ヨビパス皮下注 168 μg ペン
ヨビパス皮下注 294 μg ペン
ヨビパス皮下注 420 μg ペン

第 2 部（モジュール 2）

1.8　添付文書（案）

＊添付文書は審査段階のものであり、最新の添付文書を参照すること

帝人ファーマ株式会社

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1.8　添付文書（案）

1.8.1　添付文書（案）

〇年〇月作成（第 1 版）

貯法：凍結を避けて、
2～8℃で保存
有効期間：3 年

処方箋医薬品[注)]

副甲状腺機能低下症治療剤
パロペグテリパラチド注射剤

ヨビパス®皮下注 168 μg ペン
ヨビパス®皮下注 294 μg ペン
ヨビパス®皮下注 420 μg ペン

YORVIPATH®Subcutaneous Injection

日本標準商品分類番号
872439

承認番号	
販売開始	—

注）注意-医師等の処方箋により使用すること

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		ヨビパス皮下注 168 μg ペン	ヨビパス皮下注 294 μg ペン	ヨビパス皮下注 420 μg ペン
容量		1 筒中 0.56 mL	1 筒中 0.98 mL	1 筒中 1.4 mL
有効成分		PTH(1-34) [注1)] 168 μg に相当するパロペグテリパラチドを含有する。	PTH(1-34) [注1)] 294 μg に相当するパロペグテリパラチドを含有する。	PTH(1-34) [注1)] 420 μg に相当するパロペグテリパラチドを含有する。
添加剤	コハク酸	0.66 mg	1.16 mg	1.65 mg
	D-マンニトール	23.4 mg	40.9 mg	58.4 mg
	m-クレゾール	1.4 mg	2.5 mg	3.5 mg
	水酸化ナトリウム	適量	適量	適量
	塩酸	適量	適量	適量

注 1) 副甲状腺ホルモンの N 末端 1～34 番目のアミノ酸に相当するペプチドである。

3.2 製剤の性状

販売名	ヨビパス皮下注 168 μg ペン	ヨビパス皮下注 294 μg ペン	ヨビパス皮下注 420 μg ペン
性状	無色澄明の液		
剤形	注射剤[注 2)]		
pH	3.7～4.3		
浸透圧	256～314 mOsmol/kg		
識別（ペン本体ラベル及び注入ボタンの色）	水色	ｵﾚﾝｼﾞ色	赤紫色
1 回あたりの投与可能量	6 μg 9 μg 12 μg	15 μg 18 μg 21 μg	24 μg 27 μg 30 μg

注 2) 本剤は、薬液を充填したカートリッジを専用のペン型注入器にあらかじめ装着した注射剤である。

4. 効能又は効果

副甲状腺機能低下症

5. 効能又は効果に関連する注意

5.1　活性型ビタミン D 製剤やカルシウム剤による治療を受けている患者に対して、本剤の投与を検討すること。［7.1 参照］

5.2　副甲状腺ホルモン分泌不全の患者に対して、本剤の投与を検討すること。偽性副甲状腺機能低下症の患者では、副甲状腺ホルモンに対する反応性が低下しており本剤の効果が期待できないため、本剤の投与前に血中 PTH 濃度を測定する等、適切に鑑別診断を行うこと。

6. 用法及び用量

通常、成人には、パロペグテリパラチドを、PTH(1-34)として 1 回 18 μg を開始用量とし、1 日 1 回、皮下注射する。以後、患者の血清カルシウム濃度の十分な管理のもとに、1 日 1 回 6～60 μg の範囲で適宜用量を増減して皮下投与するが、増量又は減量は 3 μg ずつ行うこと。

7. 用法及び用量に関連する注意

7.1　活性型ビタミン D 製剤やカルシウム剤による治療により患者の血清カルシウム濃度

が基準範囲内又はわずかに下回る状態（目安として 7.8～10.6 mg/dL）となっていることを確認した上で、本剤を投与すること。［5.1 参照］

7.2 本剤の投与開始時には、以下を参考に活性型ビタミン D 製剤及びカルシウム剤の投与量を調節すること。

7.2.1 投与開始時に活性型ビタミン D 製剤を投与している場合

・血清カルシウム濃度が 8.3 mg/dL 以上の場合、本剤の初回投与時に活性型ビタミン D 製剤の投与の中止を検討すること。

・血清カルシウム濃度が 8.3 mg/dL 未満の場合、本剤の初回投与時に活性型ビタミン D 製剤を本剤の投与開始前の用量の 50%を下限に減量すること。

・カルシウム剤を投与している場合、カルシウム剤の用量は維持すること。

7.2.2 投与開始時に活性型ビタミン D 製剤を投与しておらず、カルシウム剤を投与している場合

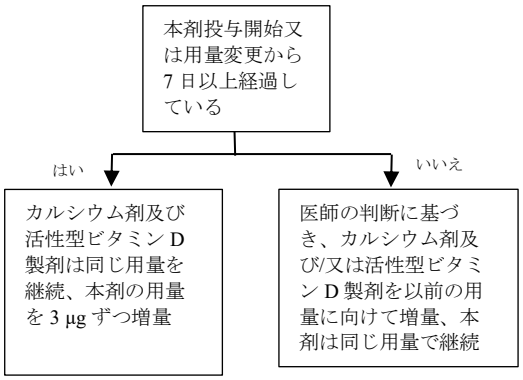
・カルシウム剤の用量が 1500 mg/日超の場合、本剤の初回投与時にカルシウム剤を 1500 mg/日を下限に減量すること。

・カルシウム剤の用量が 1500 mg/日以下の場合、本剤の初回投与時にカルシウム剤の投与を中止すること。ただし、食事から十分なカルシウムを摂取できない場合は、カルシウム剤を 600 mg/日以下の用量で投与することを検討すること。

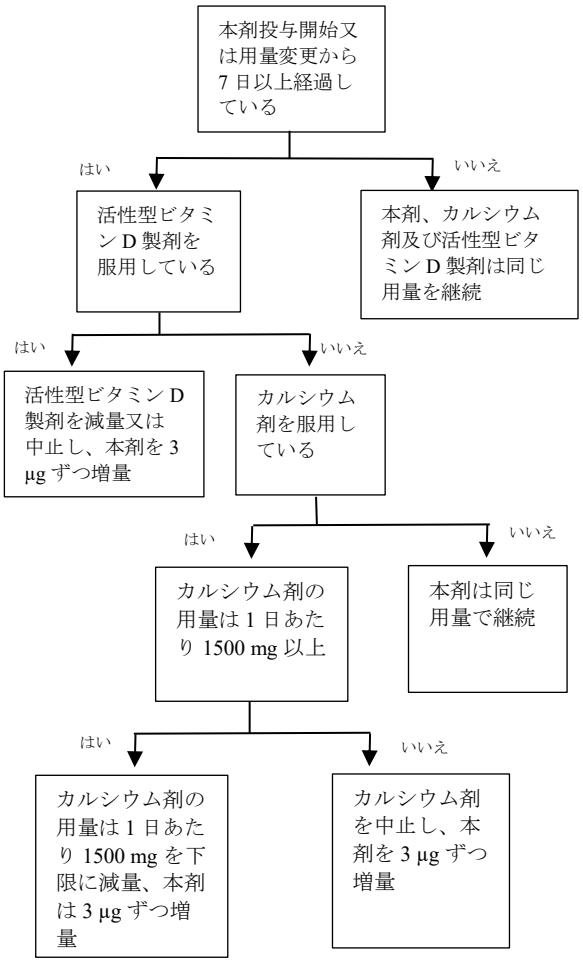
7.3 本剤の初回投与後、及び本剤、活性型ビタミン D 製剤又はカルシウム剤の投与量を変更した後は、7～14 日後を目安に血清カルシウム濃度を測定し、下図を参考に、血清カルシウム濃度が正常範囲内に維持されるように、本剤、活性型ビタミン D 製剤又はカルシウム剤の投与量を調節すること。［8.1、11.1.1 参照］

図 1 本剤、活性型ビタミン D 製剤及びカルシウム剤の投与量調節方法

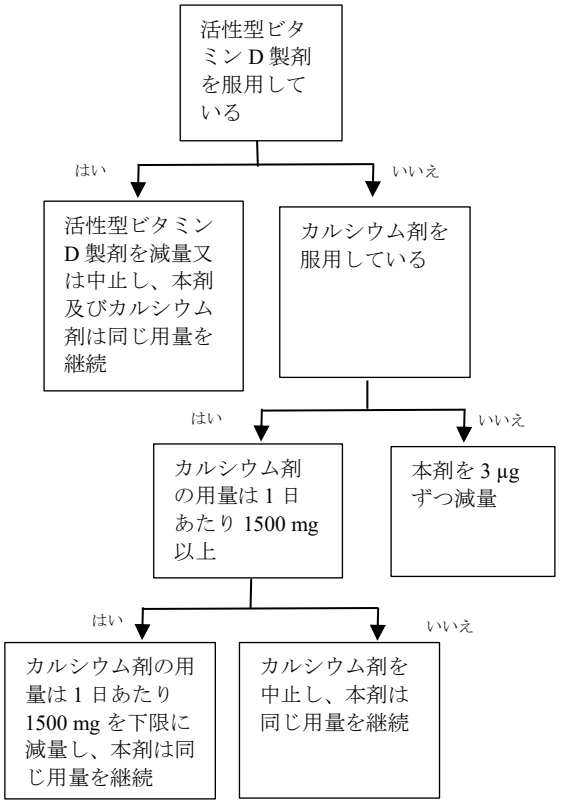
•血清カルシウム濃度 8.3 mg/dL 未満：



•血清カルシウム濃度 8.3 mg/dL 以上～10.6 mg/dL 以下：



•血清カルシウム濃度 10.7 mg/dL 以上～12.0 mg/dL 未満：



7.4 本剤の用量調節にあたっては、以下の点に留意すること。

・血清カルシウム濃度が 12.0 mg/dL 以上となった場合は、本剤を 2～3 日間を目安に休薬すること。その後、治療を再開する場合は、血清カルシウム濃度が 12.0 mg/dL 未満となったことを確認した上で、7.3 の図を参考に、患者の血清カルシウム濃度及び休薬前の本剤の用量に基づき、本剤、活性型ビタミン D 製剤及びカルシウム剤の用量を調節すること。［8.1、11.1.1 参照］

・投与を忘れた場合には、気付いた時点で直ちに投与すること。ただし、1 日に 2 回の投与は行わないこと。

・本剤の投与を 3 日以上休薬した場合は、低カルシウム血症の徴候・症状がないか確認し、血清カルシウム濃度の測定を検討すること。本剤による治療を再開する場合は、休薬前の用量から投与を開始し、その後は 7.3 の図を参考に、患者の血清カルシウム濃度に基づき、本剤、活性型ビタミン D 製剤及びカルシウム剤の用量を調節すること。

7.5 低アルブミン血症（血清アルブミン濃度が 4.0 g/dL 未満）がある場合には、補正カルシウム濃度[注 3)]を指標に用量を調節すること。

注 3) 補正カルシウム濃度（mg/dL）＝血清カルシウム濃度（mg/dL）－血清アルブミン濃度（g/dL）＋4.0

8. 重要な基本的注意

8.1 高カルシウム血症があらわれることがあるので、本剤投与中は定期的に血清カルシウム濃度を測定すること。［7.3、7.4、10.2、11.1.1 参照］

8.2 本剤の効果を十分に発揮させるため、ビタミン D が欠乏していない状態で本剤を投与することが望ましい。本剤の投与前及び投与期間中にビタミン D 欠乏が疑われる場合は、ビタミン D に関する栄養指導や生活指導等の実施を考慮すること。

8.3 起立性低血圧、めまい、立ちくらみ等があらわれることがあるので、高所での作業、自動車の運転等危険が伴う作業に従事する場合には注意させること。

8.4 本剤の自己注射にあたっては、以下の点に留意すること。

・投与法について十分な教育訓練を実施したのち、患者自ら確実に投与できることを確認した上で、医師の管理指導の下で実施すること。

・全ての器具の安全な廃棄方法について指導を徹底すること。

・添付されている取扱説明書を必ず読むよう指導すること。

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 骨肉腫発生のリスクが高いと考えられる患者

以下のような骨肉腫発生のリスクが高いと考えられる患者に対しては、患者のベネフィットとリスクを考慮して本剤の投与の可否を検討すること。［15.2.1、15.2.2 参照］

・悪性骨腫瘍及び転移性骨腫瘍のある患者

・骨に対する放射線療法中又は放射線療法後の患者

・原因不明のアルカリホスファターゼ高値を示す患者

・骨ページェット病の患者

9.2 腎機能障害患者

9.2.1 重度の腎機能障害患者（eGFR が 30 mL/min/1.73 m^2 未満）

特に投与開始時に高カルシウム血症を起こす可能性があることから、投与開始後は血清カルシウム濃度や患者の状態を十分に観察すること。重度の腎機能障害を有する又は透析中の副甲状腺機能低下症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］

9.5 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。［15.2.3 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に関するデータはない。

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

一般に生理機能が低下している。

10. 相互作用

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
ジギタリス製剤 ジゴキシン ［8.1、11.1.1 参照］	高カルシウム血症に伴い不整脈があらわれることがある。	血清カルシウム値が上昇すると、ジギタリスの作用が増強される。
ビスホスホネート系製剤 アレンドロン酸ナトリウム水和物 イバンドロン酸ナトリウム水和物 リセドロン酸ナトリウム水和物等 デノスマブ ロモソズマブ等 ［8.1、11.1.1 参照］	本剤による血清カルシウム濃度の正常化が阻害され、本剤の治療効果に影響を与える可能性がある。	これらの薬剤は血清カルシウムや骨代謝に影響を及ぼし、本剤の治療効果に影響を与える可能性がある。
テリパラチド製剤 ［8.1、11.1.1 参照］		
アバロパラチド酢酸塩製剤 ［8.1、11.1.1 参照］		
ループ系利尿薬 フロセミド アゾセミド トラセミド等 サイアザイド系利尿薬 トリクロルメチアジド ヒドロクロロチアジド等 サイアザイド系類似利尿薬 インダパミド等 ［8.1、11.1.1 参照］		
全身性コルチコステロイド薬 プレドニゾン デキサメタゾン ベタメタゾン等 ［8.1、11.1.1 参照］		
リチウム製剤 炭酸リチウム ［8.1、11.1.1 参照］		

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 高カルシウム血症（9.5%）

高カルシウム血症及び高カルシウム血症によると考えられる臨床症状が認められた場合

には、血清カルシウム濃度を測定し、必要に応じて投与の中止や輸液等の適切な処置を行うこと。［7.3、7.4、8.1、10.2 参照］

11.2 その他の副作用

種類＼頻度	10%以上	3～10%未満	3%未満
神経系障害		頭痛	浮動性めまい、体位性めまい
心臓障害			動悸
一般・全身障害および投与部位の状態	注射部位反応（紅斑、内出血、発疹等）（33.8%）		
胃腸障害		下痢、悪心	

13. 過量投与

13.1 症状

高カルシウム血症、起立性低血圧、悪心、嘔吐、めまい、頭痛等が起こる可能性がある。

13.2 処置

特異的な解毒薬はない。血清カルシウム濃度を測定し、輸液等の適切な処置を行うこと。

14. 適用上の注意

14.1 薬剤投与前の注意

14.1.1 本剤は JIS T 3226-2 に適合する A 型専用注射針を用いて使用すること。注射針は毎回新しいものを、必ず注射直前に取り付けること。

14.1.2 本剤と A 型専用注射針との装着時に液漏れ等の不具合が認められた場合には、新しい注射針に取り替える等の処置方法を患者に十分指導すること。

14.1.3 カートリッジにひびが入っている場合又は液が変色している場合は使用しないこと。

14.2 薬剤投与時の注意

14.2.1 投与部位

（1）腹部又は大腿前部に皮下注射すること。注射部位は毎回変更し、同一部位に短期間に繰り返し注射しないこと。

（2）本剤の 1 日用量が 30 μg を超える場合は、2 本のペン型注入器を用いて、異なる注射部位に 1 回ずつ計 2 回投与すること。

14.2.2 投与時

注射時は注入ボタンを 5 秒間押し続けること。

14.2.3 その他

（1）1 本のペン型注入器の本剤を複数の患者に使用しないこと。

（2）他の薬剤と混合しないこと 。

15. その他の注意

15.2 非臨床試験に基づく情報

15.2.1 雌雄ラットに本薬を皮下投与した反復投与毒性試験において、2 μg/kg/日及び 5 μg/kg/日（5 μg/kg/日投与時の遊離 PTH の AUC 比はヒトに本剤 60 μg/日を投与した場合の約 2 倍）で骨吸収作用を示唆する変化（鼻骨の空隙率の増加等）が、10 μg/kg/日以上（遊離 PTH の AUC 比は、ヒトに本剤 60 μg/日を投与した場合の約 5 倍以上）では骨形成作用を示唆する変化（大腿骨・胸骨の骨増加等）が認められた。また、20 μg/kg/日（遊離 PTH の AUC 比はヒトに本剤 60 μg/日を投与した場合の約 9 倍）で骨端線の異常（異形成）が認められた [1]。［9.1.1 参照］

15.2.2 本薬のがん原性試験は実施されていない。テリパラチド製剤（骨粗鬆症治療剤）では、雌雄ラットに皮下投与したがん原性試験において、骨肉腫を含む骨腫瘍性病変の発生頻度が増加したとの報告がある。［9.1.1 参照］

15.2.3 テリパラチド（遺伝子組換え）の動物試験では、ウサギで胎児毒性（胚死亡）が、マウスで胎児の骨格変異又は異常のわずかな増加が、ラットで出生児の体重増加抑制及び自

発運動量の低下が認められている。ラットに本薬 30 μg/kg/日又はウサギに本薬 6 μg/kg/日（遊離 PTH の AUC 比は、ヒトに本剤 60 μg/日を投与した場合と比較して、それぞれ約 7.9 倍及び 6.6 倍）を投与した試験では、胚・胎児発生への影響を示唆する所見は認められていない[2]。［9.5 参照］

