; gamma1 heavy chain humanized (1-458) [VH (*Homo sapiens* IGHV2-70*12 (92.9%) -(IGHD) - IGHJ6*01 (100%)) CDR-IMGT [10.7.20] (26-35.53-59.98-117) (1-128) -*Homo sapiens* IGHG1*08p (100%) G1m3,1 (CH1 R120 (225) (129-226), hinge 1-15 (227-241), CH2 (242-351), CH3 D12 (367), L14 (369) (352-456), CHS (457-458)) (129-458)], (231-215')-disulfide with lambda light chain *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV1-51*01 (100%) - IGLJ2*01 (90.9%) K123>E (106)) CDR-IMGT [8.3.11] (26-33.51-53.90-100) (1'-110') -*Homo sapiens* IGLC2*01 (98.1%) S45>G (156), T82>K (167) (111'-216')]; dimer (237-237":240-240")-bisdisulfide, produced in a Chinese hamster ovary (CHO) cell line derived from CHO-K1, glycoform alfa
regdanvimab	immunoglobuline G1-lambda anti-[*Homo sapiens* protéine spike (S) du coronavirus 2 du syndrome respiratoire aigu sévère (SARS-CoV-2), domaine de liaison au récepteur (RBD)], anticorps monoclonal humanisé et *Homo sapiens*; chaîne lourde gamma1 humanisée (1-458) [VH (*Homo sapiens* IGHV2-70*12 (92.9%) -(IGHD) - IGHJ6*01 (100%)) CDR-IMGT [10.7.20] (26-35.53-59.98-117) (1-128) -*Homo sapiens* IGHG1*08p (100%) G1m3,1 (CH1 R120 (225) (129-226), charnière 1-15 (227-241), CH2 (242-351), CH3 D12 (367), L14 (369) (352-456), CHS (457-458)) (129-458)], (231-215')-disulfure avec la chaîne légère lambda *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV1-51*01 (100%) -IGLJ2*01 (90.9%) K123>E (106)) CDR-IMGT [8.3.11] (26-33.51-53.90-100) (1'-110') -*Homo sapiens* IGLC2*01 (98.1%) S45>G (156), T82>K (167) (111'-216')]; dimère (237-237":240-240")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) dérivant de la lignée cellulaire CHO-K1, glycoforme alfa

regdanvimab

inmunoglobulina G1-lambda anti-[*Homo sapiens* proteína espícula (S) del coronavirus 2 del síndrome respiratorio agudo severo (SRAS-CoV-2), dominio de unión al receptor (RBD)], anticuerpo monoclonal humanizado y *Homo sapiens*; cadena pesada gamma1 humanizada (1-458) [VH (*Homo sapiens* IGHV2-70*12 (92.9%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [10.7.20] (26-35.53-59.98-117) (1-128) -*Homo sapiens* IGHG1*08p (100%) G1m3,1 (CH1 R120 (225) (129-226), bisagra 1-15 (227-241), CH2 (242-351), CH3 D12 (367), L14 (369) (352-456), CHS (457-458)) (129-458)], (231-215')-disulfuro con la cadena ligera lambda *Homo sapiens* (1'-216') [V-LAMBDA (*Homo sapiens* IGLV1-51*01 (100%) -IGLJ2*01 (90.9%) K123>E (106)) CDR-IMGT [8.3.11] (26-33.51-53.90-100) (1'-110') -*Homo sapiens* IGLC2*01 (98.1%) S45>G (156), T82>K (167) (111'-216')]; dímero (237-237":240-240")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular derivada de CHO-K1, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QITLKESGPT LVKPTQTLTL TCSFSGFSLS TSGVGVGWIR QPPGKALEWL  50
ALIDWDDNKY HTTSLKTRLT ISKDTSKNQV VLTMTNMDPV DTATYYCARI 100
PGFLRYRNRY YYYGMDVWGQ GTTVTVSSAS TKGPSVFPLA PSSKSTSGGT 150
AALGCLVKDY FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP 200
SSSLGTQTYI CNVNHKPSNT KVDKRVEPKS CDKTHTCPPC PAPELLGGPS 250
VFLFPPKPKD TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT 300
KPREEQYNST YRVVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA 350
KGQPREPQVY TLPPSRDELT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN 400
NYKTTPPVLD SDGSFFLYSK LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK 450
SLSLSPGK                                               458
```

Light chain / Chaîne légère / Cadena ligera

```
ELVLTQPPSV SAAPGQKVTI SCSGSSSNIG NNYVSWYQQL PGTAPKLLIY  50
DNNKRPSGIP DRFSGSKSGT SATLGITGLQ TGDEADYYCG TWDSSLSAGV 100
FGGGTELTVL GQPKAAPSVT LFPPSSEELQ ANKATLVCLI SDFYPGAVTV 150
AWKADGSPVK AGVETTKPSK QSNNKYAASS YLSLTPEQWK SHRSYSCQVT 200
HEGSTVEKTV APTECS                                      216
```

Post-translational modifications

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

Intra-H (C23-C104) 22-97 155-211 272-332 378-436
22"-97" 155"-211" 272"-332" 378"-436"

Intra-L (C23-C104) 22'-89' 138'-197'
22'"-89'" 138'"-197'"

Inter-H-L (h 5-CL 126) 231-215' 231"-215'"

Inter-H-H (h 11, h 14) 237-237" 240-240"

N-terminal glutamine cyclization to pyroglutamyl (pE, 5-oxoprolyl)

H VH Q1:
1, 1"

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

H CH2 N84.4:
308, 308"

Fucosylated complex bi-antennary CHO-type glycans (G0F predominant) / glycanes de type CHO bi-antennaires complexes fucosylés (G0F prédominant) / glicanos de tipo CHO biantenarios complejos fucosilados (G0F predominante).

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal

H CHS K2:
458, 458"

reluscovtogenum ralaplasmidum

reluscovtogene ralaplasmid

DNA plasmid expressing a consensus sequence* of the full-length SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) spike (S) glycoprotein, with an N-terminal IgE leader sequence, under control of the human CMV promoter (hCMV promoter) and a bovine growth hormone poly-adenylation signal (bGH poly(A)). The plasmid also contains a pUC origin of replication and a kanamycin antibiotic resistance gene.
*based upon sequences published on GISAID (Global Initiative on Sharing All Influenza Data) in early 2020.

réluscovtogène ralaplasmide	plasmide d'ADN exprimant une séquence consensus* complète de la glycoprotéine spike (S) du SARS-CoV-2 (coronavirus 2 du syndrome respiratoire aigu sévère), avec une séquence leader N-terminale d'IgE, sous contrôle du promoteur du CMV humain (promoteur hCMV) et d'un signal de polyadénylation de l'hormone de croissance bovine (bGH poly(A)). Le plasmide contient également une origine de réplication pUC et un gène de résistance à la kanamycine. *basé sur des séquences publiées dans GISAID (Global Initiative on Sharing All Influenza Data) début 2020.
reluscovtogén ralaplasmida	plásmido de DNA que expresa una secuencia consenso* completa de la glicoproteína de la espícula (S) de SARS-CoV-2 (coronavirus 2 del síndrome respiratorio agudo severo), con una secuencia líder N-terminal de la IgE, bajo el control del promotor de CMV humano (promotor hCMV) y una señal de poliadenilación de la hormona de crecimiento bovina (bGH poly(A)). El plásmido contiene también un origen de replicación pUC y un gen de resistencia al antibiótico kanamicina. *basada en secuencias publicadas en GISAID (Global Initiative on Sharing All Influenza Data) a principios de 2020.

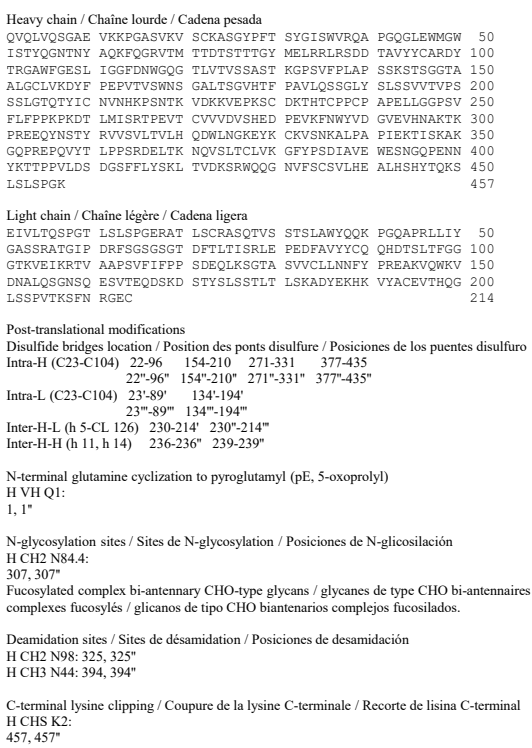
sotrovimabum #

sotrovimab	immunoglobulin G1-kappa, anti-[*Homo sapiens* severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike (S) protein, receptor binding domain (RBD)], *Homo sapiens* monoclonal antibody; gamma1 heavy chain *Homo sapiens* (1-457) [VH (*Homo sapiens* IGHV1-18*01 (92.9%) -(IGHD) -IGHJ5*01 (92.9%)) CDR-IMGT [8.8.20] (26-33.51-58.97-116) (1-127) -*Homo sapiens* IGHG1*01 G1m17,1, G1v24 CH3 L107, S114(CH1 K120 (224) (128-225), hinge 1-15 (226-240), CH2 (241-350), CH3 D12 (366), L14 (368), M107>L (438), N114>S (444) (351-455), CHS (456-457)) (128-457)], (230-214')-disulfide with kappa light chain *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (96.7%) -IGKJ4*01 (100%)) CDR-IMGT [7.3.8] (27-33.51-53.90-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dimer (236-236":239-239")-bisdisulfide, produced in a Chinese hamster ovary (CHO)-K1 cell line, glycoform alfa
sotrovimab	immunoglobuline G1-kappa anti-[*Homo sapiens* protéine spike (S) du coronavirus 2 du syndrome respiratoire aigu sévère (SARS-CoV-2), domaine de liaison au récepteur (RBD)], anticorps monoclonal *Homo sapiens*;

chaîne lourde gamma1 *Homo sapiens* (1-457) [VH (*Homo sapiens* IGHV1-18*01 (92.9%) -(IGHD) -IGHJ5*01 (92.9%)) CDR-IMGT [8.8.20] (26-33.51-58.97-116) (1-127) -*Homo sapiens* IGHG1*01 G1m17,1, G1v24 CH3 L107, S114 (CH1 K120 (224) (128-225), charnière 1-15 (226-240), CH2 (241-350), CH3 D12 (366), L14 (368), M107>L (438), N114>S (444) (351-455), CHS (456-457)) (128-457)], (230-214')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (96.7%) -IGKJ4*01 (100%)) CDR-IMGT [7.3.8] (27-33.51-53.90-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dimère (236-236":239-239")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-K1, glycoforme alfa

sotrovimab

inmunoglobulina G1-kappa anti-[*Homo sapiens* proteína espícula (S) del coronavirus 2 del síndrome respiratorio agudo severo (SRAS-CoV-2), dominio de unión al receptor (RBD)], anticuerpo monoclonal *Homo sapiens*;
cadena pesada gamma1 *Homo sapiens* (1-457) [VH (*Homo sapiens* IGHV1-18*01 (92.9%) -(IGHD) -IGHJ5*01 (92.9%)) CDR-IMGT [8.8.20] (26-33.51-58.97-116) (1-127) -*Homo sapiens* IGHG1*01 G1m17,1, G1v24 CH3 L107, S114 (CH1 K120 (224) (128-225), bisagra 1-15 (226-240), CH2 (241-350), CH3 D12 (366), L14 (368), M107>L (438), N114>S (444) (351-455), CHS (456-457)) (128-457)], (230-214')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (96.7%) -IGKJ4*01 (100%)) CDR-IMGT [7.3.8] (27-33.51-53.90-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dímero (236-236":239-239")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-K1, forma glicosilada alfa



Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGASVKV SCKASGYPFT SYGISWVRQA PGQGLEWMGW  50
ISTYQGNTNY AQKFQGRVTM TTDTSTTTGY MELRRLRSDD TAVYYCARDY 100
TRGAWFGESL IGGFDNWGQG TLVTVSSAST KGPSVFPLAP SSKSTSGGTA 150
ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY SLSSVVTVPS 200
SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKTHTCPPCP APELLGGPSV 250
FLFPPKPKDT LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK 300
PREEQYNSTY RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK 350
GQPREPQVYT LPPSRDELTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN 400
YKTTPPVLDS DGSFFLYSKL TVDKSRWQQG NVFSCSVLHE ALHSHYTQKS 450
LSLSPGK                                               457
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Light chain / Chaîne légère / Cadena ligera