16. 薬物動態

16.1 血中濃度

16.1.1 単回投与

日本人健康成人男性に本剤 50、75、100 μg を単回皮下投与したときの血漿中遊離 PTH（1-34）の薬物動態パラメータは以下のとおりであった[3]。

表 1 単回皮下投与後の血漿中遊離 PTH（1-34）の薬物動態パラメータ

用量（μg）	C_{max}（pg/mL）	$AUC_{0\text{-}120\ h}$（pg· h/mL）	t_{max}（h）
50（n=7）	7.19（10.6）	340（17.8）	8.00（4.00-16.17）
75（n=7）	10.3（20.6）	484（9.3）	8.00（1.97-16.05）
100（n=7）	14.1（22.5）	621（19.2）	4.00（2.00-7.98）

幾何平均値（幾何 CV%）、t_{max}：中央値（最小値-最大値）
遊離 PTH（1-34）：本剤から遊離した PTH（1-34）を測定

16.1.2 反復投与

（1）健康成人

外国人健康成人に本剤 12～24 μg を 1 日 1 回 10 日間反復皮下投与したときの血漿中遊離 PTH（1-34）の薬物動態パラメータは以下のとおりであった[3)、4)]。

表 2 反復皮下投与後の血漿中遊離 PTH（1-34）の薬物動態パラメータ

用量（μg）	評価時点	C_{max}（pg/mL）	AUC_{tau}（pg· h/mL）	t_{max}（h）	$t_{1/2}$（h）
12（n=8）	1 日目	－	－	－	－
	10 日目	3.78（18.6）	68.0（21.4）	4.00（4.00-16.02）	63.7（27.0）
16（n=8）	1 日目	2.45（19.3）	46.2（14.2）	8.00（4.00-16.00）	－
	10 日目	4.46（20.3）	87.7（23.5）	4.00（4.00-12.00）	34.8（40.7）
20（n=8）	1 日目	3.05（17.7）	54.7（17.4）	4.00（3.75-16.00）	－
	10 日目	5.77（19.0）	112（20.5）	6.07（4.03-16.05）	51.3（9.6）
24（n=8）	1 日目	3.81（15.4）	66.8（15.9）	8.00（4.00-16.00）	－
	10 日目	7.43（22.6）	150（19.1）	7.88（4.00-12.00）	46.9（13.2）

幾何平均値（幾何 CV%）、t_{max}：中央値（最小値-最大値）
遊離 PTH（1-34）：本剤から遊離した PTH（1-34）を測定

（2）副甲状腺機能低下症患者

外国人副甲状腺機能低下症の成人患者 12 例に本剤 12～45 μg（平均 24.5 μg）を 1 日 1 回反復皮下投与したときの定常状態における血漿中遊離 PTH 濃度推移は以下のとおりであり、投与後 24 時間を通じて正常範囲内[注 4)]を維持した[5]。

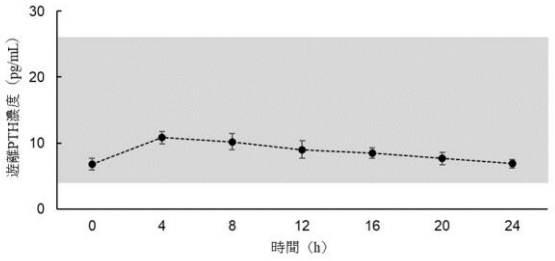


図 2 反復皮下投与したときの血漿中遊離 PTH 濃度推移

平均値±標準誤差（各測定ポイントにおける例数 n = 7~12）
遊離 PTH：遊離 PTH（1-34）濃度と遊離 PTH（1-33）濃度を合算

注 4）遊離 PTH の正常範囲（約 4~26 pg/mL）は、血漿中の内因性 PTH（1-84）濃度の正常範囲（10~65 pg/mL）と、内因性 PTH（1-84）に対する PTH（1-34）の分子量の比から算出された。

16.3 分布

健康成人、腎機能障害者及び副甲状腺機能低下症患者 281 例から得られたデータに基づく母集団薬物動態解析により、体重 70 kg の外国人健康成人女性に本剤を皮下投与したときの遊離 PTH の見かけの分布容積（平均値（CV%））は 8.7(18) L と推定された[6]。

16.4 代謝

パロペグテリパラチドは生理的条件下でリンカー部位が加水分解され、PTH（1-34）及びPTH（1-34）の活性代謝物である PTH（1-33）を放出する。PTH（1-34）及び PTH（1-33）は同様の活性を有する。［18.1 参照］

16.6 特定の背景を有する患者

16.6.1 腎機能障害者

腎機能障害の程度が異なる被験者に本剤 50 μg を単回皮下投与したときの遊離 PTH（1-34）、総 PTH 及び mPEG の薬物動態パラメータを、腎機能が正常（eGFR 90 mL/min/1.73 m^2 以上）な被験者（13 例）と比較した結果は以下のとおりであった[3]。重度腎機能障害を有する被験者では、内因性 PTH（1-84）濃度が高いことに起因し、遊離 PTH（1-34）の曝露量が適切に評価されていない可能性がある[7]。［9.2.1 参照］

表 3 腎機能障害者における単回皮下投与後の遊離 PTH（1-34）、総 PTH 及び mPEG の薬物動態パラメータ

腎機能障害の程度 eGFR（mL/min/1.73 m^2）	遊離 PTH（1-34）		総PTH		mPEG	
	C_{max} 幾何平均値の比［90%信頼区間］	AUC_{last} 幾何平均値の比［90%信頼区間］	C_{max} 幾何平均値の比［90%信頼区間］	AUC_{last} 幾何平均値の比［90%信頼区間］	C_{max} 幾何平均値の比［90%信頼区間］	AUC_{last} 幾何平均値の比［90%信頼区間］
軽度（60 ≦ eGFR ＜90）（n=9）	1.13［0.956-1.33］	1.43［1.01-2.03］	1.19［0.716-1.97］	1.29［0.764-2.16］	1.31［0.820-2.09］	1.59［0.874-2.88］
中等度（30 ≦ eGFR ＜60）（n=8）	1.17［0.859-1.60］	1.34［0.712-2.50］	0.741［0.408-1.35］	0.834［0.484-1.44］	0.942［0.543-1.64］	1.18［0.788-1.78］
重度（eGFR＜30）（n=8）	2.83［1.82-4.40］	13.80［5.83-32.50］	0.718［0.394-1.31］	0.740［0.339-1.62］	1.01［0.646-1.57］	1.25［0.579-2.71］

遊離 PTH（1-34）：本剤から遊離した PTH（1-34）を測定
総 PTH：本剤中の PTH(1-34)及び PTH（1-33）を測定。ただし、遊離 PTH 及び内因性 PTH（1-84）も併せて測定された。
mPEG：本剤中の mPEG 及び本剤から遊離した mPEG を測定

16.6.2 高齢者

母集団薬物動態解析の結果、年齢（19～76 歳）は遊離 PTH の曝露量に影響を及ぼさないことが示唆された[6]。

17. 臨床成績

17.1 有効性及び安全性に関する試験

17.1.1 海外第Ⅲ相試験

活性型ビタミン D 製剤及びカルシウム剤による治療を受けている副甲状腺機能低下症患者 82 例を対象に、プラセボ対照無作為化二重盲験並行群間比較試験を実施した（本剤群 61 例、プラセボ群 21 例）。用法は、プラセボ又は本剤を 1 日 1 回皮下投与とされた。本剤の開始用量は 18 μg とされ、その後は患者ごとに、血清カルシウム値が正常となり、かつ活性型ビタミン D 製剤及びカルシウム剤からの離脱が可能となるよう、6～60 μg の範囲で用量が調節された[8]。

主要評価項目は盲検期終了時（投与 26 週時）のレスポンダーの割合とされ、レスポンダーはアルブミン補正血清カルシウム濃度が正常範囲（8.3～10.6 mg/dL）、活性型ビタミン D 製剤からの離脱、カルシウム剤からの離脱、投与 26 週時より 4 週間以内に治験薬を増量していない、のすべてを満たす場合とされた[9]。

盲検期終了時のレスポンダーの割合について、本剤群は 78.7%（48/61 例）、プラセボ群は 4.8%（1/21 例）、群間差［95%信頼区間］は 73.9%［52.8, 85.4］であり、プラセボに対する本剤の優越性が示された（p＜0.0001、副甲状腺機能低下症の成因（術後、その他）で層別化した Cochran-Mantel-Haenszel 検定、有意水準両側 5%）。試験期間中の本剤群の投与量（中央値［範囲］）は、投与 4 週時では 21.0［12, 30］ μg、投与 26 週時では 21.0［9, 39］ μg であった。

盲検期終了時までの副作用の発現割合は本剤群で 49.2%（30/61 例）、プラセボ群で 38.1%（8/21 例）であり、本剤群の主な副作用は、注射部位反応 31.1%（19/61 例）、頭痛 9.8%（6/61 例）、高カルシウム血症 9.8%（6/61 例）、悪心 8.2%（5/61 例）であった。

17.1.2 国内第Ⅲ相試験

活性型ビタミン D 製剤及びカルシウム剤による治療を受けている副甲状腺機能低下症患者 13 例を対象に、非盲検非対照試験を実施した。用法は、本剤を 1 日 1 回皮下投与、本剤の開始用量は 18 μg とされ、その後は患者ごとに、血清カルシウム値が正常となり、かつ活性型ビ

タミン D 製剤及びカルシウム剤からの離脱が可能となるよう、6～60 μg の範囲で用量が調節された[10]。

主要評価項目は有効性評価期終了時（投与 26 週時）のレスポンダーの割合とされ、レスポンダーはアルブミン補正血清カルシウム濃度が正常範囲（8.3～10.6 mg/dL）、活性型ビタミン D 製剤からの離脱、カルシウム製剤からの離脱、のすべてを満たす場合とされた[10]。

有効性評価期終了時のレスポンダーの割合は、92.3%（12/13 例）、投与 52 週時のレスポンダーの割合は、91.7%（11/12 例）であった。試験期間中の投与量（中央値［範囲］）は、投与 4 週時では 21.0［12, 27］ μg、投与 26 週時では 21.0［12, 30］ μg、投与 52 週時では 22.5［12, 33］ μg であった。

副作用は投与 52 週時までに 30.8%（4/13 例）に認められ、認められた副作用は、注射部位紅斑、投薬過誤、高カルシウム血症、高カルシウム尿症が各 7.7%（1/13 例）であった。

なお、国内第Ⅲ相試験において、本剤の 1 日投与量が 30 μg を超える場合、下表のとおりに 2 本のペンを組み合わせて投与された。

用量	用法	ペン型注入器の組み合わせ
33 μg/日	18 μg/日＋15μg/日	294 μg/0.98mL ペン 2 本 （オレンジ色の押しボタン付き）
36 μg/日	18 μg/日＋18 μg/日	
39 μg/日	21 μg/日＋18 μg/日	
42 μg/日	21 μg/日＋21 μg/日	
45 μg/日	24 μg/日＋21 μg/日	420 μg/1.4 mL ペン 1 本 （赤紫色の押しボタン付き） ＋ 294 μg/0.98mL ペン 1 本 （オレンジ色の押しボタン付き）
48 μg/日	24 μg/日＋24 μg/日	420 μg/1.4 mL ペン 2 本 （赤紫色の押しボタン付き）
51 μg/日	27 μg/日＋24 μg/日	
54 μg/日	27 μg/日＋27 μg/日	
57 μg/日	30 μg/日＋27 μg/日	
60 μg/日	30 μg/日＋30 μg/日	

18. 薬効薬理

18.1 作用機序

パロペグテリパラチドは、PTH（1-34）にリンカーを介してメトキシポリエチレングリコールを結合させたプロドラッグであり、皮下投与後、リンカー部分が加水分解することにより、PTH（1-34）が持続的に遊離する[11]。

PTH（1-34）及び主な代謝物である PTH（1-33）は、内因性 PTH（1-84）と同様に PTH 受容体に作用し、骨組織からのカルシウムの動員や腎臓の尿細管からのカルシウム再吸収の促進、小腸における活性型ビタミン D 合成亢進を介した間接的なカルシウム輸送の促進により、血中カルシウム濃度を上昇させる。また、腎臓のリン再吸収を抑制すること等により、血中リン濃度を低下させる。［16.4 参照］

18.2 副甲状腺機能低下症の動物モデルでの薬理作用

副甲状腺機能低下症モデルラットにおいて、パロペグテリパラチドを 28 日間反復皮下投与した結果、試験期間を通じて血中カルシウム濃度が上昇し、血中リン濃度が低下した。また、骨形成マーカー及び骨吸収マーカーの上昇、海綿骨の骨密度の低下が認められた[11]。

19. 有効成分に関する理化学的知見

一般的名称：

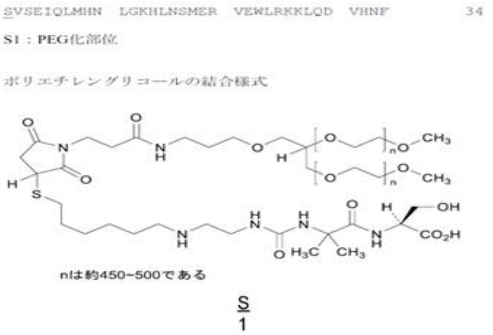
パロペグテリパラチド

（Palopegteriparatide）（JAN）

分子式：$C_{181}H_{291}N_{55}O_{51}S_2$（ペプチド部分）

分子量：約 48,000（ペプチド部分：4,117.72）

化学構造式：



S
1

N-({2-[(6-{[1-{3-[(3-{2,3-bis[α-methylpoly(oxyethylene)-ω-oxy]propoxy}propyl)amino]-3-oxopropyl}-2,5-dioxopyrrolidin-3-yl]sulfanyl}hexyl)amino]ethyl}carbamoyl)-2-methylAla-Ser

本質：パロペグテリパラチドは、ヒト副甲状腺ホルモン類縁体であり、ヒト副甲状腺ホルモンの 1～34 番目のアミノ酸に相当し、メトキシポリエチレングリコール（分子量：約 43,000）が切断可能なリンカーを介して結合している（PEG 結合部位：S1）。パロペグテリパラチドは、34 個のアミノ酸残基からなる PEG 化合成ペプチド（分子量：約 48,000）である。

20. 取扱い上の注意

使用開始後はキャップにより遮光して室温（30℃以下）に保管し，2 週間以内に使用すること。残った場合は廃棄すること。

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

＜ヨビパス皮下注 168 μg ペン＞

1 筒

＜ヨビパス皮下注 294 μg ペン＞

1 筒

＜ヨビパス皮下注 420 μg ペン＞

1 筒

23. 主要文献

1) 社内報告: 反復投与毒性試験（ラット）. 20XX.（2025 年 X 月 XX 日承認、CTD2.6.6.3.1）

2) 社内報告: 生殖発生毒性試験（マウス、ラット、ウサギ）. 20XX.（2025 年 X 月 XX 日承認、CTD2.6.6.6）

3) 社内報告：海外第 I 相試験（健康成人）. 20XX.（2025 年 X 月 XX 日承認、CTD2.7.6.3、5.3.3.1、5.3.3.3）

4) Karpf DB,et al.: J Bone Miner Res. 2020 ; 35(8) : 1430-40.

5) 社内報告：海外第Ⅱ相試験（副甲状腺機能低下症患者）. 20XX.（2025 年 X 月 XX 日承認、CTD5.3.5.1）

6) 社内報告 : 母集団薬物動態解析（健康成人、腎機能障害者、副甲状腺機能低下症患者）. 20XX.（2025 年 X 月 XX 日承認、CTD2.7.2.3、CTD5.3.3.5）

7) 社内報告：海外第 I 相試験（腎機能障害患者）. 20XX.(2025 年 X 月 XX 日承認、CTD5.3.3.3）

8) 社内報告：海外第Ⅲ相試験（副甲状腺機能低下症）. 20XX.（2025 年 X 月 XX 日承認、CTD2.7.3.2、、2.7.4.2、2.7.6.6、5.3.5.1）

9) Khan AA, et al.: J Bone Miner Res. 2023；38(1)：14-25.

10) 社内報告：国内第Ⅲ相試験（副甲状腺機能低下症）. 20XX.(2025 年 X 月 XX 日承認、CTD 2.7.3.2、2.7.6.7、5.3.5.2 ）

11) Holeten-Andersen L, et al.: J Bone Miner Res. 2019; 34(11): 2075-86.

24. 文献請求先及び問い合わせ先

帝人ファーマ株式会社 メディカル情報グループ

〒100-8585　東京都千代田区霞が関 3 丁目 2 番 1 号

フリーダイヤル　0120-189-315

26. 製造販売業者等

26.1 製造販売元

帝人ファーマ株式会社

東京都千代田区霞が関 3 丁目 2 番 1 号

ヨビパス®／YORVIPATH® is the registered trademark of Ascendis Pharma Bone Disease A/S, Hellerup, Denmark.

1.8.2 「効能又は効果」（案）及びその設定の根拠

1.8.2.1 効能又は効果（案）

4. 効能又は効果 副甲状腺機能低下症 5. 効能又は効果に関連する注意 5.1 活性型ビタミン D 製剤やカルシウム剤による治療を受けている患者に対して、本剤の投与を検討すること。［7.1 参照］ 5.2 副甲状腺ホルモン分泌不全の患者に対して、本剤の投与を検討すること。偽性副甲状腺機能低下症の患者では、副甲状腺ホルモンに対する反応性が低下しており本剤の効果が期待できないため、本剤の投与前に血中 PTH 濃度を測定する等、適切に鑑別診断を行うこと。

1.8.2.2 効能又は効果の設定根拠

TCP-304 試験は海外第III相検証試験で、副甲状腺機能低下症の成人患者を対象に ACP-014 の有効性、安全性、忍容性、及び QOL を評価することを目的とした、26 週間の多施設共同、無作為化、二重盲検、プラセボ対照試験、及び 3 年間の非盲検継続投与試験であった。

治験薬の投与を受けた 82 名（ACP-014 群：61 名、プラセボ群：21 名）を ITT 解析対象集団及び安全性解析対象集団に含めた。被験者の多くが 26 週間の盲検期を完了した。盲検期に、有害事象のために治験薬の投与を中止した被験者は 3 名（ACP-014 群：1 名、プラセボ群：2 名）であった。

TCP-304 試験では、レスポンダーの定義は盲検期終了時（Week 26）に、以下に示す主要評価項目をすべて満たすこととした。

1) アルブミン補正血清カルシウム濃度が基準範囲（8.3～10.6 mg/dL）
2) 活性型ビタミン D 投与からの離脱（4 週間以内の活性型ビタミン D の 1 日用量が 0 かつ頓用での使用が 7 日以内）
3) 治療用量（600 mg/日以下）のカルシウム投与からの離脱（4 週間以内のカルシウムの 1 日用量が 600 mg/日以下かつ頓用での使用が 7 日以内）
4) Week 26 来院前 4 週間以内に治験薬の増量を必要としない

盲検期終了時（Week 26）にレスポンダーと判定された被験者の割合は、ACP-014 群で 78.7%（48/61 名、95% CI：66.3, 88.1）及びプラセボ群で 4.8%（1/21 名、95% CI：0.1, 23.8）であり、統計学的に有意な差が認められた（P< 0.0001）。

TCP-305 試験は日本人の副甲状腺機能低下症の成人患者を対象とした国内第 III 相試験で、海外第 III 相試験である TCP-304 試験を補足することを目的とした、26 週間の多施設共同、単群非盲検試験、及び 3 年間の継続投与試験であった。

本治験には 13 名が組み入れられた。全員が ACP-014 の投与を受け、有効性評価期を完了した。ただし、そのうち 1 名は有効性評価期を完了したが、医師の判断（治験薬の服薬コンプライアンス不良が疑われた）で継続投与期には移行しなかった。本被験者は Day 187 に治験薬投与を中止した（治験薬の最終投与日は Day 186）。12 名が継続投与期に移行し、データカットオフ時点で全員が Week 52 までを完了した。

TCP-305 試験では、レスポンダーの定義を Week 26 に以下のすべてを満たすこととした。

1) アルブミン補正血清カルシウム濃度が基準範囲（8.3～10.6 mg/dL）2) 活性型ビタミン D 投与からの離脱

3) 治療用量のカルシウム投与からの離脱（すなわち Week 26 及びその前日の 1 日のカルシウム用量が 600 mg 以下）

Week 26 に複合エンドポイントを達成してレスポンダーと判定された被験者の割合は 92.3%（12/13 名、95% CI：64.0, 99.8）であった。

すべての被験者が「活性型ビタミン D 投与からの離脱」及び「治療用量のカルシウム投与からの離脱」に該当した。1 名を除く全員が「アルブミン補正血清カルシウム濃度が基準範囲」に該当した。Week 26 に血清カルシウム濃度が基準範囲外であった被験者の血清カルシウム濃度は 7.9 mg/dL であり、当該被験者の Week 26 以前のカルシウム濃度はベースラインを除き基準範囲であった。

また、Week 52 の有効性の主要解析の結果として、主要評価項目と同様の解析を Week 52 に実施した。継続投与期に移行した被験者の 91.7%（11/12 名、95% CI：61.5, 99.8）が Week 52 にレスポンダー基準を満たした。すべての被験者が活性型ビタミン D 及び治療用量のカルシウム投与からの離脱（すなわち、600 mg/日以下のカルシウム投与）を達成した。また、12 名中 11 名でアルブミン補正血清カルシウムが基準範囲となった。

TCP-305 試験の結果から、日本人でも TCP-304 試験の結果と同様の傾向が認められ、副甲状腺機能低下症患者に対する ACP-014 の有効性が確認された。

以上のことから、本剤の効能又は効果を「副甲状腺機能低下症」と設定した。

1.8.2.3 効能又は効果に関連する注意の設定根拠

5.1 本剤で実施した臨床試験では、治験薬投与開始まで活性型ビタミン D 製剤又はカルシウム製剤による治療を行っている副甲状腺機能低下症患者を対象としているため設定した。

5.2 PTH に対する反応性が低下して PTH 抵抗性となり（偽性副甲状腺機能低下症）、低カルシウム血症の状況で PTH 濃度が上昇している患者は、本剤による治療対象ではないため設定した。

1.8.3 「用法及び用量」（案）、「用法及び用量に関連する注意」（案）及び設定根拠

6. 用法及び用量

通常、成人には、パロペグテリパラチドを、PTH（1-34）として 1 回 18 μg を開始用量とし、1 日 1 回、皮下注射する。以後、患者の血清カルシウム濃度の十分な管理のもとに、1 日 1 回 6～60 μg の範囲で適宜用量を増減して皮下投与するが、増量又は減量は 3 μg ずつ行うこと。

7. 用法及び用量に関連する注意

7.1 活性型ビタミン D 製剤やカルシウム剤による治療により患者の血清カルシウム濃度が基準範囲内又はわずかに下回る状態（目安として 7.8～10.6 mg/dL）となっていることを確認した上で、本剤を投与すること。［5.1 参照］

7.2 本剤の投与開始時には、以下を参考に活性型ビタミン D 製剤及びカルシウム剤の投与量を調節すること。

7.2.1 投与開始時に活性型ビタミン D 製剤を投与している場合

・血清カルシウム濃度が 8.3 mg/dL 以上の場合、本剤の初回投与時に活性型ビタミン D 製剤の投与の中止を検討すること。

・血清カルシウム濃度が 8.3 mg/dL 未満の場合、本剤の初回投与時に活性型ビタミン D 製剤を本剤の投与開始前の用量の 50%を下限に減量すること。

・カルシウム剤を投与している場合、カルシウム剤の用量は維持すること。

7.2.2 投与開始時に活性型ビタミン D 製剤を投与しておらず、カルシウム剤を投与している場合

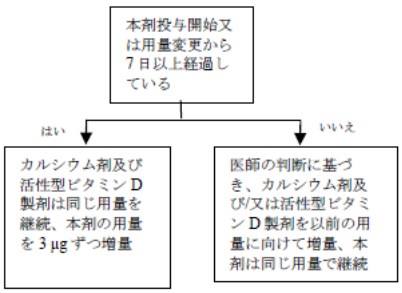
・カルシウム剤の用量が 1500 mg/日超の場合、本剤の初回投与時にカルシウム剤を 1500 mg/日を下限に減量すること。

・カルシウム剤の用量が 1500 mg/日以下の場合、本剤の初回投与時にカルシウム剤の投与を中止すること。ただし、食事から十分なカルシウムを摂取できない場合は、カルシウム剤を 600 mg/日以下の用量で投与することを検討すること。

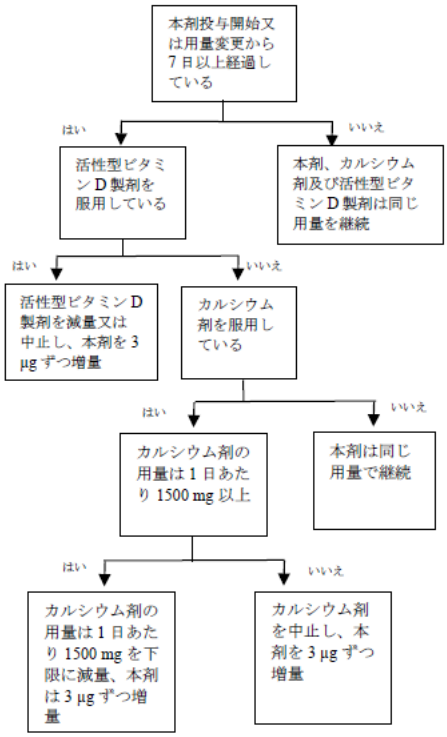
7.3 本剤の初回投与後、及び本剤、活性型ビタミン D 製剤又はカルシウム剤の投与量を変更した後は、7～14 日後を目安に血清カルシウム濃度を測定し、下図を参考に、血清カルシウム濃度が正常範囲内に維持されるように、本剤、活性型ビタミン D 製剤又はカルシウム剤の投与量を調節すること。［8.1、11.1.1 参照］

図 1 本剤、活性型ビタミン D 製剤及びカルシウム剤の投与量調節方法

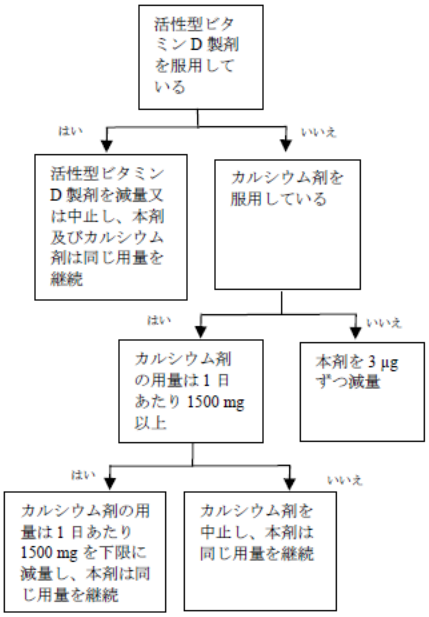
･血清カルシウム濃度 8.3 mg/dL 未満：



・血清カルシウム濃度 8.3 mg/dL 以上～10.6 mg/dL 以下：



・血清カルシウム濃度 10.7 mg/dL 以上～12.0 mg/dL 未満　：



7.4 本剤の用量調節にあたっては、以下の点に留意すること。

・血清カルシウム濃度が 12.0 mg/dL 以上となった場合は、本剤を 2～3 日間を目安に休薬すること。その後、治療を再開する場合は、血清カルシウム濃度が 12.0 mg/dL 未満となったことを確認した上で、7.3 の図を参考に、患者の血清カルシウム濃度及び休薬前の本剤の用量に基づき、本剤、活性型ビタミン D 製剤及びカルシウム剤の用量を調節すること。[8.1、 11.1.1 参照]

・投与を忘れた場合には、気付いた時点で直ちに投与すること。ただし、1 日に 2 回の投与は行わないこと。

・本剤の投与を 3 日以上休薬した場合は、低カルシウム血症の徴候・症状がないか確認し、血清カルシウム濃度の測定を検討すること。本剤による治療を再開する場合は、休薬前の用量から投与を開始し、その後は 7.3 の図を参考に、患者の血清カルシウム濃度に基づき、本剤、活性型ビタミン D 製剤及びカルシウム剤の用量を調節すること。

7.5 低アルブミン血症（血清アルブミン濃度が 4.0 g/dL 未満）がある場合には、補正カルシウム濃度注 3)を指標に用量を調節すること。

注 3) 補正カルシウム濃度（mg/dL）＝血清カルシウム濃度（mg/dL）－
血清アルブミン濃度（g/dL）＋4.0

1.8.3.1　用法・用量の設定根拠

CT-103 試験（健康成人を対象とした海外第 I 相試験）の結果から、ACP-014 12～20 μg/日の用量範囲で有効性が認められ、忍容性も良好であることが示唆された。健康成人では、血管拡張症状に基づき ACP-014 20 μg/日が MTD と判断され、ACP-014 12 μg/日はアルブミン補正血清カルシ

ウムの上昇が認められた最低用量であった。副甲状腺機能低下症患者では、ACP-014 20 μg/日を超える用量が有効で、忍容性も良好である可能性が考えられた。

TCP-201 試験（副甲状腺機能低下症患者を対象とした海外第 II 相試験）では、4 週間の盲検期に ACP-014 を固定用量（15、18、又は 21 μg/日）で投与した。また、アルブミン補正血清カルシウム濃度が基準範囲（8.3～10.6 mg/dL）に保つために、補給用量のカルシウム剤及び活性型ビタミン D の用量を調節した。OLE 期では、ACP-014 の用量を 6～60 μg/日の範囲で至適用量まで調節した。また、CT-103 試験では ACP-014 4 μg の用量幅の用量変更で PD の反応に差異が認められたことから、用量調節する際の用量幅として ACP-014 3 μg を選択した。遊離 PTH 濃度は Day 7 までに定常状態に近づいていることから、被験者ごとの用量調節は 7 日間隔で測定した血清カルシウム濃度に基づいて設定した。その結果、有害事象の発現割合に関して、ACP-014 15～21 μg/日の間で、低カルシウム血症又は高カルシウム血症に関連する有害事象を含め大きな差は認められなかった。いずれの固定用量でも有効性及び良好な忍容性が認められたが、ACP-014 18 μg/日は、ACP-014 21 μg/日と比較して高カルシウム血症の発現割合が低く、臨床的に意味のある低カルシウム血症も認められなかった［5.3.5.1-1 TCP-201 試験 12.2.1 項、12.2.2 項］。

TCP-304 試験では、開始用量を ACP-014 18 μg/日とし、用量調節アルゴリズムに従って 6～60 μg/日の範囲で 3 μg/日ずつ至適用量まで用量を調節した［5.3.5.1-2 TCP-304 試験 治験実施計画書 Figure 3］。治験薬に加え、カルシウム及び活性型ビタミン D の用量も用量調節アルゴリズムに従って調節した。盲検期（26 週間）の結果から、ACP-014 の開始用量を 18 μg/日とし、アルブミン補正血清カルシウム濃度の測定値に基づき至適用量まで調節することが支持された。盲検期終了時（Week 26）、被験者の多くでアルブミン補正血清カルシウム濃度が基準範囲であった。Week 26 の ACP-014 の用量の範囲は 9～39 μg/日であり、被験者ごとに異なる用量の必要性が示唆された［5.3.5.1-2 TCP-304 試験 Table 14.1.3.2］。

TCP-305 試験では、TCP-304 試験と同様に開始用量を 18 μg/日とし、用量調節アルゴリズムに従って 6～60 μg/日の用量範囲で 3 μg/日ずつ至適用量まで調節した［5.3.5.2-1 TCP-305 試験 治験実施計画書 1.2 項 図 2］。TCP-305 試験でも、Week 26 で治療用量のカルシウム及び活性型ビタミン D 投与から離脱した被験者の多くでアルブミン補正血清カルシウム濃度が基準範囲であった。Week 26 までの TCP-014 の用量の範囲は 12～45 μg/日であり、日本人集団でも、海外試験と同様の用量で有効性が認められた。

これら臨床試験の結果に基づき、ACP-014 は 18 μg/日で投与を開始し、その後は血清カルシウム濃度に基づいて、実診療での来院頻度も踏まえて、7～14 日間隔で被験者ごとに適切な維持用量（既存の治療薬を中止して正常な血清カルシウム濃度を維持する用量として 6～60 μg/日）まで調節する投与方法を設定した。また、用量調節する際の用量幅は 3 μg とした。

1.8.3.2 「用法及び用量に関連する注意」の設定根拠

1. 投与開始時の血清カルシウム濃度
   本剤は血清カルシウム濃度上昇作用を有するため、血清カルシウム濃度が高値の患者に

投与された場合、血清カルシウム濃度が過度に上昇し、起立性低血圧、悪心、嘔吐、めまい、無力症、頻脈及び頭痛等を生じる可能性がある。したがって、患者の血清カルシウム濃度が高値でないことを確認の上で、本剤の投与を開始することが必要である。TCP-304 試験及び TCP-305 試験では選択基準として、アルブミン補正血清カルシウム濃度 7.8～10.6 mg/dL と設定し、安全性に大きな問題は認められなかったことから、本剤開始時の血清カルシウム濃度の目安を 7.8～10.6 mg/dL と設定した。

2. 本剤、活性型ビタミンD製剤及びカルシウム剤の投与量

本剤投与開始時及び投与開始後の本剤並びに併用している活性型ビタミン D 製剤及びカルシウム剤の投与量を含めて、血清カルシウム濃度を正常に維持できる投与量を調節する必要があるため、設定した。

1.8.4　「使用上の注意」（案）及び設定根拠

使用上の注意（案）	設定根拠
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. 本剤の成分に対する過敏症の既往歴がある患者に本剤を投与した場合、過敏症が発現する可能性が高いため設定した。
8. 重要な基本的注意 8.1 高カルシウム血症があらわれることがあるので、本剤投与中は定期的に血清カルシウム濃度を測定すること。[7.3、7.4、10.2、11.1.1 参照] 8.2 本剤の効果を十分に発揮させるため、ビタミン D が欠乏していない状態で本剤を投与することが望ましい。本剤の投与前及び投与期間中にビタミン D 欠乏が疑われる場合は、ビタミン D に関する栄養指導や生活指導等の実施を考慮すること。 8.3 起立性低血圧、めまい、立ちくらみ等があらわれることがあるので、高所での作業、自動車の運転等危険が伴う作業に従事する場合には注意させること。 8.4 本剤の自己注射にあたっては、以下の点に留意すること。 ・投与法について十分な教育訓練を実施したのち、患者自ら確実に投与できることを確認した上で、医師の管理指導の下で実施すること。 ・全ての器具の安全な廃棄方法について指導を徹底すること。 ・添付されている取扱説明書を必ず読むよう指導すること。	8.1 本剤の初回投与後、又は本剤、活性型ビタミン D 製剤やカルシウム剤の投与量を変更した際に、高カルシウム血症の徴候があらわれる可能性があるため設定した。 8.2 本剤は、25-(OH)ビタミン D をカルシトリオールに変換することによって、血清中のカルシウムとリンを正常な濃度に維持している。25-(OH)ビタミンDが欠乏している場合、本剤の効果が十分に発揮することが難しくなるため、設定した。 8.3 本剤の薬理作用である血管拡張作用による起立性低血圧を起こす可能性がある。臨床試験で血管拡張作用に関連する有害事象（体位性めまい、起立性頻脈症候群、起立血圧低下、頭痛、起立性低血圧、動悸及び失神を含む）が認められたため設定した。 8.4 対象となる患者に対し、自己注射に関する十分な教育訓練と使用済み器具の安全な廃棄方法の指導を行う旨の注意喚起が必要と判断し、設定した。