```
EIVLTQSPGT LSLSPGERAT LSCRASQTVS STSLAWYQQK PGQAPRLLIY  50
GASSRATGIP DRFSGSGSGT DFTLTISRLE PEDFAVYYCQ QHDTSLTFGG 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                       214
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 154-210 271-331 377-435
22"-96" 154"-210" 271"-331" 377"-435"
Intra-L (C23-C104) 23'-89' 134'-194'
23'"-89'" 134'"-194'"
Inter-H-L (h 5-CL 126) 230-214' 230"-214'"
Inter-H-H (h 11, h 14) 236-236" 239-239"

N-terminal glutamine cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
307, 307"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

Deamidation sites / Sites de désamidation / Posiciones de desamidación
H CH2 N98: 325, 325"
H CH3 N44: 394, 394"

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
457, 457"

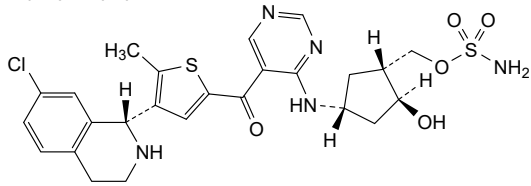
subasumstatum

subasumstat — {(1*R*,2*S*,4*R*)-4-[(5-{4-[(1*R*)-7-chloro-1,2,3,4-tetrahydroisoquinolin-1-yl]-5-methylthiophene-2-carbonyl}pyrimidin-4-yl)amino]-2-hydroxycyclopentyl}methyl sulfamate

subasumstat — sulfamate de {(1*R*,2*S*,4*R*)-4-[(5-{4-[(1*R*)-7-chloro-1,2,3,4-tétrahydroisoquinoléin-1-yl]-5-méthylthiophène-2-carbonyl}pyrimidin-4-yl)amino]-2-hydroxycyclopentyl}méthyle

subasumstat — sulfamato de {(1*R*,2*S*,4*R*)-4-[(5-{4-[(1*R*)-7-cloro-1,2,3,4-tetrahidroisoquinolein-1-il]-5-metiltiofeno-2-carbonil}pirimidin-4-il)amino]-2-hidroxiciclopentil}metilo

$C_{25}H_{28}ClN_5O_5S_2$



tixagevimabum #

tixagevimab — immunoglobulin G1-kappa, anti-[*Homo sapiens* severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike (S) protein, receptor binding domain (RBD)], *Homo sapiens* monoclonal antibody; gamma1 heavy chain *Homo sapiens* (1-453) [VH (*Homo sapiens* IGHV1-58*01 (98.0%) -(IGHD) -IGHJ3*02 (93.8%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Homo sapiens* IGHG1*03 G1m3, nG1m1, G1v21 CH2 Y15.1, T16, E18, G1v39 CH2 F1.3, E1.2, S116 (CH1 R120 (220) (124-221), hinge 1-15 (222-236), CH2 L1.3>F (240), L1.2>E (241), M15.1>Y (258), S16>T (260), T18>E (262), P116>S (337) (237-346), CH3 E12 (362), M14 (364) (347-451), CHS (452-453)) (124-453)], (226-216')-disulfide with kappa light chain *Homo sapiens* (1'-216') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (98.9%) -IGKJ1*01 (100%)) CDR-IMGT [7.3.10] (27-33.51-53.90-99) (1'-109') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (155), V101 (193) (110'-216')]; dimer (232-232":235-235")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

tixagévimab — immunoglobuline G1-kappa anti-[*Homo sapiens* protéine spike (S) du coronavirus 2 du syndrome respiratoire aigu sévère (SARS-CoV-2), domaine de liaison au récepteur (RBD)], anticorps monoclonal *Homo sapiens;*
chaîne lourde gamma1 *Homo sapiens* (1-453) [VH (*Homo sapiens* IGHV1-58*01 (98.0%) -(IGHD) -IGHJ3*02 (93.8%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Homo sapiens* IGHG1*03 G1m3, nG1m1, G1v21 CH2 Y15.1, T16, E18, G1v39 CH2 F1.3, E1.2, S116 (CH1 R120 (220) (124-221), charnière 1-15 (222-236), CH2 L1.3>F (240), L1.2>E (241), M15.1>Y (258), S16>T (260), T18>E (262), P116>S (337) (237-346), CH3 E12 (362), M14 (364) (347-451), CHS (452-453)) (124-453)], (226-216')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-216') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (98.9%) -IGKJ1*01 (100%)) CDR-IMGT [7.3.10] (27-33.51-53.90-99) (1'-109') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (155), V101 (193) (110'-216')]; dimère (232-232":235-235")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

tixagevimab

inmunoglobulina G1-kappa anti-[*Homo sapiens* proteína espícula (S) del coronavirus 2 del síndrome respiratorio agudo severo (SRAS-CoV-2), dominio de unión al receptor (RBD)], anticuerpo monoclonal *Homo sapiens*;
cadena pesada gamma1 *Homo sapiens* (1-453) [VH (*Homo sapiens* IGHV1-58*01 (98.0%) -(IGHD) -IGHJ3*02 (93.8%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Homo sapiens* IGHG1*03 G1m3, nG1m1, G1v21 CH2 Y15.1, T16, E18, G1v39 CH2 F1.3, E1.2, S116 (CH1 R120 (220) (124-221), bisagra 1-15 (222-236), CH2 L1.3>F (240), L1.2>E (241), M15.1>Y (258), S16>T (260), T18>E (262), P116>S (337) (237-346), CH3 E12 (362), M14 (364) (347-451), CHS (452-453)) (124-453)], (226-216')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-216') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (98.9%) -IGKJ1*01 (100%)) CDR-IMGT [7.3.10] (27-33.51-53.90-99) (1'-109') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (155), V101 (193) (110'-216')]; dímero (232-232":235-235")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QMQLVQSGPE VKKPGTSVKV SCKASGFTFM SSAVQWVRQA RGQRLEWIGW  50
IVIGSGNTNY AQKFQERVTI TRDMSTSTAY MELSSLRSED TAVYYCAAPY 100
CSSISCNDGF DIWGQGTMVT VSSASTKGPS VFPLAPSSKS TSGGTAALGC 150
LVKDYFPEPV TVSWNSGALT SGVHTFPAVL QSSGLYSLSS VVTVPSSSLG 200
TQTYICNVNH KPSNTKVDKR VEPKSCDKTH TCPPCPAPEF EGGPSVFLFP 250
PKPKDTLYIT REPEVTCVVV DVSHEDPEVK FNWYVDGVEV HNAKTKPREE 300
QYNSTYRVVS VLTVLHQDWL NGKEYKCKVS NKALPASIEK TISKAKGQPR 350
EPQVYTLPPS REEMTKNQVS LTCLVKGFYP SDIAVEWESN GQPENNYKTT 400
PPVLDSDGSF FLYSKLTVDK SRWQQGNVFS CSVMHEALHN HYTQKSLSLS 450
PGK                                                     453
```

Light chain / Chaîne légère / Cadena ligera

```
EIVLTQSPGT LSLSPGERAT LSCRASQSVS SSYLAWYQQK PGQAPRLLIY  50
GASSRATGIP DRFSGSGSGT DFTLTISRLE PEDFAVYYCQ HYGSSRGWTF 100
GQGTKVEIKR TVAAPSVFIF PPSDEQLKSG TASVVCLLNN FYPREAKVQW 150
KVDNALQSGN SQESVTEQDS KDSTYSLSST LTLSKADYEK HKVYACEVTH 200
QGLSSPVTKS FNRGEC                                       216
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 101-106 150-206 267-327 373-431
22"-96" 101"-106" 150"-206" 267"-327" 373"-431"
Intra- H (CDR3) 101-106
101"-106"
Intra-L (C23-C104) 23'-89' 136'-196'
23'"-89'" 136'"-196'"
Inter-H-L (h 5-CL 126) 226-216' 226"-216'"
Inter-H-H (h 11, h 14) 232-232" 235-235"

N-terminal glutamine cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
303, 303"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
453, 453"

tozinameranum #

tozinameran

messenger RNA (mRNA), 5'-capped, encoding a full-length, codon-optimised pre-fusion stabilised conformation variant (K986P and V987P) of the SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2, GenBank: MN908947.3) spike (S) glycoprotein, flanked by 5' and 3' untranslated regions and a 3' poly(A) tail; contains N1-methylpseudouridine instead of uridine (*all*-U>$m^1\Psi$).

tozinaméran	ARN messager (ARNm), protégé en 5', codant pour un variant de pré-fusion stabilisé en conformation (K986P et V987P) de la glycoprotéine spike (S) du SARS-CoV-2 (coronavirus 2 du syndrome respiratoire aigu sévère, GenBank: MN908947.3) complet, avec des codons optimisés, flanqués de régions 5' et 3' non traduites et d'une queue poly(A) 3'; contient de la N1-méthylpseudouridine au lieu de l'uridine (*tout*-U>m$^1\Psi$).
tozinamerán	RNA mensajero (mRNA), protegido en 5', que codifica para una variante pre-fusión de conformación estabilizada (K986P and V987P) de la glicoproteína de la espícula (S) del SRAS-CoV-2 (coronavirus 2 del síndrome respiratorio agudo severo, GenBank: MN908947.3) completa, con codones optimizados, flanqueada por regiones 5' y 3' no traducidas y una cola poly(A) en 3'; contiene N1-metilpseudouridina en lugar de uridina (*all*-U>m$^1\Psi$).