使用上の注意（案）	設定根拠
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 骨肉腫発生のリスクが高いと考えられる患者 以下のような骨肉腫発生のリスクが高いと考えられる患者に対しては、患者のベネフィットとリスクを考慮して本剤の投与の可否を検討すること。［15.2.1、15.2.2 参照］ ・悪性骨腫瘍及び転移性骨腫瘍のある患者 ・骨に対する放射線療法中又は放射線療法後の患者 ・原因不明のアルカリホスファターゼ高値を示す患者 ・骨ページェット病の患者	9.1.1 左記の患者では本剤の試験は実施していない。慎重に投与する必要があるため設定した。 テリパラチド（骨粗鬆症治療剤）と本剤では骨に対する作用機序が異なると考えられ、また、本剤は副甲状腺機能低下患者において、生理学的範囲内の PTH 曝露を提供する補充療法を意図したものであるものの、テリパラチド製剤（骨粗鬆症治療剤）について、雌雄ラットを用いたがん原性試験において投与量及び投与期間に依存して骨肉腫を含む骨腫瘍性病変の発生頻度が増加したとの報告がある。
9.2 腎機能障害患者 9.2.1 重度の腎機能障害患者（eGFR が 30 mL/min/1.73 m2 未満） 特に投与開始時に高カルシウム血症を起こす可能性があることから、投与開始後は血清カルシウム濃度や患者の状態を十分に観察すること。重度の腎機能障害を有する又は透析中の副甲状腺機能低下症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］	9.2.1 国内外における本剤の臨床試験では、重度の腎機能障害患者は症例登録対象外と設定していたため、重度の腎機能障害患者を有する副甲状腺機能低下症患者における有効性及び安全性の結果は得られていない。このため、重度の腎機能障害を有する副甲状腺機能低下症患者に本剤を投与する場合は、注意深く観察しながら、慎重に投与する必要があるため記載した。
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。［15.2.3 参照］	9.5 非臨床試験において、生殖毒性に関して本剤に関連した有害作用は認められていない。一方で、テリパラチド製剤（骨粗鬆症治療剤）において、マウスまたはウサギの胚・胎児発生毒性試験において影響が認められている。また、本剤は、妊娠又は妊娠している可能性のある女性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。
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に関するデータはない。	9.6 本剤がヒト乳汁中に移行するかどうかは不明であることから設定した。
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 小児等に対する使用経験がないため設定した。

<table>
<tr><th>使用上の注意（案）</th><th>設定根拠</th></tr>
<tr><td>9.8 高齢者
一般に生理機能が低下している。</td><td>9.8 一般的な注意として記載した。</td></tr>
<tr><td>10. 相互作用
10.2 併用注意（併用に注意すること）
<table>
<tr><th>薬剤名等</th><th>臨床症状・措置方法</th><th>機序・危険因子</th></tr>
<tr><td>ジギタリス製剤
ジゴキシン
［8.1、11.1.1 参照］</td><td>高カルシウム血症に伴い不整脈があらわれることがある。</td><td>血清カルシウム値が上昇すると、ジギタリスの作用が増強される。</td></tr>
<tr><td>ビスホスホネート系製剤
アレンドロン酸ナトリウム水和物
イバンドロン酸ナトリウム水和物
リセドロン酸ナトリウム水和物等
デノスマブ
ロモソズマブ等
［8.1、11.1.1 参照］</td><td rowspan="8">本剤による血清カルシウム濃度の正常化が阻害され、本剤の治療効果に影響を与える可能性がある。</td><td rowspan="8">これらの薬剤は血清カルシウムや骨代謝に影響を及ぼし、本剤の治療効果に影響を与える可能性がある。</td></tr>
<tr><td>テリパラチド製剤
［8.1、11.1.1 参照］</td></tr>
<tr><td>アバロパラチド酢酸塩製剤
［8.1、11.1.1 参照］</td></tr>
<tr><td>ループ系利尿薬
フロセミド
アゾセミド
トラセミド等
サイアザイド系利尿薬
トリクロルメチアジド
ヒドロクロロチアジド等
サイアザイド系類似利尿薬
インダパミド等
［8.1、11.1.1 参照］</td></tr>
<tr><td>全身性コルチコステロイド薬
プレドニゾロン
デキサメタゾン
ベタメタゾン等
［8.1、11.1.1 参照］</td></tr>
<tr><td>リチウム製剤
炭酸リチウム
［8.1、11.1.1 参照］</td></tr>
</table>
</td><td>10.2
・ジギタリス製剤
本剤の薬理作用により、一過性の血清カルシウム値上昇がみられ、ジギタリス製剤の作用が増強される可能性が考えられるため設定した。

・ビスホスホネート系製剤、デノスマブ、ロモソズマブ、テリパラチド製剤、アバロパラチド酢酸塩製剤、ループ系利尿薬、サイアザイド系利尿薬、サイアザイド系類似利尿薬、全身性コルチコステロイド薬、リチウム製剤などの薬剤との併用により、本剤による血清カルシウム濃度の正常化が阻害され、本剤の治療効果に影響を与える可能性があるため設定した。</td></tr>
<tr><td>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 高カルシウム血症（9.5%）
高カルシウム血症及び高カルシウム血症によると考えられる臨床症状が認められた場合には、血清カルシウム濃度を測定し、必要に応じて投与の中止や輸液等の適切な処置を行うこと。［7.3、7.4、8.1、10.2 参照］</td><td>11.1.1 本剤の国内外で実施された臨床試験及び海外製造販売後の使用において重篤な高カルシウム血症が認められていることを踏まえて設定した。
11.2 CCSI、海外第Ⅲ相臨床試験及び国内第Ⅲ相臨床試験（TCP-304 試験及び TCP-305 試験）の結果に基づき設定した。</td></tr>
</table>

<table>
<tr><th>使用上の注意（案）</th><th>設定根拠</th></tr>
<tr><td>11.2 その他の副作用
<table>
<tr><th>種類＼頻度</th><th>10%以上</th><th>3～10%未満</th><th>3%未満</th></tr>
<tr><td>神経系障害</td><td></td><td>頭痛</td><td>浮動性めまい、体位性めまい</td></tr>
<tr><td>心臓障害</td><td></td><td></td><td>動悸</td></tr>
<tr><td>一般・全身障害および投与部位の状態</td><td>注射部位反応（紅斑、内出血、発疹等）（33.8%）</td><td></td><td></td></tr>
<tr><td>胃腸障害</td><td></td><td>下痢、悪心</td><td></td></tr>
</table></td><td></td></tr>
<tr><td>13. 過量投与
13.1 症状
高カルシウム血症、起立性低血圧、悪心、嘔吐、めまい、頭痛等が起こる可能性がある。
13.2 処置
特異的な解毒薬はない。血清カルシウム濃度を測定し、輸液等の適切な処置を行うこと。</td><td>13.1、13.2 本剤は血中カルシウム上昇作用を有するため、過量投与が行われた場合、血清カルシウム濃度が過度に上昇する危険性があるため設定した。</td></tr>
<tr><td>14. 適用上の注意
14.1 薬剤投与前の注意
14.1.1 本剤は JIS T 3226-2 に適合する A 型専用注射針を用いて使用すること。注射針は毎回新しいものを、必ず注射直前に取り付けること。
14.1.2 本剤と A 型専用注射針との装着時に液漏れ等の不具合が認められた場合には、新しい注射針に取り替える等の処置方法を患者に十分指導すること。
14.1.3 カートリッジにひびが入っている場合又は液が変色している場合は使用しないこと。
14.2 薬剤投与時の注意
14.2.1 投与部位
（1）腹部又は大腿前部に皮下注射すること。注射部位は毎回変更し、同一部位に短期間に繰り返し注射しないこと。
（2）本剤の 1 日用量が 30 μg を超える場合は、2 本のペン型注入器を用いて、異なる注射部位に 1 回ずつ計 2 回投与すること。
14.2.2 投与時
注射時は注入ボタンを 5 秒間押し続けること。
14.2.3 その他
（1）1 本のペン型注入器の本剤を複数の患者に使用しないこと。
（2）他の薬剤と混合しないこと。</td><td>14.1.1 本ペン型注入器にあった注射針を規定するために設定した。
14.1.2～14.1.3 既存の皮下注ペン製剤の記載を参考に設定した。
14.2.1 第Ⅲ相試験ではこれらの部位に皮下投与を行い、安全上の問題は報告されていないこと及び本剤の欧州における SmPC を参考に設定した。
14.2.2 本剤の設計検証試験により投与量精度を検証した結果から設定した。
14.2.3 本剤の SmPC 6.2 Incompatibilities 及び 6.6 Special precautions for disposal and other handling を参考に、一般的な注意として設定した。</td></tr>
</table>

使用上の注意（案）	設定根拠
15. その他の注意 15.2　非臨床試験に基づく情報 15.2.1 雌雄ラットに本薬を皮下投与した反復投与毒性試験において、2 μg/kg/日及び 5 μg/kg/日（5 μg/kg/日投与時の遊離 PTH の AUC 比はヒトに本剤 60 μg/日を投与した場合の約 2 倍）で骨吸収作用を示唆する変化（鼻骨の空隙率の増加等）が、10 μg/kg/日以上（遊離 PTH の AUC 比は、ヒトに本剤 60 μg/日を投与した場合の約 5 倍以上）では骨形成作用を示唆する変化（大腿骨・胸骨の骨増加等）が認められた。また、20 μg/kg/日（遊離 PTH の AUC 比はヒトに本剤 60 μg/日を投与した場合の約 9 倍）で骨端線の異常（異形成）が認められた。［9.1.1 参照］ 15.2.2 本薬のがん原性試験は実施されていない。テリパラチド製剤（骨粗鬆症治療剤）では、雌雄ラットに皮下投与したがん原性試験において、骨肉腫を含む骨腫瘍性病変の発生頻度が増加したとの報告がある。［9.1.1 参照］ 15.2.3 テリパラチド（遺伝子組換え）の動物試験では、ウサギで胎児毒性（胚死亡）が、マウスで胎児の骨格変異又は異常のわずかな増加が、ラットで出生児の体重増加抑制及び自発運動量の低下が認められている。ラットに本薬 30 μg/kg/日又はウサギに本薬 6 μg/kg/日（遊離 PTH の AUC 比は、ヒトに本剤 60 μg/日を投与した場合と比較して、それぞれ約 7.9 倍及び 6.6 倍）を投与した試験では、胚・胎児発生への影響を示唆する所見は認められていない。［9.5 参照］	15.2 15.2.1 本剤のラットを用いた反復投与毒性試験において、2 μg/kg/日及び 5 μg/kg/日では骨吸収作用を示唆する変化が、10 μg/kg/日以上では骨形成作用が認められている。また、最高用量では骨端線異形成が観察されているため設定した。 15.2.2 テリパラチド製剤（骨粗鬆症治療剤）について、雌雄ラットを用いたがん原性試験において投与量及び投与期間に依存して骨肉腫を含む骨腫瘍性病変の発生頻度が増加したとの報告がある。テリパラチド（骨粗鬆症治療剤）と本剤では骨に対する作用機序が異なると考えられ、また、本剤は副甲状腺機能低下患者において生理学的範囲内の PTH 曝露を提供する補充療法を意図したものであるものの、重要な情報であると判断して設定した。 15.2.3　本剤では生殖発生毒性への影響は認められていないが、テリパラチド製剤（骨粗鬆症治療剤）において、マウスまたはウサギの胚・胎児発生毒性試験において影響が認められたため設定した。

ヨビパス皮下注 168 μg ペン
ヨビパス皮下注 294 μg ペン
ヨビパス皮下注 420 μg ペン

第 1 部（モジュール 1）

1.9　一般的名称に係る文書

帝人ファーマ株式会社

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1.9　一般的名称に係る文書..... 3

1.9　一般的名称に係る文書

（1）日本医薬品一般的名称（Japanese Accepted Names, JAN）

パロペグテリパラチドは、以下のとおり令和 5 年 12 月 15 日付で医薬品の一般的名称の指定を受けた。

令和 5 年 12 月 15 日付け医薬薬審発 1215 第 1 号 厚生労働省医薬局医薬品審査管理課長通知「医薬品の一般的名称について」に掲載。

医薬品一般的名称	英名	日本名
	Palopegteriparatide	パロペグテリパラチド

登録番号　304-8-B12

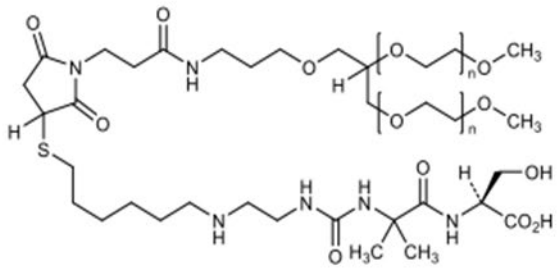
JAN（日本名）：パロペグテリパラチド

JAN（英　名）：Palopegteriparatide

SVSEIQLMHN LGKHLNSMER VEWLRKKLQD VHNF　　34

S1：PEG化部位

ポリエチレングリコールの結合様式



nは約450~500である

S
1

N-({2-[(6-{[1-{3-[(3-{2,3-bis[α-methylpoly(oxyethylene)-ω-oxy]propoxy}propyl)amino]-3-oxopropyl}-2,5-dioxopyrrolidin-3-yl]sulfanyl}hexyl)amino]ethyl}carbamoyl)-2-methylAla-Ser

$C_{181}H_{291}N_{55}O_{51}S_2$（ペプチド部分）

パロペグテリパラチドは，ヒト副甲状腺ホルモン類縁体であり，ヒト副甲状腺ホルモンの 1～34 番目のアミノ酸に相当し，メトキシポリエチレングリコール（分子量：約 43,000）が切断可能なリンカーを介して結合している（PEG 結合部位：S1）．パロペグテリパラチドは，34 個のアミノ酸残基からなる PEG 化合成ペプチド（分子量：約 48,000）である．

Palopegteriparatide is a human parathyroid hormone analogue corresponding to amino acid residues 1 – 34 of human parathyroid hormone, to which a methoxy polyethylene glycol (molecular weight: ca. 43,000) is bound via a cleavable linker (pegylation site: S1). Palopegteriparatide is a pegylated synthetic peptide (molecular weight: ca. 48,000) consisting of 34 amino acid residues.

（2）International Nonproprietary Names（INN）

INN：palopegteriparatide

r-INN List 86（WHO Drug Information, Vol. 35, No. 3, 2021）

医薬薬審発 1215 第１号
令 和 ５ 年 12 月 15 日

各都道府県衛生主管部（局）長　殿

厚生労働省医薬局医薬品審査管理課長
（　　公　　印　　省　　略　　）

医薬品の一般的名称について

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

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

別添

（別表２）INN に収載された品目の我が国における医薬品一般的名称

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

登録番号　304-8-B12

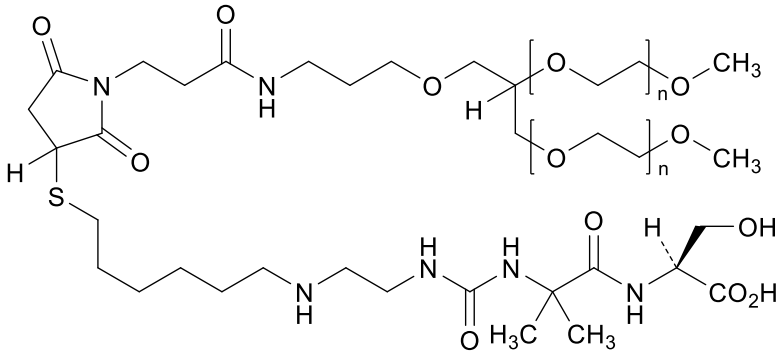
JAN（日本名）：パロペグテリパラチド

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SVSEIQLMHN LGKHLNSMER VEWLRKKLQD VHNF 34

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nは約450~500である

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登録番号 305-1-B5

JAN（日本名）：イフィナタマブ　デルクステカン（遺伝子組換え）

JAN（英　名）：Ifinatamab Deruxtecan (Genetical Recombination)

アミノ酸配列及びジスルフィド結合

H 鎖

```
QVQLVQSGAE VKKPGSSVKV SCKASGYTFT NYVMHWVRQA PGQGLEWMGY     50
INPYNDDVKY NEKFKGRVTI TADESTSTAY MELSSLRSED TAVYYCARWG     100
YYGSPLYYFD YWGQGTLVTV 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
```

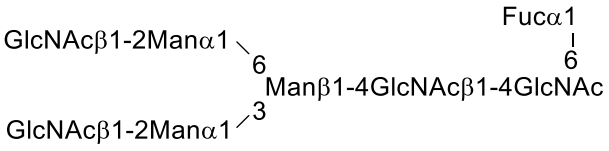
L 鎖

```
EIVLTQSPAT LSLSPGERAT LSCRASSRLI YMHWYQQKPG QAPRPLIYAT     50
SNLASGIPAR FSGSGSGTDF TLTISSLEPE DFAVYYCQQW NSNPPTFGQG     100
TKVEIKRTVA APSVFIFPPS DEQLKSGTAS VVCLLNNFYP REAKVQWKVD     150
NALQSGNSQE SVTEQDSKDS TYSLSSTLTL SKADYEKHKV YACEVTHQGL     200
SSPVTKSFNR GEC                                             213
```

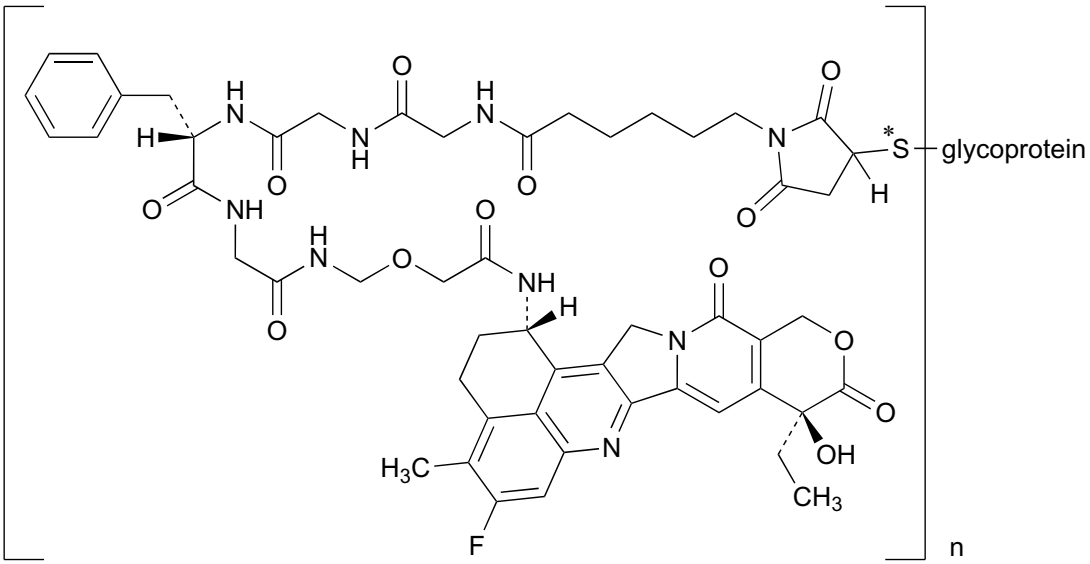
H 鎖 Q1：部分的ピログルタミン酸；H 鎖 C225，H 鎖 C231，H 鎖 C234，L 鎖 C213：薬物結合可能部位；H 鎖 N302：糖鎖結合；H 鎖 K452：部分的プロセシング