zansecimabum #

zansecimab	immunoglobulin G4-kappa, anti-[*Homo sapiens* ANGPT2 (angiopoietin 2)], humanized monoclonal antibody; gamma4 heavy chain humanized (1-447) [VH (*Homo sapiens* IGHV1-18*01 (86.7%) -(IGHD) -IGHJ4*01 (93.3%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -*Homo sapiens* IGHG4*01, G4v5 h P10,G4v4 CH2 A1.3, A1.2 (CH1 (122-219), hinge 1-12 S10>P (229) (220-231), CH2 F1.3>A (235), L1.2>A (236) (232-341), CH3 (342-446), CHS K>del (447)) (122-447)], (135-214')-disulfide with kappa light chain humanized (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (83.2%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dimer (227-227":230-230")-bisdisulfide, produced in a Chinese hamster ovary (CHO) cell line derived from CHO-GSKO, glycoform alfa
zansécimab	immunoglobuline G4-kappa anti-[*Homo sapiens* ANGPT2 (angiopoietin 2)], anticorps monoclonal humanisé; chaîne lourde gamma4 humanisée (1-447) [VH (*Homo sapiens* IGHV1-18*01 (86.7%) -(IGHD) - IGHJ4*01 (93.3%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -*Homo sapiens* IGHG4*01 G4v5 h P10,G4v4 CH2 A1.3, A1.2 (CH1 (122-219), charnière 1-12 S10>P (229) (220-231), CH2 F1.3>A (235), L1.2>A (236) (232-341), CH3 (342-446), CHS K>del (447)) (122-447)], (135-214')-disulfure avec la chaîne légère kappa humanisée (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (83.2%) - IGKJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dimère (227-227":230-230")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) dérivant de la lignée cellulaire CHO-GSKO, glycoforme alfa
zansecimab	inmunoglobulina G4-kappa anti-[*Homo sapiens* ANGPT2 (angiopoyetina 2)], anticuerpo monoclonal humanizado;

cadena pesada gamma4 humanizada (1-447) [VH (*Homo sapiens* IGHV1-18*01 (86.7%) -(IGHD) - IGHJ4*01 (93.3%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -*Homo sapiens* IGHG4*01 G4v5 h P10,G4v4 CH2 A1.3, A1.2 (CH1 (122-219), bisagra 1-12 S10>P (229) (220-231), CH2 F1.3>A (235), L1.2>A (236) (232-341), CH3 (342-446), CHS K>del (447)) (122-447)], (135-214')-disulfuro con la cadena ligera kappa humanizada (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (83.2%) -IGKJ4*01 (100%)) CDR-IMGT [6.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (153), V101 (191) (108'-214')]; dímero (227-227":230-230")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular derivada de CHO-GSKO, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGASVKV SCKASGYSFT DYNMVWVRQA PGQGLEWMGY  50
IDPYNGGTGY NQKFEGRVTM TTDTSTSTAY MELRSLRSDD TAVYYCARTR 100
DRYDVWYFDV WGQGTLVTVS SASTKGPSVF PLAPCSRSTS ESTAALGCLV 150
KDYFPEPVTV SWNSGALTSG VHTFPAVLQS SGLYSLSSVV TVPSSSLGTK 200
TYTCNVDHKP SNTKVDKRVE SKYGPPCPPC PAPEAAGGPS VFLFPPKPKD 250
TLMISRTPEV TCVVVDVSQE DPEVQFNWYV DGVEVHNAKT KPREEQFNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKGLP SSIEKTISKA KGQPREPQVY 350
TLPPSQEEMT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD 400
SDGSFFLYSR LTVDKSRWQE GNVFSCSVMH EALHNHYTQK SLSLSLG    447
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Light chain / Chaîne légère / Cadena ligera

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DIQMTQSPSS VSASVGDRVT ITCKASQDVY IAVAWYQQKP GKAPKLLIYW  50
ASTRDTGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCHQ YSSYPPTFGG 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 148-204 262-322 368-426
22"-96" 148"-204" 262"-322" 368"-426"
Intra-L (C23-C104) 23'-88' 134'-194'
23'"-88"' 134'"-194'"
Inter-H-L (CH1 10-CL 126) 135-214' 135"-214'"
Inter-H-H (h 8, h 11) 227-227" 230-230"

N-terminal glutamine cyclization to pyroglutamyl (pE, 5-oxoprolyl)
H VH Q1:
1, 1"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
298, 298"
Fucosylated complex bi-antennary CHO-type glycans (G0F predominant) / glycanes de type CHO bi-antennaires complexes fucosylés (G0F prédominant) / glicanos de tipo CHO biantenarios complejos fucosilados (G0F predominante).

zorecimeranum #

zorecimeran — messenger RNA (mRNA), 5'-capped, encoding a full-length codon-optimised pre-fusion stabilized conformation variant (K986P and V987P) of the SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2; NC_045512.2) spike (S) glycoprotein, flanked by 5' and 3' untranslated regions; the 3' untranslated region comprises a part of the human alpha globin gene 3' UTR sequence element, a synthetic poly(A) tail and a poly(C)-rich sequence followed by a histone stem loop sequence as a 3' tail.

zoréciméran — ARN messager (ARNm), protégé en 5', codant pour un variant de pré-fusion stabilisé en conformation (K986P et V987P) de la glycoprotéine spike (S) du SARS-CoV-2 (coronavirus 2 du syndrome respiratoire aigu sévère), NC_045512.2) complet, avec des codons optimisés, flanqués de régions 5' et 3' non traduites. La région 3' non traduite comprend une partie de l'élément de séquence 3' UTR du gène de l'alpha globine humaine, une queue poly(A) synthétique et une séquence riche en poly(C) suivie d'une séquence d'histones stem-loop comme extrémité en 3'.

zorecimerán	RNA mensajero (mRNA), protegido en 5', que codifica para una variante pre-fusión de conformación estabilizada (K986P and V987P) de la glicoproteína de la espícula (S) del SRAS-Cov-2 (coronavirus 2 del síndrome respiratorio agudo severo, NC_045512.2) completa, con codones optimizados, flanqueada por regiones 5' y 3' no traducidas. La región 3' no traducida comprende una parte del elemento secuencia 3' UTR del gen de la alfa globina humana, una cola poly(A) sintética y una secuencia rica en poly(C) seguida de una secuencia de histona stem-loop cola 3'.

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/

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

Recommended International Nonproprietary Names (Rec. INN): List 76
Dénominations communes internationales recommandées (DCI Rec.): Liste 76
Denominaciones Comunes Internacionales Recomendadas (DCI Rec.): Lista 76
(WHO Drug Information, Vol. 30, No. 3, 2016)

p.483 **blontuvetmabum #**

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

immunoglobulin G2_V-kappa-C-lambda, anti-[***Canis lupus familiaris*** MS4A1 (membrane-spanning 4-domains subfamily A member 1, CD20)], caninized monoclonal antibody; gamma2 heavy chain chimeric (1-448) [*Mus musculus* VH (*Mus musculus* IGHV1-15*01 -(IGHD) -IGHJ1*03) [8.8.6] (1-113) -*Canis lupus familiaris* IGHG2*02 (CH1 T26>Q (131) (114-211), hinge (212-229), CH2 (230-339), CH3 (340-446), CHS (447-448)) (114-448)], (128-218')-disulfide with V-kappa-C-lambda light chain chimeric (1'-219') [*Mus musculus* V-KAPPA (*Mus musculus* IGKV8-30*01 -IGKJ5*01) [12.3.9] (1'-112') -*Canis lupus familiaris* IGL1CS1*01 V45.3>I (162) (114'-219')]; dimer (225-225'':228-228'')-bisdisulfide

immunoglobuline G2_V-kappa-C-lambda, anti-[***Canis lupus familiaris*** MS4A1 (membre 1 de la sous-famille A à 4 domaines transmembranaires, CD20)], anticorps monoclonal caninisé;
chaîne lourde gamma2 chimérique (1-448) [*Mus musculus* VH (*Mus musculus* IGHV1-15*01 -(IGHD) -IGHJ1*03) [8.8.6] (1-113) -*Canis lupus familiaris* IGHG2*02 (CH1 T26>Q (131) (114-211), charnière (212-229), CH2 (230-339), CH3 (340-446), CHS (447-448)) (114-448)], (128-218')-disulfure avec la chaîne légère V-kappa-C-lambda chimérique (1'-219') [*Mus musculus* V-KAPPA (*Mus musculus* IGKV8-30*01 -IGKJ5*01) [12.3.9] (1'-112') -*Canis lupus familiaris* IGL1CS1*01 V45.3>I (162) (114'-219')]; dimère (225-225'':228-228'')-bisdisulfure

inmunoglobulina G2_V-kappa-C-lambda, anti-[***Canis lupus familiaris*** MS4A1 (miembro 1 de la subfamilia A con 4 dominios transmembranarios, CD20)], anticuerpo monoclonal caninizado;
cadena pesada gamma2 quimérica (1-448) [*Mus musculus* VH (*Mus musculus* IGHV1-15*01 -(IGHD) -IGHJ1*03) [8.8.6] (1-113) -*Canis lupus familiaris* IGHG2*02 (CH1 T26>Q (131) (114-211), bisagra (212-229), CH2 (230-339), CH3 (340-446), CHS (447-448)) (114-448)], (128-218')-disulfuro con la cadena ligera V-kappa-C-lambda quimérica (1'-219') [*Mus musculus* V-KAPPA (*Mus musculus* IGKV8-30*01 -IGKJ5*01) [12.3.9] (1'-112') -*Canis lupus familiaris* IGL1CS1*01 V45.3>I (162) (114'-219')]; dímero (225-225'':228-228'')-bisdisulfuro

p.534 **tamtuvetmabum #**
-535 tamtuvetmab *replace the description by the following one*
tamtuvetmab *remplacer la description par la suivante*
tamtuvetmab *sustitúyase la descripción por la siguiente*

immunoglobulin G2_V-kappa-C-lambda, anti-[***Canis lupus familiaris*** CD52], caninized monoclonal antibody;
gamma2 heavy chain chimeric (1-456) [chimeric VH (*Rattus norvegicus* IGHV7S6*01 (97.00%) -(IGHD) -*Canis lupus familiaris* IGHJ-E2RCC8) [8.10.12] (1-121) -*Canis lupus familiaris* IGHG2*02 (CH1 (122-219), hinge (220-237), CH2 (238-347), CH3 (348-454), CHS (455-456))(122-456)], (136-212')-disulfide with V-kappa-C-lambda light chain chimeric (1'-213') [*Rattus norvegicus* V-KAPPA (*Rattus norvegicus* IGKV22S7 (93.70%) -IGKJ1*01) [6.3.9] (1'-107') -*Canis lupus familiaris* IGLC1S1*01 V45.3>I (156) (108'-213')]; dimer (233-233":236-236")-bisdisulfide

immunoglobuline G2_V-kappa-C-lambda, anti-[***Canis lupus familiaris*** CD52], anticorps monoclonal caninisé;
chaîne lourde gamma2 chimérique (1-456) [VH chimérique (*Rattus norvegicus* IGHV7S6*01 (97.00%) -(IGHD) -*Canis lupus familiaris* IGHJ-E2RCC8) [8.10.12] (1-121) -*Canis lupus familiaris* IGHG2*02 (CH1 (122-219), charnière (220-237), CH2 (238-347), CH3 (348-454), CHS (455-456)) (122-456)], (136-212')-disulfure avec la chaîne légère V-kappa-C-lambda chimérique (1'-213') [*Rattus norvegicus* V-KAPPA (*Rattus norvegicus* IGKV22S7 (93.70%) -IGKJ1*01) [6.3.9] (1'-107') -*Canis lupus familiaris* IGLC1S1*01 V45.3>I (156) (108'-213')]; dimère (233-233":236-236")-bisdisulfure

inmunoglobulina G2_V-kappa-C-lambda, anti-[***Canis lupus familiaris*** CD52], anticuerpo monoclonal caninizado;
cadena pesada gamma2 quimérica (1-456) [VH quimérico (*Rattus norvegicus* IGHV7S6*01 (97.00%) -(IGHD) -*Canis lupus familiaris* IGHJ-E2RCC8) [8.10.12] (1-121) -*Canis lupus familiaris* IGHG2*02 (CH1 (122-219), bisagra (220-237), CH2 (238-347), CH3 (348-454), CHS (455-456))(122-456)], (136-212')-disulfuro con la cadena ligera V-kappa-C-lambda quimérica (1'-213') [*Rattus norvegicus* V-KAPPA (*Rattus norvegicus* IGKV22S7 (93.70%) -IGKJ1*01) [6.3.9] (1'-107') -*Canis lupus familiaris* IGLC1S1*01 V45.3>I (156) (108'-213')]; dímero (233-233":236-236")-bisdisulfuro