H 鎖 C225－L 鎖 C213，H 鎖 C231－H 鎖 C231，H 鎖 C234－H 鎖 C234：ジスルフィド結合（薬物が結合していないとき）

主な糖鎖の推定構造



デルクステカン部位の構造式



n は平均 4 である

*抗体部分のシステイン残基の硫黄原子

$C_{6528}H_{10032}N_{1724}O_{2024}S_{46}$（タンパク質部分，4 本鎖）

H 鎖 $C_{2235}H_{3426}N_{584}O_{683}S_{17}$

L 鎖 $C_{1029}H_{1594}N_{278}O_{329}S_{6}$

イフィナタマブ　デルクステカンは，抗体薬物複合体（分子量：約 153,000）であり，遺伝子組換えモノクローナル抗体の平均 4 個のシステイン残基に，カンプトテシン誘導体とリンカーからなるデルクステカン（(3*RS*)-1-[(10*S*)-10-ベンジル-1-{[(1*S*,9*S*)-9-エチル-5-フルオロ-9-ヒドロキシ-4-メチル-10,13-ジオキソ-2,3,9,10,13,15-ヘキサヒドロ-1*H*,12*H*-ベンゾ[*de*]ピラノ[3',4':6,7]インドリジノ[1,2-*b*]キノリン-1-イル]アミノ}-1,6,9,12,15,18-ヘキサオキソ-3-オキサ-5,8,11,14,17-ペンタアザトリコサン-23-イル]-2,5-ジオキソピロリジン-3-イル基（$C_{52}H_{57}FN_9O_{13}$；分子量：1,035.06））が結合している．抗体部分は，遺伝子組換え抗 CD276 モノクローナル抗体であり，その相補性決定部はマウス抗体に，その他はヒト IgG1 に由来し，CHO 細胞により産生される．タンパク質部分は，452 個のアミノ酸残基からなる H 鎖（γ1 鎖）2 本及び 213 個のアミノ酸残基からなる L 鎖（κ 鎖）2 本で構成される糖タンパク質（分子量：約 149,000）である．

Ifinatamab Deruxtecan is an antibody-drug-conjugate (molecular weight: ca. 153,000) consisting of Deruxtecan ((3*RS*)-1-[(10*S*)-10-benzyl-1-{[(1*S*,9*S*)-9-ethyl-5-fluoro-9-hydroxy-4-methyl-10,13-dioxo-2,3,9,10,13,15-hexahydro-1*H*,12*H*-benzo[*de*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinolin-1-yl]amino}-1,6,9,12,15,18-hexaoxo-3-oxa-5,8,11,14,17-pentaazatricosan-23-yl]-2,5-dioxopyrrolidin-3-yl group ($C_{52}H_{57}FN_9O_{13}$; molecular weight: 1,035.06)), which is composed of camptothecin derivative and linker, attached to an average of four cysteine residues of a recombinant monoclonal antibody. The antibody moiety is a recombinant anti-CD276 monoclonal antibody, the complementarity-determining regions of which are derived from mouse antibody and other regions are derived from human IgG1 and produced in CHO cells. The protein moiety is a glycoprotein (molecular weight: ca. 149,000) composed of 2 H-chains (γ1-chains) consisting of 452 amino acid residues each and 2 L-chains (κ-chains) consisting of 213 amino acid residues each.

※　JAN 以外の情報は、参考として掲載しました。

International Nonproprietary Names for Pharmaceutical Substances (INN)

RECOMMENDED International Nonproprietary Names: List 86

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 86

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 86

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*

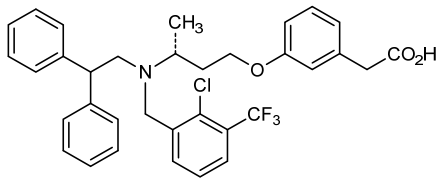
abequolixronum

abequolixron — (3-{(3*R*)-3-[{[2-chloro-3-(trifluoromethyl)phenyl]methyl}(2,2-diphenylethyl)amino]butoxy}phenyl)acetic acid

abéquolixron — acide (3-{(3*R*)-3-[{[2-chloro-3-(trifluorométhyl)phényl]méthyl}(2,2-diphényléthyl)amino]butoxy}phényl)acétique

abecuolixron — ácido (3-{(3*R*)-3-[{[2-cloro-3-(trifluorometil)fenil]metil}(2,2-difeniletil)amino]butoxi}fenil)acético

$C_{34}H_{33}ClF_3NO_3$



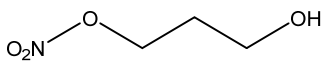
abrucomstatum

abrucomstat — 3-hydroxypropyl nitrate

abrucomstat — nitrate de 3-hydroxypropyle

abrucomstat — nitrato de 3-hidroxipropilo

$C_3H_7NO_4$



acasunlimabum #

acasunlimab — immunoglobulin G1-lambda/kappa, anti-[*Homo sapiens* CD274 (programmed death ligand 1, PDL1, PD-L1, B7 homolog 1, B7H1)], and anti-[*Homo sapiens* TNFRSF9 (tumor necrosis factor receptor (TNFR) superfamily member 9, 4-1BB, CD137)], humanized and *Homo sapiens* monoclonal antibody, bispecific;

	gamma1 heavy chain anti-CD274 humanized (1-450) [VH anti-CD274 humanized (*Homo sapiens* IGHV3-23*01 (87.6%) -(IGHD) -IGHJ1*01 (100%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -*Homo sapiens* IGHG1*03, G1m3, nG1m1, G1v41 CH2 F1.3, E1.2 (CH1 R120 (218) (122-219), hinge 1-15 (220-234), CH2 L1.3>F (238), L1.2>E (239), D27>A (269) (235-344), CH3 E12 (360), M14 (362), F85.1>L (409) (345-449), CHS K>del (450)) (122-450)], (224-213')-disulfide with lambda light chain anti-CD274 *Homo sapiens* (1'-214') [V-LAMBDA (*Homo sapiens* IGLV3-21*02 (97.9%) -IGLJ2*01 (100%)) CDR-IMGT [6.3.11] (26-31.49-51.88-98) (1'-108') -*Homo sapiens* IGLC2*01 (100%) (109'-214')]; gamma1 heavy chain anti-TNFRSF9 humanized (1''-446'') [VH anti-TNFRSF9 humanized (*Homo sapiens* IGHV3-49*04 (86%) -(IGHD) -IGHJ2*01 (92.9%)) CDR-IMGT [8.7.11] (26-33.51-57.96-106) (1''-117'') -*Homo sapiens* IGHG1*03, G1m3, nG1m1 (CH1 R120 (214) (118''-215''), hinge 1-15 (216''-230''), CH2 L1.3>F (234), L1.2>E (235), D27>A (265) (231''-340''), CH3 E12 (356), M14 (358), K88>R (409) (341''-445''), CHS K>del (446)) (118''-446'')], (220''-217''')-disulfide with kappa light chain anti-TNFRSF9 humanized (1'''-217''') [V-KAPPA anti-TNFRSF9 humanized (*Homo sapiens* IGKV1-33*01 (85.7%) -IGKJ1*01 (90%)) CDR-IMGT [6.3.12] (27-32.50-52.89-100) (1'''-110''') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (156), V101 (194) (111'''-217''')]; dimer (230-226'':233-229'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa
acasunlimab	immunoglobuline G1-lambda/kappa, anti-[*Homo sapiens* CD274 (ligand 1 de mort programmée, PDL1, PD-L1, homologue 1 de B7, B7H1)] et anti-[*Homo sapiens* TNFRSF9 (membre 9 de la superfamille des récepteurs du facteur de nécrose tumorale, 4-1BB, CD137)], anticorps monoclonal humanisé et *Homo sapiens,* bispécifique; chaîne lourde gamma1 anti-CD274 humanisée (1-450) [VH anti-CD274 humanisé (*Homo sapiens* IGHV3-23*01 (87.6%) -(IGHD) -IGHJ1*01 (100%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -*Homo sapiens* IGHG1*03, G1m3, nG1m1, G1v41 CH2 F1.3, E1.2 (CH1 R120 (218) (122-219), charnière 1-15 (220-234), CH2 L1.3>F (238), L1.2>E (239), D27>A (269) (235-344), CH3 E12 (360), M14 (362), F85.1>L (409) (345-449), CHS K>del (450)) (122-450)], (224-213')-disulfure avec la chaîne légère lambda anti-CD274 *Homo sapiens* (1'-214') [V-LAMBDA (*Homo sapiens* IGLV3-21*02 (97.9%) -IGLJ2*01 (100%)) CDR-IMGT [6.3.11] (26-31.49-51.88-98) (1'-108') -*Homo sapiens* IGLC2*01 (100%) (109'-214')]; chaîne lourde gamma1 anti-TNFRSF9 humanisée (1''-446'') [VH anti-TNFRSF9 humanisé (*Homo sapiens* IGHV3-49*04 (86%) -(IGHD) -IGHJ2*01 (92.9%)) CDR-IMGT [8.7.11] (26-33.51-57.96-106) (1''-117'') -*Homo sapiens* IGHG1*03, G1m3, nG1m1 (CH1 R120 (214) (118''-215''), charnière 1-15 (216''-230''), CH2 L1.3>F (234), L1.2>E (235), D27>A (265) (231''-340''), CH3 E12 (356), M14 (358), K88>R (409) (341''-445''), CHS K>del (446)) (118''-446'')], (220''-217''')-disulfure avec la chaîne légère kappa anti-TNFRSF9 humanisée (1'''-217''') [V-KAPPA anti-TNFRSF9 humanisé (*Homo sapiens* IGKV1-33*01 (85.7%) -IGKJ1*01 (90%)) CDR-IMGT [6.3.12] (27-32.50-52.89-100) (1'''-110''') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (156), V101 (194) (111'''-217''')]; dimère (230-226'':233-229'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa
acasunlimab	inmunoglobulina G1-lambda/kappa, anti-[*Homo sapiens* CD274 (ligando 1 de muerte programada, PDL1, PD-L1, homólogo 1 de B7, B7H1)] y anti-[*Homo sapiens* TNFRSF9 (miembro 9 de la superfamilia de los receptores del factor de necrosis tumoral, 4-1BB, CD137)], anticuerpo monoclonal humanizado y *Homo sapiens,* biespecífico;

cadena pesada gamma1 anti-CD274 humanizada (1-450) [VH anti-CD274 humanizado (*Homo sapiens* IGHV3-23*01 (87.6%) -(IGHD) -IGHJ1*01 (100%)) CDR-IMGT [8.8.14] (26-33.51-58.97-110) (1-121) -*Homo sapiens* IGHG1*03, G1m3, nG1m1, G1v41 CH2 F1.3, E1.2 (CH1 R120 (218) (122-219), bisagra 1-15 (220-234), CH2 L1.3>F (238), L1.2>E (239), D27>A (269) (235-344), CH3 E12 (360), M14 (362), F85.1>L (409) (345-449), CHS K>del (450)) (122-450)], (224-213')-disulfuro con la cadena ligera lambda anti-CD274 *Homo sapiens* (1'-214') [V-LAMBDA (*Homo sapiens* IGLV3-21*02 (97.9%) -IGLJ2*01 (100%)) CDR-IMGT [6.3.11] (26-31.49-51.88-98) (1'-108') -*Homo sapiens* IGLC2*01 (100%) (109'-214')];
cadena pesada gamma1 anti-TNFRSF9 humanizada (1"-446") [VH anti-TNFRSF9 humanizado (*Homo sapiens* IGHV3-49*04 (86%) -(IGHD) -IGHJ2*01 (92.9%)) CDR-IMGT [8.7.11] (26-33.51-57.96-106) (1"-117") -*Homo sapiens* IGHG1*03, G1m3, nG1m1 (CH1 R120 (214) (118"-215"), bisagra 1-15 (216"-230"), CH2 L1.3>F (234), L1.2>E (235), D27>A (265) (231"-340"), CH3 E12 (356), M14 (358), K88>R (409) (341"-445"), CHS K>del (446)) (118"-446")], (220"-217"')-disulfuro con la cadena ligera kappa anti-TNFRSF9 humanizada (1"'-217"') [V-KAPPA anti-TNFRSF9 humanizado (*Homo sapiens* IGKV1-33*01 (85.7%) -IGKJ1*01 (90%)) CDR-IMGT [6.3.12] (27-32.50-52.89-100) (1"'-110"') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (156), V101 (194) (111"'-217"')]; dímero (230-226":233-229")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada (anti-CD274)

```
EVQLLEPGGG LVQPGGSLRL SCEASGSTFS TYAMSWVRQA PGKGLEWVSG  50
FSGSGGFTFY ADSVRGRFTI SRDSSKNTLF LQMSSLRAED TAVYYCAIPA 100
RGYNYGSFQH WGQGTLVTVS SASTKGPSVF PLAPSSKSTS GGTAALGCLV 150
KDYFPEPVTV SWNSGALTSG VHTFPAVLQS SGLYSLSSVV TVPSSSLGTQ 200
TYICNVNHKP SNTKVDKRVE PKSCDKTHTC PPCPAPEFEG GPSVFLFPPK 250
PKDTLMISRT PEVTCVVVAV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY 300
NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP 350
QVYTLPPSRE EMTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP 400
VLDSDGSFLL YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG 450
```

Heavy chain / Chaîne lourde / Cadena pesada (anti-TNFRSF9)

```
EVQLVESGGG LVQPGRSLRL SCTASGFSLN DYWMSWVRQA PGKGLEWVGY  50
IDVGGSLYYA ASVKGRFTIS RDDSKSIAYL QMNSLKTEDT AVYYCARGGL 100
TYGFDLWGQG TLVTVSSAST KGPSVFPLAP SSKSTSGGTA ALGCLVKDYF 150
PEPVTVSWNS GALTSGVHTF PAVLQSSGLY SLSSVVTVPS SSLGTQTYIC 200
NVNHKPSNTK VDKRVEPKSC DKTHTCPPCP APEFEGGPSV FLFPPKPKDT 250
LMISRTPEVT CVVVAVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT 350
LPPSREEMTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTPPVLDS 400
DGSFFLYSRL TVDKSRWQQG NVFSCSVMHE ALHNHYTQKS LSLSPG     446
```

Light chain / Chaîne légère / Cadena ligera (anti-CD274)

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

Light chain / Chaîne légère / Cadena ligera (anti-TNFRSF9)

```
DIVMTQSPSS LSASVGDRVT ITCQASEDIS SYLAWYQQKP GKAPKRLIYG  50
ASDLASGVPS RFSASGSGTD YTFTISSLQP EDIATYYCHY YATISGLGVA 100
FGGGTKVEIK 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) 22-96 148-204 265-325 371-429
22"-95" 144"-200" 261"-321" 367"-425"
Intra-L (C23-C104) 22'-87' 136'-195'
23'"-88'" 137'"-197'"
Inter-H-L (h 5-CL 126) 224-213' 220"-217'"
Inter-H-H (h 11, h 14) 230-226" 233-229"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
301, 297"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

acavameranum #

acavameran — messenger RNA (mRNA), 5' capped, encoding tumour necrosis factor ligand superfamily member 4 (TNFSF4, OX40 ligand, OX40L, glycoprotein Gp34), flanked by 5' and 3' untranslated regions and a 3' polyA tail; contains N1-methylpseudouridine instead of uridine (*all*-U>$m^1\Psi$).

acavaméran — ARN messager (ARNm), protégé par une coiffe en 5', codant le membre 4 de la superfamille des ligands du facteur de nécrose tumorale (TNFSF4; ligand OX40, OX40L, glycoprotéine Gp34), flanqué de régions non traduites en 5' et 3' et d'une queue polyA en 3'; contient de la N1-méthylpseudouridine au lieu de l'uridine (*all*-U>$m^1\Psi$).

acavamerán — RNA mensajero (mRNA), protegido en 5', que codifica para el miembro 4 de la superfamilia de ligandos del factor de necrosis tumoral (TNFSF4, ligando de OX40, OX40L, glicoproteína Gp34), flanqueado por regiones no traducidas en 5' y 3' y una cola polyA en 3'; contiene N1-metilpseudouridina en lugar de uridina (*all*-U>$m^1\Psi$).

acazicolceptum #

acazicolcept — human inducible T-cell co-stimulator ligand (ICOS ligand) N-terminal fragment (1-122) (variant (N^{52}>H, N^{57}>Y, Q^{100}>R), fused via peptidyl linker ^{123}GGGGSGGGGS^{132} to a human immunoglobulin G1 Fc fragment (133-363) variant (L^{151}>A, L^{152}>E, G^{154}>A, C-terminal K^{364} deleted), dimer, glycosylated, produced in Chinese hamster ovary (CHO) cells;
[N^{52}>H, N^{57}>Y, Q^{100}>R] human inducible T-cell co-stimulator ligand (ICOS ligand, ICOSL, CD275) N-terminal fragment (1-122) fused via a $(G_4S)_2$ linker (123-132) to a human immunoglobulin G1 C-terminal K>del Fc fragment (133-363) [*Homo sapiens* IGHG1*01; hinge 133-147; CH2 148-257 (L151A, L152E, G154A); CH3 258-362; CHS 363], dimer (143-143':146-146')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

acazicolcept — fragment N-terminal (1-122) du ligand costimulateur de la cellule T inductible humaine (ligand ICOS) (variant (N^{52}>H, N^{57}>Y, Q^{100}>R), fusionné via un linker peptidique ^{123}GGGGSGGGGS^{132} à un fragment Fc (133-363) de l'immunoglobuline G1 humaine, variant (L^{151}>A, L^{152}>E, G^{154}>A, C-terminal K^{364} supprimé), dimère, glycosylé, produit dans des cellules ovariennes de hamster chinois (CHO);
fragment N-terminal (1-122) du ligand costimulateur de la cellule T inductible humaine (ligand d'ICOS, ICOSL, CD275) [N^{52}>H, N^{57}>Y, Q^{100}>R] fusionné via un linker $(G_4S)_2$ (123-132) au fragment Fc (133-363) C-terminal K>del de l'immunoglobuline G1 humaine [*Homo sapiens* IGHG1*01; charnière 133-147; CH2 148-257 (L151A, L152E, G154A); CH3 258-362; CHS 363], dimère (143-143':146-146')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

acazicolcept — ligando coestimulador de las células T inducible humano (ligando ICOS) fragmentoN-terminal (1-122) (variante (N^{52}>H, N^{57}>Y, Q^{100}>R), fusionado a través de un enlace peptidil ^{123}GGGGSGGGGS^{132} al fragmento de una inmunoglobulina humana G1 Fc (133-363) variante (L^{151}>A, L^{152}>E, G^{154}>A, C-terminal K^{364} eliminada), dímero, glicosilado, producido en células ováricas de hámster chino (CHO);

[N^{52}>H, N^{57}>Y, Q^{100}>R] ligando humano de coestimulador inducible de células T (ligando de ICOS, ICOSL, CD275), fragmento N-terminal (1-122), fusionado a través de un péptido $(G_4S)_2$ (123-132) con un fragmento Fc C-terminal K>del de la inmunoglobulina G1 humana (133-363) [*Homo sapiens* IGHG1*01; bisagra 133-147; CH2 148-257 (L151A, L152E, G154A); CH3 258-362; CHS 363], dímero (143-143':146-146')-bisdisulfuro, producido en células ováricas de hámster chino (CHO), glicoforma alfa

Sequence / Séquence / Secuencia