Recommended International Nonproprietary Names (Rec. INN): List 77
Dénominations communes internationales recommandées (DCI Rec.): Liste 77
Denominaciones Comunes Internacionales Recomendadas (DCI Rec.): Lista 77
(WHO Drug Information, Vol. 31, No. 1, 2017)

p.118 **ranevetmabum #**
-119 ranevetmab *replace the description by the following one*
ranevetmab *remplacer la description par la suivante*
ranevetmab *sustitúyase la descripción por la siguiente*

immunoglobulin G1-kappa, anti-[***Canis lupus familiaris*** NGF (nerve growth factor, nerve growth factor beta polypeptide, NGFB, beta-NGF)], caninized monoclonal antibody;
gamma1 heavy chain (1-453) [caninized VH (*Rattus norvegicus* IGHV5S13*01 (71.40%) -(IGHD)-IGHJ4*01) [8.7.16] (1-122) -*Canis lupus familiaris* IGHG1*01 (CH1 (123-219), hinge (220-233), CH2 (234-343), CH3 (344-451), CHS (452-453)) (123-453)], (137-213')-disulfide with kappa light chain (1'-217') [caninized V-KAPPA (*Rattus norvegicus* IGKV12S34*01 (76.80%) -IGKJ2-3*01) [6.3.9] (1'-107') -*Canis lupus familiaris* IGKC*01 (108'-213') -4-mer (214'-217')]; dimer (224-224'':226-226'':232-232'')-trisdisulfide

immunoglobuline G2-kappa, anti-[***Canis lupus familiaris*** NGF (facteur de croissance du nerf, facteur de croissance du nerf polypeptide bêta, NGFB, bêta-NGF)], anticorps monoclonal caninisé;
chaîne lourde gamma2 (1-453) [VH caninisé (*Rattus norvegicus* IGHV5S13*01 (71.40%) -(IGHD)-IGHJ4*01) [8.7.16] (1-122) -*Canis lupus familiaris* IGHG1*01 (CH1 (123-219), charnière (220-233), CH2 (234-343), CH3 (344-451), CHS (452-453)) (123-453)], (137-213')-disulfure avec la chaîne légère kappa (1'-217') [V-KAPPA caninisé (*Rattus norvegicus* IGKV12S34*01 (76.80%) -IGKJ2-3*01) [6.3.9] (1'-107') -*Canis lupus familiaris* IGKC*01 (108'-213') -4-mer (214'-217')]; dimère (224-224'':226-226'':232-232'')-trisdisulfure

inmunoglobulina G2-kappa, anti-[***Canis lupus familiaris*** NGF (factor de crecimiento de los nervios, factor de crecimiento de nervios polipéptido beta, NGFB, beta-NGF)], anticuerpo monoclonal caninizado;
cadena pesada gamma2 (1-453) [VH caninizado (*Rattus norvegicus* IGHV5S13*01 (71.40%) -(IGHD)-IGHJ4*01) [8.7.16] (1-122) -*Canis lupus familiaris* IGHG1*01 (CH1 (123-219), bisagra (220-233), CH2 (234-343), CH3 (344-451), CHS (452-453)) (123-453)], (137-213')-disulfuro con la cadena ligera kappa (1'-217') [V-KAPPA caninizado (*Rattus norvegicus* IGKV12S34*01 (76.80%) -IGKJ2-3*01) [6.3.9] (1'-107') -*Canis lupus familiaris* IGKC*01 (108'-213') -4-mer (214'-217')]; dímero (224-224'':226-226'':232-232'')-trisdisulfuro

Recommended International Nonproprietary Names (Rec. INN): List 79
Dénominations communes internationales recommandées (DCI Rec.): Liste 79
Denominaciones Comunes Internacionales Recomendadas (DCI Rec.): Lista 79
(WHO Drug Information, Vol. 32, No. 1, 2018)

p.170	*suprimáse*	*insertese*
	t**o**glato de tigilanol	t**i**glato de tigilanol

Recommended International Nonproprietary Names (Rec. INN): List 81
Dénominations communes internationales recommandées (DCI Rec.): Liste 81
Denominaciones Comunes Internacionales Recomendadas (DCI Rec.): Lista 81
(WHO Drug Information, Vol. 31, No. 1, 2017)

olenasufligenum relduparvovecum #

olenasufligene relduparvovec	*A revised sequence has been uploaded to the INN MedNet, which includes three nucleotide insertions within the CAG promoter compared to the previous version, increasing the total length of the vector to 4075bp. The table of features was revised accordingly.*
olénasufligène relduparvovec	*Une séquence révisée a été téléchargée sur MedNet DCI, et comprend trois insertions de nucléotides dans le promoteur CAG par rapport à la version précédente, augmentant la longueur totale du vecteur à 4075 pb. Le tableau des caractéristiques a été révisé en conséquence.*
olenasufligén relduparvovec	*Se cargó una secuencia revisada en MedNet DCI e incluye tres inserciones de nucleótidos dentro del promotor CAG en comparación con la versión anterior, aumentando la longitud total del vector a 4075 pb. La tabla de características se revisó en consecuencia.*

Recommended International Nonproprietary Names (Rec. INN): List 83
Dénominations communes internationales recommandées (DCI Rec.): Liste 83
Denominaciones Comunes Internacionales Recomendadas (DCI Rec.): Lista 83
(WHO Drug Information, Vol. 34, No. 1, 2020)

p.41 -42 **efbemalenograstimum alfa #**

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

human granulocyte colony-stimulating factor (G-CSF) fragment fused via a peptidyl linker to a human immunoglobulin G2 Fc fragment variant, dimer:
[human granulocyte colony-stimulating factor (G-CSF, pluripoietin) short **[V^{36}, S^{37}, E^{38}>del]** isoform (1-174)]-[GSG$_3$S(G$_4$S)$_2$ linker (175-190)]-[human immunoglobulin G2 Fc fragment (223 C-terminal residues) (*Homo sapiens* IGHG2*01 (natural S^{344}>A variant); hinge (191-197), CH2 (P^{297}>S) (198-306), CH3 (307-411), CHS (412-413) (191-413)] fusion protein, dimer (193-193':196-196')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

fragment du facteur de stimulation des colonies de granulocytes humain (G-CSF) lié par un peptide à un variant du fragment Fc de l'immunoglobuline humaine G2, dimère:
[facteur humain de stimulation des colonies de granulocytes (G-CSF, pluripoïétine) **[V^{36}, S^{37}, E^{38}>del]** isoforme courte (1-174)]-[GSG$_3$S(G$_4$S)$_2$ linker (175-190)]-[fragment Fc de l'immunoglobuline humaine G2 (résidus 223 C-terminaux) (*Homo sapiens* IGHG2*01 (variant natural S^{344}>A); charnière (191-197), CH2 (P^{297}>S) (198-306), CH3 (307-411), CHS (412-413) (191-413)] protéine de fusion, dimère (193-193':196-196')-bisdisulfure, produit par des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

fragmento del factor de estimulación de las colonias de granulocitos humano (G-CSF) que se une por un péptido a una variante del fragment Fc de la inmunoglobulina humana G2, dímero:
[factor humano de estimulación de las colonias de granulocitos (G-CSF, pluripoyetina) [**V^{36}, S^{37}, E^{38}**>del] isoforma corta (1-174)]-[$GSG_3S(G_4S)_2$ conector (175-190)]-[fragmento Fc de la inmunoglobulina humana G2 (residuo 223 C-terminal) (*Homo sapiens* IGHG2*01 (variante natural S^{344}>A); bisagra (191-197), CH2 (P^{297}>S) (198-306), CH3 (307-411), CHS (412-413) (191-413)] proteína de fusión, dímero (193-193':196-196')-bisdisulfuro, producido en las células ováricas de hamsters chinos (CHO), glicoforma alfa

Sequence / Séquence / Secuencia:

```
TPLGPASSLP QSFLLKCLEQ VRKIQGDGAA LQEKLCATYK LCHPEELVLL  50
GHSLGIPWAP LSSCPSQALQ LAGCLSQLHS GLFLYQGLLQ ALEGISPELG 100
PTLDTLQLDV ADFATTIWQQ MEELGMAPAL QPTQGAMPAF ASAFQRRAGG 150
VLVASHLQSF LEVSYRVLRH LAQPGSGGGS GGGGSGGGGS VECPPCPAPP 200
VAGPSVFLFP PKPKDTLMIS RTPEVTCVVV DVSHEDPEVQ FNWYVDGVEV 250
HNAKTKPREE QFNSTFRVVS VLTVVHQDWL NGKEYKCKVS NKGLPASIEK 300
TISKTKGQPR EPQVYTLPPS REEMTKNQVS LTCLVKGFYP SDIAVEWESN 350
GQPENNYKTT PPMLDSDGSF FLYSKLTVDK SRWQQGNVFS CSVMHEALHN 400
HYTQKSLSLS PGK                                         413
```

Disulfide bridge location / Position de la pont disulfure / Posición del puente disulfuro:
intra-G-CSF: 36-42, 64-74, 36'-42', 64'-74'
intra-IgG2 Fc: 227-287, 333-391, 227'-287', 333'-391'
inter-IgG2 Fc: 193-193', 196-196'

Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación
N-linked glycans: Asn263, Asn263'
O-linked glycans: Thr133, Thr133'

p.298 -299 **narsoplimabum #**

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

immunoglobulin G4-lambda, anti-[*Homo sapiens* MASP2 (mannan-binding lectin serine peptidase 2, mannan-binding lectin serine protease 2, mannan-binding lectin serine protease 1 pseudogene 1, MASP1P1)], *Homo sapiens* monoclonal antibody; gamma**4** heavy chain *Homo sapiens* (1-445) [VH (*Homo sapiens* IGHV2-26*01 (94.0%) -(IGHD) -IGHJ4*01 (100%)) [10.7.10] (1-118) -*Homo sapiens* IGHG4*01 (CH1 (119-216), hinge 1-12 S10>P (226) (217-228), CH2 (229-338), CH3 (339-443), CHS (444-445)) (119-445)], (132-211')-disulfide with lambda light chain *Homo sapiens* (1'-212') [V-LAMBDA (*Homo sapiens* IGLV3-1*01 (93.5%) -IGLJ2*01 (100%)) [6.3.9] (1'-106') -*Homo sapiens* IGLC2*01 (100%) (107'-212')];
dimer (224-224":227-227")-bisdisulfide, produced in Chinese hamster ovary (CHO)-S cell line, glycoform alfa

immunoglobuline G4-lambda, anti-[*Homo sapiens* MASP2 (sérine peptidase 2 de la lectine liant le mannane, sérine protéase 2 de la lectine liant le mannane, pseudogène 1 de la protéase 1 de la lectine liant le mannane, MASP1P1)], anticorps monoclonal *Homo sapiens*;
chaîne lourde gamma**4** *Homo sapiens* (1-445) [VH (*Homo sapiens* IGHV2-26*01 (94.0%) -(IGHD) -IGHJ4*01 (100%)) [10.7.10] (1-118) -*Homo sapiens* IGHG4*01 (CH1 (119-216), charnière 1-12 S10>P (226) (217-228), CH2 (229-338), CH3 (339-443), CHS (444-445)) (119-445)], (132-211')-disulfure avec la chaîne légère lambda *Homo sapiens* (1'-212') [V-LAMBDA (*Homo sapiens* IGLV3-1*01 (93.5%) -IGLJ2*01 (100%)) [6.3.9] (1'-106') -*Homo sapiens* IGLC2*01 (100%) (107'-212')];
dimère (224-224":227-227")-bisdisulfure, produit dans des cellules ovariennes de hamsters chinois (CHO) lignée cellulaire S, glycoforme alfa

inmunoglobulina G4-lambda, anti-[*Homo sapiens* MASP2 (serina peptidasa 2 de la lectina que se une al manano, serina proteasa 2 de la lectina unida al manano, pseudogen 1 de la proteasa 1 de la lectina unida al manano, MASP1P1)], anticuerpo monoclonal *Homo sapiens*; cadena pesada gamma**4** *Homo sapiens* (1-445) [VH (*Homo sapiens* IGHV2-26*01 (94.0%) -(IGHD) -IGHJ4*01 (100%)) [10.7.10] (1-118) -*Homo sapiens* IGHG4*01 (CH1 (119-216), bisagra 1-12 S10>P (226) (217-228), CH2 (229-338), CH3 (339-443), CHS (444-445)) (119-445)], (132-211')-disulfuro con la cadena ligera lambda *Homo sapiens* (1'-212') [V-LAMBDA (*Homo sapiens* IGLV3-1*01 (93.5%) -IGLJ2*01 (100%)) [6.3.9] (1'-106') -*Homo sapiens* IGLC2*01 (100%) (107'-212')]; dímero (224-224":227-227")-bisdisulfuro, producido en las células ováricas de hamsters chinos (CHO) línea celular S, glicoforma alfa

Proposed International Nonproprietary Names (Prop. INN): List 122
Dénominations communes internationales proposées (DCI Prop.): Liste 122
Denominaciones Comunes Internacionales Propuestas (DCI Prop.): Lista 122
(WHO Drug Information, Vol. 33, No. 2, 2019)

p.831 **eflepedocokinum alfa#**
-832 eflépédocokine alfa *remplacer la description par la suivante*
eflepedocokina alfa *sustitúyase la descripción por la siguiente*

interleukine 22 humaine (IL22, cytokine Zcyto18, facteur inductible dérivé des lymphocytes T lié à IL10, IL-TIF) (1-146), fusionnée via un peptide liant $GSG_3S(G_4S)_2$ (147-162) au fragment Fc C-terminal de l'immunoglobuline G2 humaine (163-385), P^{269}>S-mutant **S**^{316}>A-variant, dimère (165-165':168-168')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

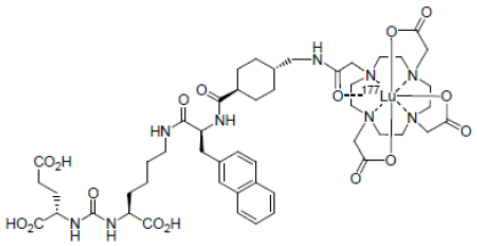
interleukina 22 humana (IL22, citoquina Zcyto18, factor inducible derivado de los linfocitos T relacionado con IL10, IL-TIF) (1-146), fusionada a través de un péptido que se une a $GSG_3S(G_4S)_2$ (147-162) con el fragmento Fc C-terminal de la inmunoglobulina G2 humana (163-385), P^{269}>S-mutante **S**^{316}>A-variante, dímero (165-165':168-168')-bisdisulfuro, producido en las células ováricas de hamster chino (CHO), glicoforma alfa

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.

<table>
<tr><td>化学名・別名</td><td>【日本名】ルテチウムビピボチドテトラキセタン（^{177}Lu）
【英名】Lutetium (^{177}Lu) vipivotide tetraxetan（INN）
【化学名】
英名：2-[4-[2-[[4-[[(2S)-1-[[(5S)-5-carboxy-5-[[(1S)-1,3-dicarboxypropyl]carbamoylamino]pentyl]amino]-3-naphthalen-2-yl-1-oxopropan-2-yl]carbamoyl]cyclohexyl]methylamino]-2-oxoethyl]-4,7,10-tris(carboxylatomethyl)-1,4,7,10-tetrazacyclododec-1-yl]acetate; lutetium-177(3+)</td></tr>
<tr><td>構造式</td><td></td></tr>
<tr><td>効能・効果</td><td>PSMA 陽性の遠隔転移を有する去勢抵抗性前立腺癌</td></tr>
<tr><td>用法・用量</td><td>通常、成人にはルテチウムビピボチドテトラキセタン(^{177}Lu)として 1 回 7.4GBq を 6 週間間隔で最大 6 回静脈内投与する。なお、患者の状態により適宜減量する。</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：ルテチウムビピボチドテトラキセタン（^{177}Lu）
製剤：プルヴィクト静注［1 バイアル（7.5～12.5mL）中ルテチウムビピボチドテトラキセタン（^{177}Lu）7.4GBq（検定日時）を含有］</td></tr>
<tr><td>毒性</td><td>拡張型単回投与毒性試験
被験物質：^{175}Lu-PSMA-617 溶液[a]
<table>
<tr><th>動物種</th><th>投与経路</th><th>投与量 (mg/kg)</th><th>無毒性量 (mg/kg)</th><th>主な所見</th></tr>
<tr><td>ラット</td><td>静脈内</td><td>0, 2, 4</td><td>4</td><td>瀕死・死亡例なし
概略の致死量：> 4 mg/kg
毒性所見なし</td></tr>
<tr><td>ミニブタ</td><td>静脈内</td><td>0, 0.2, 0.6, 1.8</td><td>1.8</td><td>瀕死・死亡例なし
概略の致死量：> 1.8 mg/kg
≥ 0.2 mg/kg:
Day 2 剖検時：投与部位に血管及び血管周囲の壊死を伴う急性炎症
Day 15 剖検時：Day 2 剖検時と同様の変化がみられたが，回復傾向が認められた。</td></tr>
</table>
a ^{175}Lu-PSMA-617 及び PSMA-617 を約 1：1 の割合で含有した酢酸ナトリウム緩衝液

反復投与毒性試験
被験物質：非標識 PSMA-617
<table>
<tr><th>動物種</th><th>投与期間</th><th>投与経路</th><th>投与量 (µg/kg/day)</th><th>無毒性量 (µg/kg/day)</th><th>主な所見</th></tr>
<tr><td>ラット</td><td>4 週間</td><td>静脈内</td><td>0, 40, 160, 400</td><td>400</td><td>瀕死・死亡例なし
毒性所見なし</td></tr>
</table></td></tr>
</table>

副　作　用	【前立腺特異的膜抗原（PSMA）陽性の遠隔転移を有する去勢抵抗性前立腺癌対象の国内臨床試験における日本人の副作用発現率】 副作用発現率　20/30＝66.7% 副作用の種類　件数 便秘　6 例（20.0%） 血小板数減少　6 例（20.0%） 貧血　5 例（16.7%） 口内乾燥　4 例（13.3%） 倦怠感　4 例（13.3%） 悪心　3 例（10.0%） 食欲減退　3 例（10.0%） 味覚不全　3 例（10.0%） （承認申請時までの集計）
会　　社	ノバルティスファーマ株式会社　製剤：輸入

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2　第 4 部 16
3　第 5 部 23

1 第 3 部

添付資料番号	タイトル	試験実施期間及び試験実施場所	報種類（国内／外国）	評価／参考
3.2 データ又は報告書				
3.2.S 原薬 Vipivotide tetraxetan				
3.2.S.1 一般情報				
3.2.S.1.1	5004904_SM_A_S11_[redacted]	–	外国	参考
3.2.S.1.2	5004904_SM_A_S12_[redacted]	–	外国	参考
3.2.S.1.3	5004904_SM_A_S13_[redacted]	–	外国	参考
3.2.S.2 製造				
3.2.S.2.1	5004904_SM_A_S21_[redacted]	–	外国	参考
3.2.S.2.2_1	5004904_SM_A_S22_[redacted]	–	外国	参考
3.2.S.2.2_2	5004904_SM_A_S22_[redacted]	–	外国	参考
3.2.S.2.2_3	5004904_AF_DS_[redacted]	–	外国	参考
3.2.S.2.3_1	5004904_SM_A_S23_[redacted]	–	外国	参考
3.2.S.2.3_2	5004904_SM_A_S23_[redacted]	–	外国	参考
3.2.S.2.4_1	5004904_SM_A_S24_[redacted]	–	外国	参考
3.2.S.2.4_2	5004904_SM_A_S24_[redacted]	–	外国	参考
3.2.S.2.5_1	5004904_SM_A_S25_[redacted]	–	外国	参考
3.2.S.2.5_2	5004904_SM_A_S25_[redacted]	–	外国	参考
3.2.S.2.6_1	5004904_SM_A_S26_[redacted]	–	外国	参考
3.2.S.2.6_2	5004904_SM_A_S26_[redacted]	–	外国	参考
3.2.S.3 特性				
3.2.S.3.1	5004904_SM_A_S31_[redacted]	–	外国	参考

添付資料番号	タイトル	試験実施期間及び試験実施場所	報種類（国内／外国）	評価／参考
3.2.S.3.2_1	5004904_SM_A_S32_[redacted]	－	外国	参考
3.2.S.3.2_2	5004904_SM_A_S32_[redacted]	－	外国	参考
3.2.S.4　原薬の管理				
3.2.S.4.1_1	5004904_SM_A_S41_[redacted]	－	外国	参考
3.2.S.4.1_2	5004904_SM_A_S41_[redacted]	－	外国	参考
3.2.S.4.1_3	5004904_AF_DS_[redacted]	－	外国	参考
3.2.S.4.2_1	5004904_SM_A_S42_[redacted]	－	外国	参考
3.2.S.4.2_2	5004904_SM_A_S42_[redacted]	－	外国	参考
3.2.S.4.3_1	5004904_SM_A_S43_[redacted]	－	外国	参考
3.2.S.4.3_2	5004904_SM_A_S43_[redacted]	－	外国	参考
3.2.S.4.4_1	5004904_SM_A_S44_[redacted]	－	外国	参考
3.2.S.4.4_2	5004904_SM_A_S44_[redacted]	－	外国	参考
3.2.S.4.5_1	5004904_SM_A_S45_[redacted]	－	外国	参考
3.2.S.4.5_2	5004904_SM_A_S45_[redacted]	－	外国	参考
3.2.S.5　標準品又は標準物質				
3.2.S.5	5004904_SM_A_S5_[redacted]	－	外国	参考
3.2.S.6　容器及び施栓系				
3.2.S.6_1	5004904_SM_A_S6_[redacted]	－	外国	参考
3.2.S.6_2	5004904_SM_A_S6_[redacted]	－	外国	参考
3.2.S.7　安定性				
3.2.S.7.1_1	5004904_SM_A_S71_[redacted]	－	外国	参考
3.2.S.7.1_2	5004904_SM_A_S71_[redacted]	－	外国	参考
3.2.S.7.1_3	5004904_AF_DS_[redacted]	－	外国	参考