```
DTQEKEVRAM VGSDVELSCA CPEGSRFDLN DVYVYWQTSE SKTVVTYHIP    50
QHSSLEYVDS RYRNRALMSP AGMLRGDFSL RLFNVTPQDE QKFHCLVLSR   100
SLGFQEVLSV EVTLHVAANF SVGGGGSGGG GSEPKSSDKT HTCPPCPAPE   150
AEGAPSVFLF PPKPKDTLMI SRTPEVTCVV VDVSHEDPEV KFNWYVDGVE   200
VHNAKTKPRE EQYNSTYRVV SVLTVLHQDW LNGKEYKCKV SNKALPAPIE   250
KTISKAKGQP REPQVYTLPP SRDELTKNQV SLTCLVKGFY PSDIAVEWES   300
NGQPENNYKT TPPVLDSDGS FFLYSKLTVD KSRWQQGNVF SCSVMHEALH   350
NHYTQKSLSL SPG                                           363
```

Mutation sites / Sites de mutation / Posiciones de mutación
N52, N52'>H, N57, N57'>Y, Q100, Q100'>R, L151, L151'>A, L152, L152'>E, G154, G154'>A
K364, K364'>del

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posición del puentes disulfuro

intra-ICOSL	19-95		intra-Fc	178-238	284-342
	19'-95'			178'-238'	284'-342'
inter-Fc	143-143'	146-146'			

Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación
ICOSL: N84, N119, N84', N119';
Fc: N214, N214'

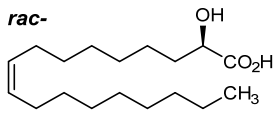
acidum idroxioleicum

idroxioleic acid — *rac*-(2*R*,9*Z*)-2-hydroxyoctadec-9-enoic acid

acide idroxioléique — acide *rac*-(2*R*,9*Z*)-2-hydroxyoctadéc-9-énoïque

ácido idroxioleico — ácido *rac*-(2*R*,9*Z*)-2-hidroxioctadec-9-enoico

$C_{18}H_{34}O_3$



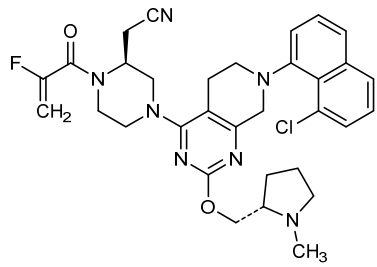
adagrasibum

adagrasib — {(2*S*)-4-[7-(8-chloronaphthalen-1-yl)-2-{[(2*S*)-1-methylpyrrolidin-2-yl]methoxy}-5,6,7,8-tetrahydropyrido[3,4-*d*]pyrimidin-4-yl]-1-(2-fluoroprop-2-enoyl)piperazin-2-yl}acetonitrile

adagrasib — {(2*S*)-4-[7-(8-chloronaphtalén-1-yl)-2-{[(2*S*)-1-méthylpyrrolidin-2-yl]méthoxy}-5,6,7,8-tétrahydropyrido[3,4-*d*]pyrimidin-4-yl]-1-(2-fluoroprop-2-énoyl)pipérazin-2-yl}acétonitrile

adagrasib — {(2*S*)-4-[7-(8-cloronaftalen-1-il)-2-{[(2*S*)-1-metilpirrolidin-2-il]metoxi}-5,6,7,8-tetrahidropirido[3,4-*d*]pirimidin-4-il]-1-(2-fluoroprop-2-enoil)piperazin-2-il}acetonitrilo

$C_{32}H_{35}ClFN_7O_2$



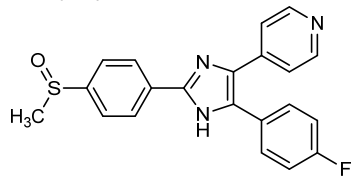
adezmapimodum

adezmapimod — *rac*-4-[5-(4-fluorophenyl)-2-{4-[(*R*)-methanesulfinyl]phenyl}-1*H*-imidazol-4-yl]pyridine

adezmapimod — *rac*-4-[5-(4-fluorophényl)-2-{4-[(*R*)-méthanesulfinyl]phényl}-1*H*-imidazol-4-yl]pyridine

adezmapimod — *rac*-4-[5-(4-fluorofenil)-2-{4-[(*R*)-metanosulfinil]fenil}-1*H*-imidazol-4-il]piridina

$C_{21}H_{16}FN_3OS$



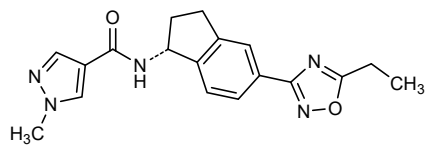
aficamtenum

aficamten — *N*-[(1*R*)-5-(5-ethyl-1,2,4-oxadiazol-3-yl)-2,3-dihydro-1*H*-inden-1-yl]-1-methyl-1*H*-pyrazole-4-carboxamide

aficamtène — *N*-[(1*R*)-5-(5-éthyl-1,2,4-oxadiazol-3-yl)-2,3-dihydro-1*H*-indén-1-yl]-1-méthyl-1*H*-pyrazole-4-carboxamide

aficamten — *N*-[(1*R*)-5-(5-etil-1,2,4-oxadiazol-3-il)-2,3-dihidro-1*H*-inden-1-il]-1-metil-1*H*-pirazol-4-carboxamida

$C_{18}H_{19}N_5O_2$

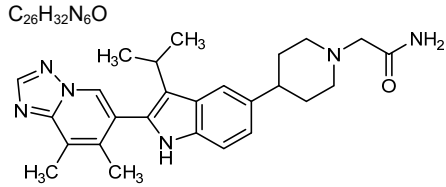


afimetoranum

afimetoran — 2-{4-[2-(7,8-dimethyl[1,2,4]triazolo[1,5-*a*]pyridin-6-yl)-3-(propan-2-yl)-1*H*-indol-5-yl]piperidin-1-yl}acetamide

afimétoran — 2-{4-[2-(7,8-diméthyl[1,2,4]triazolo[1,5-*a*]pyridin-6-yl)-3-(propan-2-yl)-1*H*-indol-5-yl]pipéridin-1-yl}acétamide

afimetorán — 2-{4-[2-(7,8-dimetil[1,2,4]triazolo[1,5-*a*]piridin-6-il)-3-(propan-2-il)-1*H*-indol-5-il]piperidin-1-il}acetamida



alomfilimabum #

alomfilimab	immunoglobulin G1-kappa, anti-[*Homo sapiens* ICOS (inducible T-cell costimulatory, activation-inducible lymphocyte immunomediatory molecule, AILIM, CD278)], *Homo sapiens* monoclonal antibody; gamma1 heavy chain *Homo sapiens* (1-454) [VH (*Homo sapiens* IGHV3-20*04 (94.9%) -(IGHD) -IGHJ4*01 (92.9%) T122>I (118)) CDR-IMGT [8.8.17] (26-33.51-58.97-113) (1-124) -*Homo sapiens* IGHG1*01 (100%), G1m17,1 (CH1 K120 (221) (125-222), hinge 1-15 (223-237), CH2 (238-347), CH3 D12 (363), L14 (365) (348-452), CHS (453-454)) (125-454)], (227-215')-disulfide with kappa light chain *Homo sapiens* (1'-215') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (92.7%) -IGKJ3*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')]; dimer (233-233":236-236")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa
alomfilimab	immunoglobuline G1-kappa, anti-[*Homo sapiens* ICOS (costimulateur inductible du lymphocyte T, molécule immunomédiateur lymphocytaire inductible par activation, AILIM, CD278)], anticorps monoclonal *Homo sapiens*; chaîne lourde gamma1 *Homo sapiens* (1-454) [VH (*Homo sapiens* IGHV3-20*04 (94.9%) -(IGHD) -IGHJ4*01 (92.9%) T122>I (118)) CDR-IMGT [8.8.17] (26-33.51-58.97-113) (1-124) -*Homo sapiens* IGHG1*01 (100%), G1m17,1 (CH1 K120 (221) (125-222), charnière 1-15 (223-237), CH2 (238-347), CH3 D12 (363), L14 (365) (348-452), CHS (453-454)) (125-454)], (227-215')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-215') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (92.7%) -IGKJ3*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')]; dimère (233-233":236-236")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa
alomfilimab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* ICOS (coestimulador inducible del linfocito T, molécula inmunomediadora linfocitaria inducible por activación, AILIM, CD278)], anticuerpo monoclonal *Homo sapiens*; cadena pesada gamma1 *Homo sapiens* (1-454) [VH (*Homo sapiens* IGHV3-20*04 (94.9%) -(IGHD) -IGHJ4*01 (92.9%) T122>I (118)) CDR-IMGT [8.8.17] (26-33.51-58.97-113) (1-124) -*Homo sapiens* IGHG1*01 (100%), G1m17,1 (CH1 K120 (221) (125-222), bisagra 1-15 (223-237), CH2 (238-347), CH3 D12 (363), L14 (365) (348-452), CHS (453-454)) (125-454)], (227-215')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-215') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (92.7%) -IGKJ3*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')]; dímero (233-233":236-236")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG VVRPGGSLRL SCVASGVTFD DYGMSWVRQA PGKGLEWVSG  50
INWNGGDTDY SDSVKGRFTI SRDNAKNSLY LQMNSLRAED TALYYCARDF 100
YGSGSYYHVP FDYWGQGILV TVSSASTKGP SVFPLAPSSK STSGGTAALG 150
CLVKDYFPEP VTVSWNSGAL TSGVHTFPAV LQSSGLYSLS SVVTVPSSSL 200
GTQTYICNVN HKPSNTKVDK KVEPKSCDKT HTCPPCPAPE LLGGPSVFLF 250
PPKPKDTLMI SRTPEVTCVV VDVSHEDPEV KFNWYVDGVE VHNAKTKPRE 300
EQYNSTYRVV SVLTVLHQDW LNGKEYKCKV SNKALPAPIE KTISKAKGQP 350
REPQVYTLPP SRDELTKNQV SLTCLVKGFY PSDIAVEWES NGQPENNYKT 400
TPPVLDSDGS FFLYSKLTVD KSRWQQGNVF SCSVMHEALH NHYTQKSLSL 450
SPGK                                                    454
```

Light chain / Chaîne légère / Cadena ligera

```
EIVLTQSPGT LSLSPGERAT LSCRASQSVS RSYLAWYQQK RGQAPRLLIY  50
GASSRATGIP DRFSGDGSGT DFTLSISRLE PEDFAVYYCH QYDMSPFTFG 100
PGTKVDIKRT 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) 22-96 151-207 268-328 374-432
22"-96" 151"-207" 268"-328" 374"-432"
Intra-L (C23-C104) 23'-89' 135'-195'
23'"-89'" 135'"-195'"
Inter-H-L (h 5-CL 126) 227-215' 227"-215'"
Inter-H-H (h 11, h 14) 233-233" 236-236"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
304, 304"
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:
454, 454"

amlitelimabum #

amlitelimab — immunoglobulin G4-kappa, anti-[*Homo sapiens* TNFSF4 (tumor necrosis factor (TNF) superfamily member 4, OX40 ligand, OX-40L, TAX transcriptionally-activated glycoprotein 1, TXGP1, CD252)], monoclonal antibody;
gamma4 heavy chain (1-454) [VH (*Homo sapiens* IGHV3-23*04 (89.8%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [8.8.20] (26-33.51-58.97-116) (1-127)-*Homo sapiens* IGHG4*01, G4v5 h P10, G4v3 E1.2 (CH1 (128-225), hinge 1-12 S10>P (235) (226-237), CH2 L1.2>E (242) (238-347), CH3 (348-452), CHS (453-454)) (128-454)], (210-214')-disulfide with kappa light chain (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (96.8%) -IGKJ3*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 (233-233":236-236")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

amlitélimab — immunoglobuline G4-kappa, anti-[*Homo sapiens* TNFSF4 (membre 4 de la superfamille des ligands du facteur de nécrose tumorale, ligand de OX40, OX40L, glycoprotéine 1 activée transcriptionellement par TAX, TXGP1, CD252)], anticorps monoclonal;
chaîne lourde gamma4 (1-454) [VH (*Homo sapiens* IGHV3-23*04 (89.8%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [8.8.20] (26-33.51-58.97-116) (1-127)-*Homo sapiens* IGHG4*01, G4v5 h P10, G4v3 E1.2 (CH1 (128-225), charnière 1-12 S10>P (235) (226-237), CH2 L1.2>E (242) (238-347), CH3 (348-452), CHS (453-454)) (128-454)], (210-214')-disulfure avec la chaîne légère kappa (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (96.8%) -IGKJ3*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 (233-233":236-236")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

amlitelimab

inmunoglobulina G4-kappa, anti-[*Homo sapiens* TNFSF4 (miembro 4 de la superfamilia de los ligandos del factor de necrosis tumoral, ligando de OX40, OX40L, glicoproteína 1 activada transcripcionalmente por TAX, TXGP1, CD252)], anticuerpo monoclonal;
cadena pesada gamma4 (1-454) [VH (*Homo sapiens* IGHV3-23*04 (89.8%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [8.8.20] (26-33.51-58.97-116) (1-127)-*Homo sapiens* IGHG4*01, G4v5 h P10, G4v3 E1.2 (CH1 (128-225), bisagra 1-12 S10>P (235) (226-237), CH2 L1.2>E (242) (238-347), CH3 (348-452), CHS (453-454)) (128-454)], (210-214')-disulfuro con la cadena ligera kappa (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (96.8%) -IGKJ3*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 (233-233'':236-236'')-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGGSLRL SCAASGFTFS NYAMNWVRQA PGKGLEWVST  50
ISGSGGATRY ADSVKGRFTI SRDNSRNTVY LQMNSLRVED TAVFYCTKDR 100
LIMATVRGPY YYGMDVWGQG TTVTVSSAST KGPSVFPLAP CSRSTSESTA 150
ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY SLSSVVTVPS 200
SSLGTKTYTC NVDHKPSNTK VDKRVESKYG PPCPPCPAPE FEGGPSVFLF 250
PPKPKDTLMI SRTPEVTCVV VDVSQEDPEV QFNWYVDGVE VHNAKTKPRE 300
EQFNSTYRVV SVLTVLHQDW LNGKEYKCKV SNKGLPSSIE KTISKAKGQP 350
REPQVYTLPP SQEEMTKNQV SLTCLVKGFY PSDIAVEWES NGQPENNYKT 400
TPPVLDSDGS FFLYSRLTVD KSRWQEGNVF SCSVMHEALH NHYTQKSLSL 450
SLGK                                                    454
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Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS LSASVGDRVT ITCRASQSIS SYLNWYQQKP GKAPNLLIYA  50
ASSLQSGVPS RFSGSGSETD FTLTISSLQP EDFATYYCQQ SHSVSFTFGP 100
GTKVDIKRTV 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    268-328    374-432
                    22''-96''  154''-210''  268''-328''  374''-432''
Intra-L (C23-C104)  23'-88'    134'-194'
                    23'''-88'''  134'''-194'''
Inter-H-L (CH1 10-CL 126)  141-214'   141''-214'''
Inter-H-H (h 8, h 11)      233-233''  236-236''
```