添付資料番号	タイトル	試験実施期間及び試験実施場所	報種類（国内／外国）	評価／参考
3.2.S.7.2_1	5004904_SM_A_S72_[redacted]	－	外国	参考
3.2.S.7.2_2	5004904_SM_A_S72_[redacted]	－	外国	参考
3.2.S.7.3_1	5004904_SM_A_S73_[redacted]	－	外国	参考
3.2.S.7.3_2	5004904_SM_A_S73_[redacted]	－	外国	参考
3.2.S　原薬 Lutetium (177Lu) vipivotide tetraxetan				
3.2.S.1　一般情報				
3.2.S.1.1	5004905_SM_A_S11_[redacted]	－	外国	評価
3.2.S.1.2	5004905_SM_A_S12_[redacted]	－	外国	評価
3.2.S.1.3	5004905_SM_A_S13_[redacted]	－	外国	評価
3.2.S.2　製造				
3.2.S.2.1	5004905_SM_A_S21_[redacted]	－	外国	評価
3.2.S.2.2_1	5004905_SM_A_S22_[redacted]	－	外国	評価
3.2.S.2.2_2	5004905_AF_DS_MANU_[redacted]	－	外国	評価
3.2.S.2.3_1	5004905_SM_A_S23_[redacted]	－	外国	評価
3.2.S.2.3_2	5004905_SM_A_S23_[redacted]	－	外国	評価
3.2.S.2.3_3	5004905_SM_A_S23_[redacted]	－	外国	評価
3.2.S.2.3_4	Certificate of Analysis_[redacted]	－	外国	評価
3.2.S.2.4_1	5004905_SM_A_S24_[redacted]	－	外国	評価
3.2.S.2.4_2	5004905_SM_A_S24_[redacted]	－	外国	評価
3.2.S.2.4_3	Method Validation [redacted]	－	外国	評価
3.2.S.2.4_4	Method Validation_[redacted]	－	外国	評価
3.2.S.2.4_5	Method Validation Report [redacted]	－	外国	評価

添付資料番号	タイトル	試験実施期間及び試験実施場所	報種類（国内／外国）	評価／参考
3.2.S.2.4_6	External Analytical Document_[redacted]	－	外国	評価
3.2.S.2.4_7	5004905_SM_A_S24_[redacted]	－	外国	評価
3.2.S.2.4_8	5004905_SM_A_S24_[redacted]	－	外国	評価
3.2.S.2.4_9	5004905_SM_A_S24_[redacted]	－	外国	評価
3.2.S.2.4_10	AAA-REP-2092-val report	－	外国	評価
3.2.S.2.4_11	5004905_SM_A_S24_[redacted]	－	外国	評価
3.2.S.2.4_12	5004905_SM_A_S24_[redacted]	－	外国	評価
3.2.S.2.5	5004905_SM_A_S25_[redacted]	－	外国	評価
3.2.S.2.6	5004905_SM_A_S26_[redacted]	－	外国	評価
3.2.S.3　特性				
3.2.S.3.1_1	5004905_SM_A_S31_[redacted]	－	外国	評価
3.2.S.3.1_2	5004905_SM_A_S31_[redacted] (SN10980)	－	外国	評価
3.2.S.3.1_3	5004905_SM_A_S31_[redacted] (Q20_058)	－	外国	評価
3.2.S.3.1_4	5004905_SM_A_S31_[redacted]	－	外国	評価
3.2.S.3.1_5	5004905_SM_A_S31_[redacted] (01129007)	－	外国	評価
3.2.S.3.1_6	5004905_SM_A_S31_[redacted] (GEN-CMC-CR-0001)	－	外国	評価
3.2.S.3.2	5004905_SM_A_S32_[redacted]	－	外国	評価
3.2.S.4　原薬の管理				
3.2.S.4.1	5004905_SM_A_S41_[redacted]	－	外国	評価
3.2.S.4.2	5004905_SM_A_S42_[redacted]	－	外国	評価
3.2.S.4.3	5004905_SM_A_S43_[redacted]	－	外国	評価
3.2.S.4.4	5004905_SM_A_S44_[redacted]	－	外国	評価
3.2.S.4.5	5004905_SM_A_S45_[redacted]	－	外国	評価

添付資料番号	タイトル	試験実施期間及び試験実施場所	報種類（国内／外国）	評価／参考
3.2.S.5　標準品又は標準物質				
3.2.S.5	5004905_SM_A_S5_[redacted]	－	外国	評価
3.2.S.6　容器及び施栓系				
3.2.S.6	5004905_SM_A_S6_[redacted]	－	外国	評価
3.2.S.7　安定性				
3.2.S.7.1	5004905_SM_A_S71_[redacted]	－	外国	評価
3.2.S.7.2	5004905_SM_A_S72_[redacted]	－	外国	評価
3.2.S.7.3	5004905_SM_A_S73_[redacted]	－	外国	評価
3.2.P　製剤				
3.2.P.1　製剤及び処方				
3.2.P.1_1	7011238_SM_A_P1_[redacted]	－	外国	評価
3.2.P.1_2	7011238_AF_DP_COMP_[redacted]	－	外国	評価
3.2.P.2　製剤開発の経緯				
3.2.P.2_1	7011238_SM_A_P21_[redacted]	－	外国	評価
3.2.P.2_2	7011238_SM_A_P22_[redacted]	－	外国	評価
3.2.P.2_3	7011238_SM_A_P23_[redacted]	－	外国	評価
3.2.P.2_4	7011238_SM_A_P24_[redacted]	－	外国	評価
3.2.P.2_5	7011238_SM_A_P25_[redacted]	－	外国	評価
3.2.P.2_6	7011238_SM_A_P26_[redacted]	－	外国	評価
3.2.P.3　製造				
3.2.P.3.1	7011238_SM_A_P31_[redacted]	－	外国	評価
3.2.P.3.2	7011238_SM_A_P32_[redacted]	－	外国	評価
3.2.P.3.3_1	7011238_SM_A_P33_[redacted]	－	外国	評価

添付資料番号	タイトル	試験実施期間及び試験実施場所	報種類（国内／外国）	評価／参考
3.2.P.3.3_2	7011238_AF_DP_MANU_[redacted]	－	外国	評価
3.2.P.3.4	7011238_SM_A_P34_[redacted]	－	外国	評価
3.2.P.3.5_1	7011238_SM_A_P35_[redacted]	－	外国	評価
3.2.P.3.5_2	7011238_SM_A_P35_[redacted] (R-19-4474)	－	外国	評価
3.2.P.3.5_3	7011238_SM_A_P35_[redacted]	－	外国	評価
3.2.P.3.5_4	7011238_SM_A_P35_[redacted]	－	外国	評価
3.2.P.3.5_5	7011238_SM_A_P35_[redacted]	－	外国	評価
3.2.P.3.5_6	7011238_SM_A_P35_[redacted]	－	外国	評価
3.2.P.4　添加剤の管理				
3.2.P.4.1_1	7011238_SM_A_P41_[redacted]	－	外国	評価
3.2.P.4.1_2	7011238_SM_A_P41_[redacted]_VB-QK-0124-02)	－	外国	評価
3.2.P.4.1_3	7011238_SM_A_P41_[redacted]_VB-QK-9243-02)	－	外国	評価
3.2.P.4.1_4	7011238_SM_A_P41_[redacted]VB-QK-0127_02)	－	外国	評価
3.2.P.4.1_5	7011238_SM_A_P41_[redacted]_VB-QK-9280_01_2017)	－	外国	評価
3.2.P.4.1_6	7011238_SM_A_P41_[redacted]_VB-QK-9286_01)	－	外国	評価
3.2.P.4.1_7	CoA_[redacted]	－	外国	評価
3.2.P.4.1_8	CoA_[redacted]	－	外国	評価
3.2.P.4.1_9	CoA_[redacted]	－	外国	評価
3.2.P.4.1_10	7011238_SM_A_P41_[redacted]	－	外国	評価
3.2.P.4.1_11	7011238_SM_A_P41_[redacted]	－	外国	評価

添付資料番号	タイトル	試験実施期間及び試験実施場所	報種類（国内／外国）	評価／参考
3.2.P.4.1_12	7011238_SM_A_P41_[redacted]	－	外国	評価
3.2.P.4.1_13	7011238_AF_DP_EXP_[redacted]	－	外国	評価
3.2.P.4.2_1	7011238_SM_A_P42_[redacted]	－	外国	評価
3.2.P.4.2_2	7011238_SM_A_P42_[redacted]	－	外国	評価
3.2.P.4.2_3	7011238_SM_A_P42_[redacted]	－	外国	評価
3.2.P.4.3_1	7011238_SM_A_P43_[redacted]	－	外国	評価
3.2.P.4.3_2	7011238_SM_A_P43_[redacted]AP200 Rev A)	－	外国	評価
3.2.P.4.3_3	7011238_SM_A_P43_[redacted]R-VAL-16-000258)	－	外国	評価
3.2.P.4.3_4	7011238_SM_A_P43_[redacted]	－	外国	評価
3.2.P.4.3_5	7011238_SM_A_P43_[redacted]AP184 RevA)	－	外国	評価
3.2.P.4.3_6	7011238_SM_A_P43_[redacted]AP183 Rev B)	－	外国	評価
3.2.P.4.3_7	7011238_SM_A_P43_[redacted]_AP064 Rev A)	－	外国	評価
3.2.P.4.3_8	7011238_SM_A_P43_[redacted]_ADDCT002 AP001)	－	外国	評価
3.2.P.4.3_9	7011238_SM_A_P43_[redacted]	－	外国	評価
3.2.P.4.3_10	7011238_SM_A_P43_[redacted]_AP201 Rev A)	－	外国	評価
3.2.P.4.3_11	7011238_SM_A_P43_[redacted]_AP186 Rev A)	－	外国	評価
3.2.P.4.3_12	7011238_SM_A_P43_[redacted]_AP-064_Rev A)	－	外国	評価
3.2.P.4.3_13	7011238_SM_A_P43_[redacted]_R-VAL-16-000257)	－	外国	評価

添付資料番号	タイトル	試験実施期間及び試験実施場所	報種類（国内／外国）	評価／参考
3.2.P.4.4_1	7011238_SM_A_P44_[redacted]	―	外国	評価
3.2.P.4.4_2	CoA_[redacted]	―	外国	評価
3.2.P.4.4_3	7011238_SM_A_P44_[redacted]	―	外国	評価
3.2.P.4.4_4	CoA_[redacted]	―	外国	評価
3.2.P.4.4_5	7011238_SM_A_P44_[redacted]	―	外国	評価
3.2.P.4.4_6	CoA_[redacted]	―	外国	評価
3.2.P.4.5	7011238_SM_A_P45_[redacted]	―	外国	評価
3.2.P.4.6	7011238_SM_A_P46_[redacted]	―	外国	評価
3.2.P.5　製剤の管理				
3.2.P.5.1_1	7011238_SM_A_P51_[redacted]	―	外国	評価
3.2.P.5.1_2	70011238_AF_DP_SPTM_[redacted]	―	外国	評価
3.2.P.5.2	7011238_SM_A_P52_[redacted]	―	外国	評価
3.2.P.5.3_1	7011238_SM_A_P53_[redacted]	―	外国	評価
3.2.P.5.3_2	7011238_SM_A_P53_[redacted] (AAA-REP-1874-002)	―	外国	評価
3.2.P.5.3_3	7011238_SM_A_P53_[redacted] (RD 20-037-00)	―	外国	評価
3.2.P.5.3_4	7011238_SM_A_P53_[redacted]_AAA-REP-1773-005 Method Validation Report[redacted]	―	外国	評価
3.2.P.5.3_5	7011238_SM_A_P53_[redacted] (AAA-REP-2056-002)	―	外国	評価
3.2.P.5.3_6	7011238_SM_A_P53_[redacted] (AAA-REP-2648-001)	―	外国	評価
3.2.P.5.3_7	7011238_SM_A_P53_[redacted] (AAA-REP-1774-001)	―	外国	評価
3.2.P.5.3_8	7011238_SM_A_P53_[redacted] (AP292 Rev. A-AAA-REP-1871-001)	―	外国	評価
3.2.P.5.3_9	7011238_SM_A_P53_[redacted]_AP291 Rev.B-AAA-REP-1870-002)	―	外国	評価