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
304, 304''
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:
454, 454''

anbenitamabum #

anbenitamab

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, biparatopic, tetravalent;
gamma1 heavy chain anti-ERBB2 domain II humanized (1-449) [VH anti-ERBB2 domain II (*Homo sapiens* IGHV3-66*01 (78.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -*Homo sapiens* IGHG1*01, G1m7,1, G1v32 CH3 W22 (CH1 K120 (217) (120-217), hinge 1-15 (218-232), CH2 (233-342), CH3 D12 (358), L14 (360), T22>W (368), K88>A (411) (343-447), CHS (448-449)) (120-449)], (222-214')-disulfide with kappa light chain anti-ERBB2 humanized (1'-214') [V-KAPPA anti-ERBB2 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 (194) (108'-214')];

gamma1 heavy chain anti-ERBB2 domain IV humanized (1''-450'') [VH anti-ERBB2 domain IV (*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, G1m7,1, G1v33 CH3 S22, A24, V86 (CH1 K120 (217) (121''-218''), hinge 1-15 (219''-233''), CH2 (234''-343''), CH3 D12 (359), L14 (361) T22>S (369), L24>A (371), F85.1>K (408), Y86>V (410) (344''-448''), CHS (449''-450'')) (121''-450'')], (223''-214''')-disulfide with kappa light chain anti-ERBB2 humanized (1'''-214''') [V-KAPPA anti-ERBB2 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 (194) (108'''-214''')]; dimer (228-229'':231-232'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

anbénitamab

immunoglobuline G1-kappa, anti-[*Homo sapiens* ERBB2 (récepteur 2 du facteur de croissance épidermique, récepteur tyrosine-protéine kinase erbB2, EGFR2, HER2, HER-2, p185c-erbB2, NEU, CD340)], anticorps monoclonal humanisé, biparatopique, tétravalent;
chaîne lourde gamma1 anti-ERBB2 domaine II humanisée (1-449) [VH anti-ERBB2 domain II (*Homo sapiens* IGHV3-66*01 (78.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -*Homo sapiens* IGHG1*01, G1m7,1, G1v32 CH3 W22 (CH1 K120 (217) (120-217), charnière 1-15 (218-232), CH2 (233-342), CH3 D12 (358), L14 (360), T22>W (368), K88>A (411) (343-447), CHS (448-449)) (120-449)], (222-214')-disulfure avec la chaîne légère lambda anti-ERBB2 humanisée (1'-214') [V-KAPPA anti-ERBB2 (*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 (194) (108'-214')];
chaîne lourde gamma1 anti-ERBB2 domaine IV humanisée (1''-450'') [VH anti-ERBB2 domaine IV (*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, G1m7,1, G1v33 CH3 S22, A24, V86 (CH1 K120 (217) (121''-218''), charnière 1-15 (219''-233''), CH2 (234''-343''), CH3 D12 (359), L14 (361) T22>S (369), L24>A (371), F85.1>K (408), Y86>V (410) (344''-448''), CHS (449''-450'')) (121''-450'')], (223''-214''')-disulfure avec la chaîne légère kappa anti-ERBB2 humanisée (1'''-214''') [V-KAPPA anti-ERBB2 (*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 (194) (108'''-214''')]; dimère (228-229'':231-232'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

anbenitamab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* ERBB2 (receptor 2 del factor de crecimiento epidérmico, receptor tirosina-proteína kinasa erbB2, EGFR2, HER2, HER-2, p185c-erbB2, NEU, CD340)], anticuerpo monoclonal humanizado, biparatópico, tetravalente;
cadena pesada gamma1 anti-ERBB2 dominio II humanizada (1-449) [VH anti-ERBB2 dominio II (*Homo sapiens* IGHV3-66*01 (78.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -*Homo sapiens* IGHG1*01, G1m7,1, G1v32 CH3 W22 (CH1 K120 (217) (120-217), bisagra 1-15 (218-232), CH2 (233-342), CH3 D12 (358), L14 (360), T22>W (368), K88>A (411) (343-447), CHS (448-449)) (120-449)], (222-214')-disulfuro con la cadena ligera lambda anti-ERBB2 humanizada (1'-214') [V-KAPPA anti-ERBB2 (*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 (194) (108'-214')];

cadena pesada gamma1 anti-ERBB2 domnio IV humanizada (1"-450") [VH anti-ERBB2 dominio IV (*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, G1m7,1, G1v33 CH3 S22, A24, V86 (CH1 K120 (217) (121"-218"), bisagra 1-15 (219"-233"), CH2 (234"-343"), CH3 D12 (359), L14 (361) T22>S (369), L24>A (371), F85.1>K (408), Y86>V (410) (344"-448"), CHS (449"-450")) (121"-450")], (223"-214"')-disulfuro con la cadena ligera kappa anti-ERBB2 humanizada (1"'-214"') [V-KAPPA anti-ERBB2 (*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 (194) (108"'-214"')]; dímero (228-229":231-232")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada (anti-ERBB2 domain II)

```
EVQLVESGGG LVQPGGSLRL SCAASGFTFT DYTMDWVRQA PGKGLEWVAD  50
VNPNSGGSIY NQRFKGRFTL SVDRSKNTLY LQMNSLRAED TAVYYCARNL 100
GPSFYFDYWG QGTLVTVSSA STKGPSVFPL APSSKSTSGG TAALGCLVKD 150
YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY 200
ICNVNHKPSN TKVDKKVEPK SCDKTHTCPP CPAPELLGGP SVFLFPPKPK 250
DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VDGVEVHNAK TKPREEQYNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKAL PAPIEKTISK AKGQPREPQV 350
YTLPPSRDEL TKNQVSLWCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL 400
DSDGSFFLYS ALTVDKSRWQ QGNVFSCSVM HEALHNHYTQ KSLSLSPGK  449
```

Heavy chain / Chaîne lourde / Cadena pesada (anti-ERBB2 domain IV)

```
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 LTKNQVSLSC AVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFKLV SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPGK 450
```