添付資料番号	タイトル	試験実施期間及び試験実施場所	報種類（国内／外国）	評価／参考
3.2.P.5.4_1	7011238_SM_A_P54_[redacted]	－	外国	評価
3.2.P.5.4_1-1	Batch analyses data-[redacted]	－	外国	評価
3.2.P.5.4_1-2	Batch analyses data-[redacted]	－	外国	評価
3.2.P.5.4_1-3	Batch analyses data-[redacted]	－	外国	評価
3.2.P.5.4_1-4	Batch analyses data-[redacted]	－	外国	評価
3.2.P.5.4_1-5	Batch analyses data-[redacted]	－	外国	評価
3.2.P.5.4_1-6	Batch analyses data-[redacted]	－	外国	参考
3.2.P.5.4_1-7	Batch analyses data-[redacted]	－	外国	参考
3.2.P.5.4_1-8	Batch analyses data-[redacted]	－	外国	参考
3.2.P.5.4_1-9	Batch analyses data-[redacted]	－	外国	評価
3.2.P.5.4_1-10	Batch analyses data-[redacted]	－	外国	評価
3.2.P.5.4_1-11	Batch analyses data-[redacted]	－	外国	評価
3.2.P.5.4_1-12	Batch analyses data-[redacted]	－	外国	評価
3.2.P.5.4_1-13	Batch analyses data-[redacted]	－	外国	評価
3.2.P.5.4_1-14	Batch analyses data-[redacted]	－	外国	評価
3.2.P.5.4_1-15	Batch analyses data-[redacted]	－	外国	参考
3.2.P.5.4_1-16	Batch analyses data-[redacted]	－	外国	参考
3.2.P.5.4_1-17	Batch analyses data-[redacted]	－	外国	参考
3.2.P.5.4_1-18	Batch analyses data-[redacted]	－	外国	参考
3.2.P.5.5_1	7011238_SM_A_P55[redacted]	－	外国	評価
3.2.P.5.5_2	Risk_assessment_[redacted]	－	外国	評価
3.2.P.5.6	7011238_SM_A_P56_[redacted]	－	外国	評価
3.2.P.6　標準品又は標準物質				

添付資料番号	タイトル	試験実施期間及び試験実施場所	報種類（国内／外国）	評価／参考
3.2.P.6_1	7011238_SM_A_P6_[redacted]	－	外国	評価
3.2.P.6_2	7011238_SM_A_P6_[redacted]	－	外国	評価
3.2.P.6_3	7011238_SM_A_P6_[redacted]	－	外国	評価
3.2.P.6_4	7011238_SM_A_P6_[redacted]	－	外国	評価
3.2.P.7　容器及び施栓系				
3.2.P.7	7011238_SM_A_P7_[redacted]	－	外国	評価
3.2.P.8　安定性				
3.2.P.8.1_1	7011238_SM_A_P81_[redacted]	－	外国	評価
3.2.P.8.1_2	70011238_AF_DP_SCSL_[redacted]	－	外国	評価
3.2.P.8.2	7011238_SM_A_P82_[redacted]	－	外国	評価
3.2.P.8.3_1	7011238_SM_A_P83_[redacted]	－	外国	評価
3.2.P.8.3_1-1	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_1-2	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_1-3	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_1-4	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_1-5	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_1-6	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_1-7	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_1-8	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_1-9	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_1-10	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_1-11	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_1-12	Stability data-[redacted]	－	外国	参考

添付資料番号	タイトル	試験実施期間及び試験実施場所	報種類（国内／外国）	評価／参考
3.2.P.8.3_1-13	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_1-14	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_1-15	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_1-16	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_1-17	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_1-18	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_1-19	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_1-20	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_1-21	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_1-22	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_1-23	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_1-24	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_1-25	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_2	7011238_SM_A_P83_[redacted]	－	外国	評価
3.2.P.8.3_2-1	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_2-2	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_2-3	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_2-4	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_2-5	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_2-6	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_2-7	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_2-8	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_2-9	Stability data-[redacted]	－	外国	評価

添付資料番号	タイトル	試験実施期間及び試験実施場所	報種類（国内／外国）	評価／参考
3.2.P.8.3_2-10	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_2-11	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_2-12	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_3	7011238_SM_A_P83_[redacted]	－	外国	参考
3.2.P.8.3_3-1	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_3-2	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_3-3	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_4	7011238_SM_A_P83_[redacted]	－	外国	評価
3.2.P.8.3_4-1	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_4-2	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_4-3	Stability data-[redacted]	－	外国	評価
3.2.P.8.3_5	7011238_SM_A_P83_[redacted]	－	外国	参考
3.2.P.8.3_5-1	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_5-2	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_5-3	Stability data-[redacted]	－	外国	参考
3.2.P.8.3_5-4	Stability data-[redacted]	－	外国	参考
3.2.A　その他				
3.2.A.3	7011238_SM_A_A3_[redacted]	－	外国	評価
3.3　参考文献				
－	Aime S, Barge A, Botta M, et al (1996) Crystal structure and solution dynamics of the lutetium(III) chelate of DOTA. Inorganica Chimica Acta; 246: 423-9.	－	外国	－
－	Breeman WAP, van der Wansem K, Bernard BF, et al (2003) The addition of DTPA to [177Lu-DOTA0, Tyr3]octreotate prior to administration reduces rat skeleton uptake of radioactivity. European Journal of Nuclear Medicine and Molecular Imaging; 30: 312-5.	－	外国	－

添付資料番号	タイトル	試験実施期間及び試験実施場所	報種類（国内／外国）	評価／参考
—	Cada DJ, Levien T, Baker DE (2005) Pentetate Calcium Trisodium (Ca-DTPA) and Pentetate Zinc Trisodium (Zn-DTPA). Hospital Pharmacy; 40(1): 65-71.	—	外国	—
—	European Food Safety Authority (2015) Scientific Opinion on the re-evaluation of ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) as food additives. ESFA Journal; 13(5): 4087.	—	外国	—
—	Ménétrier F, Grappin L, Raynaud P, et al (2005) Treatment of accidental intakes of plutonium and americium: Guidance notes. Applied Radiation and Isotopes; 62: 829-46.	—	外国	—
—	Pentetate calcium trisodium (Ca-DTPA) injection. US Package Insert Instruction for Use. hameln pharmaceuticals gmbh, Hameln, Germany. NDA 21-749.	—	外国	—
—	Pentetate zinc trisodium (Zn-DTPA) injection. US Package Insert Instruction for Use. hameln pharmaceuticals gmbh, Hameln, Germany. NDA 21-751.	—	外国	—
—	European Pharmacopeia 2798 LUTETIUM (177Lu) SOLUTION FOR RADIOLABELLING.	—	外国	—
—	European Pharmacopeia 50700 5.7. TABLE OF PHYSICAL CHARACTERISTICS OF RADIONUCLIDES MENTIONED IN THE EUROPEAN PHARMACOPOEIA.	—	外国	—
—	Ranu P, Uma G (2012) Effect of thermal treatment on ascorbic acid content of pomegranate juice. Indian Journal of Biotechnology; 11: 309-13	—	外国	—
—	van Gorkom GNY, Lookermans EL, Van Elessen CHMJ, et al (2019) The Effect of Vitamin C (Ascorbic Acid) in the Treatment of Patients with Cancer: A Systematic Review. Nutrients; 11: 977.	—	外国	—
—	Wang W (2015) Tolerability of hypertonic injectables. International Journal of Pharmaceutics; 490: 308-15.	—	外国	—

2 第 4 部

添付資料番号	Report No./Study No.	タイトル	試験実施期間	試験実施場所	報種類（国内／外国）	評価／参考
4.2 試験報告書						
4.2.1 薬理試験						
4.2.1.1 効力を裏付ける試験						
―	―	該当資料なし	―	―	―	―
4.2.1.2 副次的薬理試験						
4.2.1.2-1	100053460-4	^{175}Lu-PSMA-617 off-target receptor binding and functional profiling	20[redacted] 年 [redacted] 月	フランス	外国	参考
4.2.1.2-2	R-0584	In Vitro Activity of ^{175}Lu-PSMA-617 and PSMA-617 on 22RV1 and KB Cells	20[redacted] 年 [redacted] 月	米国	外国	参考
4.2.1.3 安全性薬理試験						
4.2.1.3-1	20190089PEHPP	^{175}LuPSMA-617/PSMA-617 (50/50) Evalution of effects on hERG current in stably transfected HEK-293 cells	20[redacted] 年 [redacted] 月～ 20[redacted] 年 [redacted] 月	フランス	外国	評価
4.2.1.3-2	A3734	^{175}Lu-PSMA-617 solution IRWIN DOSE RANGE STUDY FOLLOWING INTRAVENOUS ADMINISTRATION IN RATS	20[redacted] 年 [redacted] 月～ 20[redacted] 年 [redacted] 月	イタリア	外国	評価
4.2.1.3-3	A3735	^{175}Lu-PSMA-617 SOLUTION EFFECTS ON RESPIRATORY FUNCTION OF THE CONSCIOUS RAT (WHOLE BODY PLETHYSMOGRAPHY)	20[redacted] 年 [redacted] 月～ 20[redacted] 年 [redacted] 月	イタリア	外国	評価
4.2.1.3-4	A3736	^{175}Lu-PSMA-617 SOLUTION EFFECTS ON THE CARDIOVASCULAR FUNCTION OF THE CONSCIOUS MINIPIG FOLLOWING INTRAVENOUS ADMINISTRATION	20[redacted] 年 [redacted] 月～ 20[redacted] 年 [redacted] 月	イタリア	外国	評価
4.2.1.4 薬力学的薬物相互作用試験						
―	―	該当資料なし	―	―	―	―
4.2.2 薬物動態試験						
4.2.2.1 分析法及びバリデーション報告書						

添付資料番号	Report No./Study No.	タイトル	試験実施期間	試験実施場所	報種類（国内／外国）	評価／参考
4.2.2.1-1	A3728	^{175}Lu-PSMA-617 SOLUTION VALIDATION OF THE ANALYTICAL METHOD AND PREPARATION PROCEDURE IN THE VEHICLE	20[redacted]年[redacted]月～20[redacted]年[redacted]月	イタリア	外国	参考
4.2.2.1-2	A3730	^{175}Lu-PSMA-617 AND PSMA-617 VALIDATION OF THE LC-MS/MS ANALYTICAL METHOD IN RAT PLASMA	20[redacted]年[redacted]月～20[redacted]年[redacted]月	イタリア	外国	参考
4.2.2.1-3	A3731	^{175}Lu-PSMA-617 AND PSMA-617 VALIDATION OF THE LC-MS/MS ANALYTICAL METHOD IN MINIPIG PLASMA	20[redacted]年[redacted]月～20[redacted]年[redacted]月	イタリア	外国	参考
4.2.2.1-4	A3729	^{175}Lu-PSMA-617 AND PSMA-617 VALIDATION OF THE ANALYTICAL METHOD FOR TEST ITEM PREPARATIONS IN TYRODE'S SOLUTION	20[redacted]年[redacted]月～20[redacted]年[redacted]月	イタリア	外国	参考
4.2.2.1-5	B19_099	Validation of HPLC-UV analytical method for quantification of PSMA-617 and derivatives	20[redacted]年[redacted]月	イタリア	外国	参考
4.2.2.1-6	B20_001	Partial validation of HPLC-UV analytical method for quantification of Gd-PSMA-617	20[redacted]年[redacted]月	イタリア	外国	参考
4.2.2.2　吸収						
―	―	該当資料なし	―	―	―	―
4.2.2.3　分布						
4.2.2.3-1	^{177}Lu-PSMA-617-ABX-Biodis-rat	Biodistribution and Kinetics of ^{177}Lu-PSMA-617 in rats	20[redacted]年[redacted]月～20[redacted]年[redacted]月	ドイツ	外国	参考
4.2.2.3-2	REPORT-0597	Non-GLP ^{175}Lu-PSMA-617 and PSMA-617 Protein Binding in Human, Rat, and Mini-pig Plasma	20[redacted]年[redacted]月	米国	外国	参考
4.2.2.3-3	Q20_046	Estimation of ^{175}Lu-PSMA-617 and PSMA-617 Blood/Plasma partitioning in human, mouse, rat, mini-pig and dog bloods.	20[redacted]年[redacted]月～20[redacted]年[redacted]月	イタリア	外国	参考
4.2.2.4　代謝						
4.2.2.4-1	REPORT-0594	Non-GLP Stability of 175Lu-PSMA-617 and PSMA-617 in Human, Rat, and Mini-pig Plasma	20[redacted]年[redacted]月	米国	外国	参考

添付資料番号	Report No./Study No.	タイトル	試験実施期間	試験実施場所	報種類（国内／外国）	評価／参考
4.2.2.4-2	REPORT-0590	Non-GLP Stability of 175Lu-PSMA-617 and PSMA-617 in Human, Rat, and Mini-Pig Liver S9 Fractions	20[redacted]年[redacted]月	米国	外国	参考
4.2.2.4-3	REPORT-0591	Non-GLP Stability of 175Lu-PSMA-617 and PSMA-617 in Human, Rat, and Mini-Pig Kidney S9 Fractions	20[redacted]年[redacted]月	米国	外国	参考
4.2.2.5 排泄						
－	－	該当資料なし	－	－	－	－
4.2.2.6 薬物動態学的薬物相互作用（非臨床）						
－	－	該当資料なし	－	－	－	－
4.2.2.7 その他の薬物動態試験						
－	－	該当資料なし	－	－	－	－
4.2.3 毒性試験						
4.2.3.1 単回投与毒性試験						
4.2.3.1-1	A3732	^{175}Lu-PSMA-617 solution SINGLE DOSE INTRAVENOUS EXTENDED TOXICITY STUDY IN RATS	20[redacted]年[redacted]月～20[redacted]年[redacted]月	イタリア	外国	評価
4.2.3.1-2	A3733	^{175}Lu-PSMA-617 solution SINGLE DOSE INTRAVENOUS EXTENDED TOXICITY STUDY IN MINIPIGS First Revision to Final Report	20[redacted]年[redacted]月～20[redacted]年[redacted]月	イタリア	外国	評価
4.2.3.2 反復投与毒性試験						
4.2.3.2-1	32508	SUBCHRONIC TOXICITY STUDY OF PSMA-617 BY INTRAVENOUS ADMINISTRATION TO MALE CD® RATS	20[redacted]年[redacted]月～20[redacted]年[redacted]月	ドイツ	外国	評価
4.2.3.3 遺伝毒性試験						
4.2.3.3.1 In Vitro 試験						
4.2.3.3.1-1	8365629	PSMA-617: Bacterial Reverse Mutation Assay	20[redacted]年[redacted]月～20[redacted]年[redacted]月	英国	外国	評価
4.2.3.3.2 In Vivo 試験						

添付資料番号	Report No./Study No.	タイトル	試験実施期間	試験実施場所	報種類（国内／外国）	評価／参考
－	－	該当資料なし	－	－	－	－
4.2.3.4　がん原性試験						
4.2.3.4.1　長期がん原性試験						
－	－	該当資料なし	－	－	－	－
4.2.3.4.2　短期又は中期がん原性試験						
4.2.3.4.3　その他の試験						
－	－	該当資料なし	－	－	－	－
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						
－	－	該当資料なし	－	－	－	－
4.2.3.5.2　胚・胎児発生に関する試験						
－	－	該当資料なし	－	－	－	－
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						
－	－	該当資料なし	－	－	－	－
4.2.3.5.4　新生児を用いた試験						
－	－	該当資料なし	－	－	－	－
4.2.3.6　局所刺激性試験						
－	－	該当資料なし	－	－	－	－
4.2.3.7　その他の毒性試験						
4.2.3.7.1　抗原性試験						
－	－	該当資料なし	－	－	－	－
4.2.3.7.2　免疫毒性試験						
－	－	該当資料なし	－	－	－	－

添付資料番号	Report No./Study No.	タイトル	試験実施期間	試験実施場所	報種類（国内／外国）	評価／参考
4.2.3.7.3　毒性発現の機序に関する試験						
―	―	該当資料なし	―	―	―	―
4.2.3.7.4　依存性試験						
―	―	該当資料なし	―	―	―	―
4.2.3.7.5　代謝物の毒性試験						
―	―	該当資料なし	―	―	―	―
4.2.3.7.6　不純物の毒性試験						
―	―	該当資料なし	―	―	―	―
4.2.3.7.7　その他の試験						
―	―	該当資料なし	―	―	―	―

添付資料番号	著者・タイトル・掲載誌	報種類（国内／外国）
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3 第 5 部

添付資料番号	Report No./Study No.	タイトル	試験実施期間	試験実施場所	報種類（国内／外国）	評価／参考	電子データの提出
5.2 全臨床試験一覧表							
5.2	－	全臨床試験一覧表	－	－	国内	評価	－
5.3 臨床試験報告書							
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							
－	－	該当資料なし	－	－	－	－	－
5.3.1.2 比較 BA 試験及び生物学的同等性（BE）試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.1.3 In Vitro-In Vivo の関連を検討した試験報告書							
－	－	該当資料なし	－	－	－	－	－
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	01360001	Validation of a Method to Characterize [^{177}Lu]-PSMA-617 in Human Urine Using HPLC with In-Line Radiodetection	20[redacted] 年[redacted] 月	米国	外国	参考	－
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							
5.3.2.1 血漿蛋白結合試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.2.2 肝代謝及び薬物相互作用試験報告書							
5.3.2.2-1	E0496	^{175}LU-PSMA-617 SOLUTION HUMAN LIVER CYP INDUCTION STUDY	20[redacted] 年[redacted] 月～20[redacted] 年[redacted] 月	イタリア	外国	参考	－
	E0496-01	Amendment no.1	20[redacted] 年[redacted] 月	イタリア	外国	参考	－

添付資料番号	Report No./Study No.	タイトル	試験実施期間	試験実施場所	報種類（国内／外国）	評価／参考	電子データの提出
5.3.2.2-2	Adacap-04-20Nov2019	*In vitro* Interaction Studies of ^{175}Lu-PSMA-617 solution with selected human Efflux (ABC) Transporters, and Uptake Transporters	20[redacted]年[redacted]月～20[redacted]年[redacted]月	ハンガリー	外国	参考	－
5.3.2.2-3	E0497	^{175}LU-PSMA-617 SOLUTION HUMAN LIVER CYP INHIBITION STUDY	20[redacted]年[redacted]月～20[redacted]年[redacted]月	イタリア	外国	参考	－
5.3.2.3　他のヒト生体試料を用いた試験報告書							
－	－	該当資料なし	－	－	－	－	－
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							
－	－	該当資料なし	－	－	－	－	－
5.3.3.2　患者における PK 及び初期忍容性試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.3.3　内因性要因を検討した PK 試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.3.4　外因性要因を検討した PK 試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.3.5　ポピュレーション PK 試験報告書							
5.3.3.5-1	AAA617 Modeling Report	Population PK Modeling and Exposure-Response Analyses on Organ Dosimetry and Acute Toxicity Based on [^{177}Lu]Lu-PSMA-617 Sub-study Data Modeling Report	20[redacted]年[redacted]月	ノバルティス	外国	参考	あり
5.3.4　臨床薬力学（PD）試験報告書							
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							
－	－	該当資料なし	－	－	－	－	－

添付資料番号	Report No./Study No.	タイトル	試験実施期間	試験実施場所	報種類（国内／外国）	評価／参考	電子データの提出
5.3.4.2 患者における PD 試験及び PK/PD 試験報告書							
－	－	該当資料なし	－	－	－	－	－
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	VISION (CAAA617A12301)-PA 総括報告書		2018 年 5 月～2021 年 1 月	ベルギー，カナダ，デンマーク，フランス，オランダ，スウェーデン，英国，米国，ドイツ	外国	評価	あり
	VISION (CAAA617A12301)-FA 総括報告書		2018 年 5 月～2023 年 12 月	ベルギー，カナダ，デンマーク，フランス，オランダ，スウェーデン，英国，米国，ドイツ	外国	評価	あり
5.3.5.1-2	PSMAfore (CAAA617B12302) 総括報告書		2021 年 6 月～2024 年 2 月（データカットオフ日）本報告時点で継続中	オーストリア，ベルギー，カナダ，チェコ，フランス，ドイツ，オランダ，ポーランド，スロバキア，スペイン，スウェーデン，スイス，英国，米国	外国	評価	あり
	PSMAfore (CAAA617B12302) C1 Kidney Dosimetry Report						
5.3.5.2 非対照試験報告書							

添付資料番号	Report No./Study No.	タイトル	試験実施期間	試験実施場所	報種類（国内／外国）	評価／参考	電子データの提出
5.3.5.2-1	CAAA617A11201 総括報告書		2022 年 1 月～2023 年 12 月（データカットオフ日）本報告時点で継続中	日本	国内	評価	あり
5.3.5.3 複数の試験成績を併せて解析した報告書							
5.3.5.3-1	SCE Appendix 1-VISION		—	—	—	—	—
5.3.5.3-2	SCS Appendix 1-VISION		—	—	—	—	あり
5.3.5.3-3	SCE Appendix 1-PSMAfore		—	—	—	—	—
5.3.5.3-4	SCS Appendix 1-PSMAfore		—	—	—	—	あり
5.3.5.3-5	SCE/SCS Appendix 1-JP		—	—	—	—	あり
5.3.5.4 その他の臨床試験報告書							
—	該当資料なし		—	—	—	—	—
5.3.6 市販後の使用経験に関する報告書							
5.3.6-1	PSUR (23-Sep-2023 to 22-Mar-2024)		—	—	—	—	—
5.3.7 患者データ一覧表及び症例記録							
—	該当資料なし		—	—	—	—	—

添付資料番号	著者・タイトル・掲載誌	報種類（国内／外国）
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