Light chain / Chaîne légère / Cadena ligera (anti-ERBB2)

```
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) 22-96 146-202 263-323 369-427
22"-96" 147"-203" 264"-324" 370"-428"
Intra-L (C23-C104) 23'-88' 134'-194'
23"'-88"' 134"'-194"'
Inter-H-L (h5-CL 126) 222-214' 223"-214"'
Inter-H-H (h11, h14) 228-229" 231-232"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
299, 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:
449, 450"

ansuvimabum #
ansuvimab

immunoglobulin G1-kappa, anti-[*Zaire ebolavirus* (Zaire Ebola virus (EBOV)) envelope glycoprotein subunit 1 (GP1) glycan cap domain], monoclonal antibody;

	gamma1 heavy chain (1-449) [VH (*Homo sapiens* IGHV3-13*01 (78.4%) -(IGHD) -IGHJ5*01 (92.9%) T122>I (113)) CDR-IMGT [8.7.13] (26-33.51-57.96-108) (1-119) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (216) (120-217), hinge 1-15 (218-232), CH2 (233-342), CH3 D12 (358), L14 (360) (343-447), CHS (448-449)) (120-449)], (222-214')-disulfide with kappa light chain (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-27*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 a Chinese hamster ovary (CHO)-DG44 cell line, glycoform alfa
ansuvimab	immunoglobuline G1-kappa, anti-[coiffe glycosylée de la sous-unité 1 de la glycoprotéine d'enveloppe (GP1) de *Zaire ebolavirus* (virus Ebola Zaïre (EBOV))], anticorps monoclonal; chaîne lourde gamma1 (1-449) [VH (*Homo sapiens* IGHV3-13*01 (78.4%) -(IGHD) -IGHJ5*01 (92.9%) T122>I (113)) CDR-IMGT [8.7.13] (26-33.51-57.96-108) (1-119) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (216) (120-217), charnière 1-15 (218-232), CH2 (233-342), CH3 D12 (358), L14 (360) (343-447), CHS (448-449)) (120-449)], (222-214')-disulfure avec la chaîne légère kappa (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-27*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) lignée cellulaire CHO-DG44, glycoforme alfa
ansuvimab	inmunoglobulina G1-kappa, anti-[cubierta glicosilada de la subunidad 1 de la glicoproteína de envoltura (GP1) de *Zaire ebolavirus* (virus Ebola Zaïre (EBOV))], anticuerpo monoclonal; cadena pesada gamma1 (1-449) [VH (*Homo sapiens* IGHV3-13*01 (78.4%) -(IGHD) -IGHJ5*01 (92.9%) T122>I (113)) CDR-IMGT [8.7.13] (26-33.51-57.96-108) (1-119) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (216) (120-217), bisagra 1-15 (218-232), CH2 (233-342), CH3 D12 (358), L14 (360) (343-447), CHS (448-449)) (120-449)], (222-214')-disulfuro con la cadena ligera kappa (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-27*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) línea celular CHO-DG44, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LIQPGGSLRL SCAASGFALR MYDMHWVRQT IDKRLEWVSA  50
VGPSGDTTYA DSVKGRFAVS RENAKNSLSL QMNSLTAGDT AIYYCVRSDR 100
GVAGLFDSWG QGILVTVSSA STKGPSVFPL APSSKSTSGG TAALGCLVKD 150
YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY 200
ICNVNHKPSN TKVDKKVEPK SCDKTHTCPP CPAPELLGGP SVFLFPPKPK 250
DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VDGVEVHNAK TKPREEQYNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKAL PAPIEKTISK AKGQPREPQV 350
YTLPPSRDEL TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL 400
DSDGSFFLYS KLTVDKSRWQ QGNVFSCSVM HEALHNHYTQ KSLSLSPGK  449
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Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS LSASVGDRIT ITCRASQAFD NYVAWYQQRP GKVPKLLISA  50
ASALHAGVPS RFSGSGSGTH FTLTISSLQP EDVATYYCQN YNSAPLTFGG 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) 22-95 146-202 263-323 369-427
22"-95" 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.

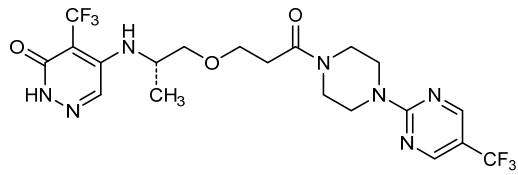
atamparibum

atamparib — 5-{[(2*S*)-1-(3-oxo-3-{4-[5-(trifluoromethyl)pyrimidin-2-yl]piperazin-1-yl}propoxy)propan-2-yl]amino}-4-(trifluoromethyl)pyridazin-3(2*H*)-one

atamparib — 5-{[(2*S*)-1-(3-oxo-3-{4-[5-(trifluorométhyl)pyrimidin-2-yl]pipérazin-1-yl}propoxy)propan-2-yl]amino}-4-(trifluorométhyl)pyridazin-3(2*H*)-one

atamparib — 5-{[(2*S*)-1-(3-oxo-3-{4-[5-(trifluorometil)pirimidin-2-il]piperazin-1-il}propoxi)propan-2-il]amino}-4-(trifluorometil)piridazin-3(2*H*)-ona

$C_{20}H_{23}F_6N_7O_3$



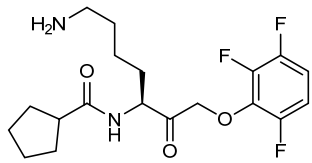
atuzaginstatum

atuzaginstat — *N*-[(3*S*)-7-amino-2-oxo-1-(2,3,6-trifluorophenoxy)heptan-3-yl]cyclopentanecarboxamide

atuzaginstat — *N*-[(3*S*)-7-amino-2-oxo-1-(2,3,6-trifluorophénoxy)heptan-3-yl]cyclopentanecarboxamide

atuzaginstat — *N*-[(3*S*)-7-amino-2-oxo-1-(2,3,6-trifluorofenoxi)heptan-3-il]ciclopentanocarboxamida

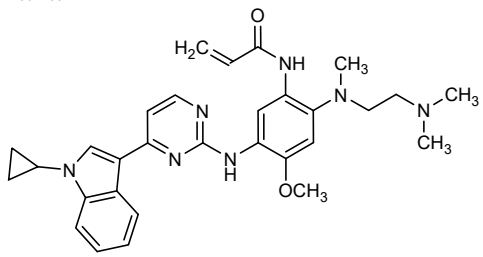
$C_{19}H_{25}F_3N_2O_3$



aumolertinibum

aumolertinib	*N*-(5-{[4-(1-cyclopropyl-1*H*-indol-3-yl)pyrimidin-2-yl]amino}-2-{[2-(dimethylamino)ethyl](methyl)amino}-4-methoxyphenyl)prop-2-enamide
aumolertinib	*N*-(5-{[4-(1-cyclopropyl-1*H*-indol-3-yl)pyrimidin-2-yl]amino}-2-{[2-(diméthylamino)éthyl](méthyl)amino}-4-méthoxyphényl)prop-2-énamide
aumolertinib	*N*-(5-{[4-(1-ciclopropil-1*H*-indol-3-il)pirimidin-2-il]amino}-2-{[2-(dimetilamino)etil](metil)amino}-4-metoxifenil)prop-2-enamida

$C_{30}H_{35}N_7O_2$



bevufenogenum nofeparvovecum #

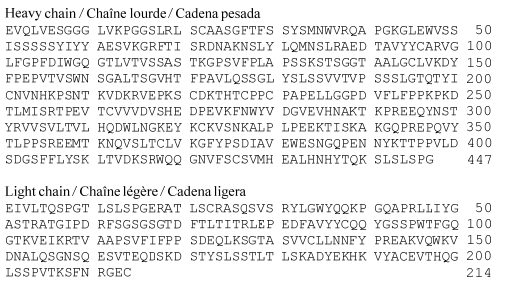
bevufenogene nofeparvovec	A non-replicating, recombinant adeno-associated virus expressing codon-optimised human phenylalanine hydroxylase (PAH). A non-replicating, recombinant adeno-associated virus, hematopoietic stem cell serotype 15 (AAVHSC15) expressing codon-optimised human phenylalanine hydroxylase (PAH) under control of a liver-specific hybrid promoter [comprising human hepatic control region-1 (HCR-1) enhancer element, human alpha-1-antitrypsin (hAAT) promoter and the SV40 small t intron)] and an SV40 polyA signal sequence, flanked by adeno-associated virus 2 (AAV2) inverted terminal repeats (ITRs).
bévufénogène noféparvovec	Un virus adéno-associé recombinant, non-répliquant, exprimant la phénylalanine hydroxylase humaine (PAH) aux codons optimisés.

	Un virus adéno-associé recombinant, non-répliquant, de cellules souches hématopoïétiques de sérotype 15 (AAVHSC15) exprimant la phénylalanine hydroxylase humaine (PAH) aux codons optimisés sous le contrôle d'un promoteur hybride spécifique du foie [consistant en un élément activateur de la région 1 de contrôle hépatique humain (HCR-1), le promoteur de l'alpha-1-antitrypsine humaine (hAAT) et du petit intron t SV40] et d'une séquence signal polyA SV40, flanquée de répétitions terminales inversées (ITRs) du virus adéno-associé 2 (AAV2).
bevufenogén nofeparvovec	Un virus adeno-asociado recombinante, no replicativo, que expresa la fenilalanina hidroxilasa humana (PAH) con codones optimizados. Un virus adeno-asociado recombinante, no replicativo, derivado de células madre hematopoyéticas serotipo 15 (AAVHSC15) que expresa la fenilalanina hidroxilasa humana (PAH) con codones optimizados, bajo el control de un promotor híbrido específico de hígado [contiene un elemento potenciador de la región de control hepático 1 humana (HCR-1), un promotor de la alfa 1 antitripsina humana (hAAT) y el intrón pequeño t de SV40] y una secuencia señal de polyA de SV40, flanqueado por las repeticiones terminales invertidas (ITRs) del virus adeno-asociado 2 (AAV2).
botensilimabum #	
botensilimab	immunoglobulin G1-kappa, anti-[*Homo sapiens* CTLA4 (cytotoxic T-lymphocyte associated protein 4, CD152)], *Homo sapiens* monoclonal antibody; gamma1 heavy chain *Homo sapiens* (1-447) [VH (*Homo sapiens* IGHV3-21*01 (99.0%) -(IGHD) -IGHJ3*02 (92.9%) M123>L (113)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) -*Homo sapiens* IGHG1*03 G1m3, nG1m1, G1v8 CH2 D3, L115, E117 (CH1 R120 (215) (119-216), hinge 1-15 (217-231), CH2 S3>D (240), A115>L (331), I117>E (333) (232-341), CH3 E12 (357), M14 (359) (342-446), CHS K>del (447)) (119-447)], (221-214')-disulfide with kappa light chain *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (94.8%) -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')]; dimer (227-227'':230-230'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa
botensilimab	immunoglobuline G1-kappa, anti-[*Homo sapiens* CTLA4 (protéine 4 associée aux lymphocytes T cytotoxiques, CD152)], anticorps monoclonal *Homo sapiens*;

chaîne lourde gamma1 *Homo sapiens* (1-447) [VH (*Homo sapiens* IGHV3-21*01 (99%) -(IGHD) - IGHJ3*02 (92.9%) M123>L (113)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) -*Homo sapiens* IGHG1*03 G1m3, nG1m1, G1v8 CH2 D3, L115, E117 (CH1 R120 (215) (119-216), charnière 1-15 (217-231), CH2 S3>D (240), A115>L (331), I117>E (333) (232-341), CH3 E12 (357), M14 (359) (342-446), CHS K>del (447)) (119-447)], (221-214')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (94.8%) - 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')]; dimère (227-227'':230-230'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

botensilimab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* CTLA4 (proteína 4 asociada con los linfocitos T citotóxicos, CD152)], anticuerpo monoclonal *Homo sapiens*;
cadena pesada gamma1 *Homo sapiens* (1-447) [VH (*Homo sapiens* IGHV3-21*01 (99%) -(IGHD) - IGHJ3*02 (92.9%) M123>L (113)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) -*Homo sapiens* IGHG1*03 G1m3, nG1m1, G1v8 CH2 D3, L115, E117 (CH1 R120 (215) (119-216), bisagra 1-15 (217-231), CH2 S3>D (240), A115>L (331), I117>E (333) (232-341), CH3 E12 (357), M14 (359) (342-446), CHS K>del (447)) (119-447)], (221-214')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (94.8%) - 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')]; 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 LVKPGGSLRL SCAASGFTFS SYSMNWVRQA PGKGLEWVSS  50
ISSSSSYIYY AESVKGRFTI SRDNAKNSLY LQMNSLRAED TAVYYCARVG 100
LFGPFDIWGQ GTLVTVSSAS TKGPSVFPLA PSSKSTSGGT AALGCLVKDY 150
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTQTYI 200
CNVNHKPSNT KVDKRVEPKS CDKTHTCPPC PAPELLGGPD VFLFPPKPKD 250
TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKALP LPEEKTISKA KGQPREPQVY 350
TLPPSREEMT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD 400
SDGSFFLYSK LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPG    447
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Light chain / Chaîne légère / Cadena ligera

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EIVLTQSPGT LSLSPGERAT LSCRASQSVS RYLGWYQQKP GQAPRLLIYG  50
ASTRATGIPD RFSGSGSGTD FTLTITRLEP EDFAVYYCQQ YGSSPWTFGQ 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
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Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 145-201 262-322 368-426
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.

cadonilimabum #

cadonilimab	immunoglobulin G1-kappa anti-[*Homo sapiens* PDCD1 (programmed cell death 1, PD-1, PD1, CD279)], each heavy chain being fused to a scFv anti-[*Homo sapiens* CTLA4 (cytotoxic T-lymphocyte-associated protein 4, CD152)], monoclonal antibody, bispecific, tetravalent; gamma1 heavy chain anti-PDCD1 fused to scFv anti-CTLA4 (1-713) [gamma-1 heavy chain(1-448) [VH anti-PDCD1 (*Homo sapiens* IGHV3-23*04 (88.7%) -(IGHD) -IGHJ6*01 (90.9%) T123>L (113)) 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)] -20-mer tetrakis(tetraglycyl-seryl) linker (449-468) -scFv heavy-lambda anti-CTLA4 (469-713) [VH anti-CTLA4 G49>C (512) (*Homo sapiens* IGHV1-2*02 (84.7%) -(IGHD) -IGHJ5*01 (90.9%) S128>A (583)) CDR-IMGT [8.8.8] (494-501.519-526.565-572) (469-583) -20-mer tetrakis(tetraglycyl-seryl) linker (584-603) -V-LAMBDA anti-CTLA4 (*Homo sapiens* IGLV7-46*01 (85.3%) -IGLJ3*02 (91.7%) G120>C (705)) CDR-IMGT [9.3.9] (629-637.655-657.694-702) (604-713)]]; (221-214')-disulfide with kappa light chain anti-PDCD1 (1'-214') [V-KAPPA (*Mus musculus* IGKV14-111*01 (86.3%) -IGKJ5*01 (100%)/*Homo sapiens* IGKV1-16*01 (80.0%) -IGKJ2*01 (81.8%) Q120>A (100), I126>L (106)) 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
cadonilimab	immunoglobuline G1-kappa anti-[*Homo sapiens* PDCD1 (protéine 1 de mort cellulaire programmée, PD-1, PD1, CD279)], chaque chaîne lourde étant fusionnée à un scFv anti-[*Homo sapiens* CTLA4 (protéine 4 associée aux lymphocytes T cytotoxiques, CD152)], anticorps monoclonal, bispécifique, tétravalent; chaîne lourde gamma1 anti-PDCD1 fusionnée au scFv anti-CTLA4 (1-713) [chaîne lourde gamma-1 (1-448) [VH anti-PDCD1 (*Homo sapiens* IGHV3-23*04 (88.7%) -(IGHD) -IGHJ6*01 (90.9%) T123>L (113)) 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)] -20-mer tétrakis(tétraglycyl-séryl) linker (449-468) -scFv lourd-lambda anti-CTLA4 (469-713) [VH anti-CTLA4 G49>C (512) (*Homo sapiens* IGHV1-2*02 (84.7%) -(IGHD) -IGHJ5*01 (90.9%) S128>A (583)) CDR-IMGT [8.8.8] (494-501.519-526.565-572) (469-583) -20-mer tétrakis(tétraglycyl-séryl) linker (584-603) -V-LAMBDA anti-CTLA4 (*Homo sapiens* IGLV7-46*01 (85.3%) -IGLJ3*02 (91.7%) G120>C (705)) CDR-IMGT [9.3.9] (629-637.655-657.694-702) (604-713)]]; (221-214')-disulfure avec la chaîne légère kappa anti-PDCD1 (1'-214') [V-KAPPA (*Mus musculus* IGKV14-111*01 (86.3%) -IGKJ5*01 (100%)/*Homo sapiens* IGKV1-16*01 (80.0%) -IGKJ2*01 (81.8%) Q120>A (100), I126>L (106)) 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

cadonilimab

inmunoglobulina G1-kappa anti-[*Homo sapiens* PDCD1 (proteína 1 de muerte celular programada, PD-1, PD1, CD279)], cada cadena pesada estando fusionada a un scFv anti-[*Homo sapiens* CTLA4 (proteína 4 asociada con los linfocitos T citotóxicos, CD152)], anticuerpo monoclonal, biespecífico, tetravalente; cadena pesada gamma1 anti-PDCD1 fusionada con scFv anti-CTLA4 (1-713) [cadena pesada gamma-1 (1-448) [VH anti-PDCD1 (*Homo sapiens* IGHV3-23*04 (88.7%) -(IGHD) -IGHJ6*01 (90.9%) T123>L (113)) 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)] -20-mer tetrakis(tetraglicil-seril) linker (449-468) -scFv pesado-lambda anti-CTLA4 (469-713) [VH anti-CTLA4 G49>C (512) (*Homo sapiens* IGHV1-2*02 (84.7%) -(IGHD) -IGHJ5*01 (90.9%) S128>A (583)) CDR-IMGT [8.8.8] (494-501.519-526.565-572) (469-583) -20-mer tetrakis(tetraglicil-seril) linker (584-603) – V-LAMBDA anti-CTLA4 (*Homo sapiens* IGLV7-46*01 (85.3%) -IGLJ3*02 (91.7%) G120>C (705)) CDR-IMGT [9.3.9] (629-637.655-657.694-702) (604-713)]];
(221-214')-disulfuro con la cadena ligera kappa anti-PDCD1 (1'-214') [V-KAPPA (*Mus musculus* IGKV14-111*01 (86.3%) -IGKJ5*01 (100%)/*Homo sapiens* IGKV1-16*01 (80.0%) -IGKJ2*01 (81.8%) Q120>A (100), I126>L (106)) 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 (anti-PDCD1 and anti-CTLA4 (scFv))

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EVQLVESGGG LVQPGGSLRL SCAASGFAFS SYDMSWVRQA PGKGLDWVAT  50
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 SLSLSPGKGG 450
GGSGGGGSGG GGSGGGGSQV QLVESGAEVK KPGASVKVSC KASGYSFTGY 500
TMNWVRQAPG QCLEWIGLIN PYNNITNYAQ KFQGRVTFTV DTSISTAYME 550
LSRLRSDDTG VYFCARLDYR SYWGQGTLVT VSAGGGGSGG GGSGGGGSGG 600
GGSQAVVTQE PSLTVSPGGT VTLTCGSSTG AVTTSNFPNW VQQKPGQAPR 650
SLIGGTNNKA SWTPARFSGS LLGGKAALTI SGAQPEDEAE YYCALWYSNH 700
WVFGCGTKLT VLR                                         713
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Light chain / Chaîne légère / Cadena ligera (anti-PDCD1)

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DIQMTQSPSS MSASVGDRVT FTCRASQDIN TYLSWFQQKP GKSPKTLIYR  50
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) 22-96 145-201 262-322 368-426 490-564 625-693
22"-96" 145"-201" 262"-322" 368"-426" 490"-564" 625-693"
Intra-H (scFv VH C49 -VL IGLJ C120) 512-705
512"-705"
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"
H scFv VH CDR2 N63:
524, 524"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaire complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

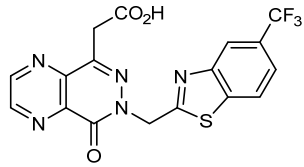
caficrestatum

caficrestat — (8-oxo-7-{[5-(trifluoromethyl)-1,3-benzothiazol-2-yl]methyl}-7,8-dihydropyrazino[2,3-*d*]pyridazin-5-yl)acetic acid

caficrestat — acide (8-oxo-7-{[5-(trifluorométhyl)-1,3-benzothiazol-2-yl]méthyl}-7,8-dihydropyrazino[2,3-*d*]pyridazin-5-yl)acétique

caficrestat — ácido (8-oxo-7-{[5-(trifluorometil)-1,3-benzotiazol-2-il]metil}-7,8-dihidropirazino[2,3-*d*]piridazin-5-il)acético

$C_{17}H_{10}F_3N_5O_3S$



cavrotolimodum

cavrotolimod — *all-P-ambo*-(17*RS*)-1-[(cholest-5-en-3β-yl)oxy]-17,20,40-trihydroxy-1,20,40-trioxo-6,9,12,15,19,21,24,27,30,33,36,39,41,44,47,50,53,56-octadecaoxa-2-aza-20λ^5,40λ^5-diphosphaoctapentacontan-58-yl *P*-thiothymidylyl-(3'→5')-2'-deoxy-*P*-thiocytidylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-deoxy-*P*-thiocytidylyl-(3'→5')-2''-deoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-deoxy-*P*-thiocytidylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5'')-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-deoxy-*P*-thiocytidylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-hydrogen 3'-thymidylate

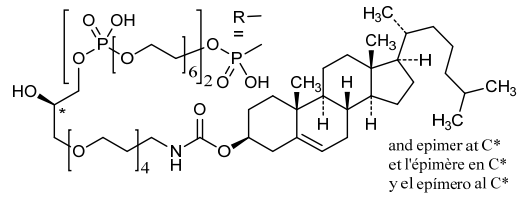
cavrotolimod — *tout-P-ambo-P*-thiothymidylyl-(3'→5')-2'-désoxy-*P*-thiocytidylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-désoxy-*P*-thiocytidylyl-(3'→5')-2''-désoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-désoxy-*P*-thiocytidylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5'')-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-désoxy-*P*-thiocytidylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-hydrogéno-3'-thymidylate de (17*RS*)-1-[(cholest-5-én-3β-yl)oxy]-17,20,40-trihydroxy-1,20,40-trioxo-6,9,12,15,19,21,24,27,30,33,36,39,41,44,47,50,53,56-octadécaoxa-2-aza-20λ^5,40λ^5-diphosphaoctapentacontan-58-yle

cavrotolimod

todo-P-ambo-P-tiotimidilil-(3'→5')-2'-desoxi-*P*-tiocitidilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-*P*-tiocitidilil-(3'→5')-2''-desoxi-*P*-tioguanilil-(3'→5')-*P*-tiotimidilil-(3'→5')-*P*-tiotimidilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-*P*-tiocitidilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-*P*-tiotimidilil-(3'→5'')-tiotimidilil-(3'→5')-*P*-tiotimidilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-*P*-tiocitidilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-*P*-tiotimidilil-(3'→5')-hidrógeno-3'-timidilato de (17*RS*)-1-[(colest-5-en-3β-il)oxi]-17,20,40-trihidroxi-1,20,40-trioxo-6,9,12,15,19,21,24,27,30,33,36,39,41,44,47,50,53,56-octadecaoxa-2-aza-20λ^5,40λ^5-difosfaoctapentacontan-58-ilo

$C_{300}H_{423}N_{71}O_{161}P_{26}S_{23}$

(3'-5')d(P-thio)(T-C-G-T-C-G-T-T-T-T-G-T-C-G-T-T-T-T-G-T-C-G-T-T)-R



cimpuciclibum

cimpuciclib

2^5-fluoro-1^2,4^6-dimethyl-1^3-(propan-2-yl)-1^3*H*-3,7-diaza-1(5)-benzimidazola-2(4,2)-pyrimidina-4(2,5)-pyridina-6(1,4)-piperidina-8(1)-cyclopropanaoctaphan-5-one

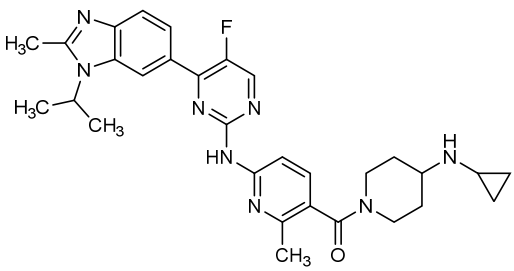
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2^5-fluoro-1^2,4^6-diméthyl-1^3-(propan-2-yl)-1^3*H*-3,7-diaza-1(5)-benzimidazola-2(4,2)-pyrimidina-4(2,5)-pyridina-6(1,4)-pipéridina-8(1)-cyclopropanaoctaphan-5-one

cimpuciclib

2^5-fluoro-1^2,4^6-dimetil-1^3-(propan-2-il)-1^3*H*-3,7-diaza-1(5)-benzimidazola-2(4,2)-pirimidina-4(2,5)-piridina-6(1,4)-piperidina-8(1)-ciclopropanaoctafan-5-ona

$C_{30}H_{35}FN_8O$



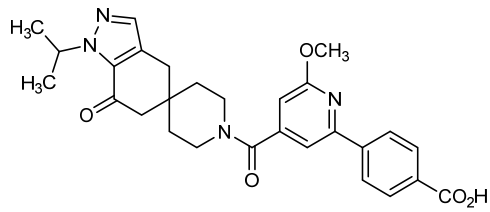
clesacostatum

clesacostat — 4-{6-methoxy-4-[7-oxo-1-(propan-2-yl)-1,4,6,7-tetrahydrospiro[indazole-5,4'-piperidine]-1'-carbonyl]pyridin-2-yl}benzoic acid

clésacostat — acide 4-{6-méthoxy-4-[7-oxo-1-(propan-2-yl)-1,4,6,7-tétrahydrospiro-[indazole-5,4'-pipéridine]-1'-carbonyl]pyridin-2-yl}benzoïque

clesacostat — ácido 4-{6-metoxi-4-[7-oxo-1-(propan-2-il)-1,4,6,7-tetrahidrospiro-[indazol-5,4'-piperidina]-1'-carbonil]piridin-2-il}benzoico

$C_{28}H_{30}N_4O_5$



cofirasersenum

cofirasersen — *all-P-ambo*-2'-*O*,4'-*C*-[(1*S*)-ethane-1,1-diyl]-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-*O*,4'-*C*-[(1*S*)-ethane-1,1-diyl]-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-*O*,4'-*C*-[(1*S*)-ethane-1,1-diyl]-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-deoxy-*P*-thioadenylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-deoxy-*P*-thioadenylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-deoxy-5-methyl-*P*-thiocytidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-*O*,4'-*C*-[(1*S*)-ethane-1,1-diyl]-5-methyl-*P*-thiouridylyl-(3'→5')-2'-*O*,4'-*C*-[(1*S*)-ethane-1,1-diyl]-*P*-thioguanylyl-(3'→5')-2'-*O*,4'-*C*-[(1*S*)-ethane-1,1-diyl]-5-methyluridine

cofirasersen — *tout-P-ambo*-2'-*O*,4'-*C*-[(1*S*)-éthane-1,1-diyl]-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-*O*,4'-*C*-[(1*S*)-éthane-1,1-diyl]-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-*O*,4'-*C*-[(1*S*)-éthane-1,1-diyl]-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-2'-désoxy-*P*-thioadénylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-désoxy-*P*-thioadénylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-2'-désoxy-5-méthyl-*P*-thiocytidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-*O*,4'-*C*-[(1*S*)-éthane-1,1-diyl]-5-méthyl-*P*-thiouridylyl-(3'→5')-2'-*O*,4'-*C*-[(1*S*)-éthane-1,1-diyl]-*P*-thioguanylyl-(3'→5')-2'-*O*,4'-*C*-[(1*S*)-éthane-1,1-diyl]-5-méthyluridine

cofirasersén — *todo-P-ambo*-2'-*O*,4'-*C*-[(1*S*)-etano-1,1-diil]-5-metil-*P*-tiocitidilil-(3'→5')-2'-*O*,4'-*C*-[(1*S*)-etano-1,1-diil]-5-metil-*P*-tiocitidilil-(3'→5')-2'-*O*,4'-*C*-[(1*S*)-etano-1,1-diil]-5-metil-*P*-tiocitidilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-2'-desoxi-*P*-tioadenilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-*P*-tioadenilil-(3'→5')-2'-desoxi-*P*-tioguanilil-

(3'→5')-2'-desoxi-5-metil-*P*-tiocitidilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-*O*,4'-*C*-[(1*S*)-etano-1,1-diil]-5-metil-*P*-tiouridilil-(3'→5')-2'-*O*,4'-*C*-[(1*S*)-etano-1,1-diil]-*P*-tioguanilil-(3'→5')-2'-*O*,4'-*C*-[(1*S*)-etano-1,1-diil]-5-metiluridina

$C_{172}H_{218}N_{57}O_{88}P_{15}S_{15}$

(3'-5') all *P*-thio C=C=C=d(G=A=T=A=G=C=T=G=G=T=)U=G=U

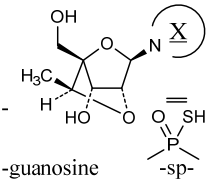
Legend:

A , G & T : 2'-deoxynucleotide

C : 2'-deoxy-5-methylcytidine

C & U : 2'-*O*,4'-*C*-[(1*S*)-ethane-1,1-diyl]-5-methylnucleotide

G : 2'-*O*,4'-*C*-[(1*S*)-ethane-1,1-diyl]-guanosine



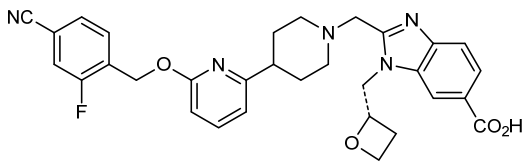
danuglipronum

danuglipron — (1²*S*)-9⁴-cyano-9²-fluoro-7-oxa-3(1,2)-benzimidazola-6(2,6)-pyridina-5(1,4)-piperidina-1(2)-oxetana-9(1)-benzenanonaphane-3⁶-carboxylic acid

danuglipron — acide (1²*S*)-9⁴-cyano-9²-fluoro-7-oxa-3(1,2)-benzimidazola-6(2,6)-pyridina-5(1,4)-pipéridina-1(2)-oxétana-9(1)-benzénanonaphane-3⁶-carboxylique

danugliprón — ácido (1²*S*)-9⁴-ciano-9²-fluoro-7-oxa-3(1,2)-benzimidazola-6(2,6)-piridina-5(1,4)-piperidina-1(2)-oxetana-9(1)-bencenanonafano-3⁶-carboxílico

$C_{31}H_{30}FN_5O_4$

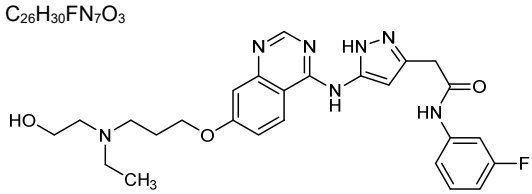


defosbarasertibum

defosbarasertib — 2-{5-[(7-{3-[ethyl(2-hydroxyethyl)amino]propoxy}quinazolin-4-yl)amino]-1*H*-pyrazol-3-yl}-*N*-(3-fluorophenyl)acetamide

défosbarasertib — 2-{5-[(7-{3-[éthyl(2-hydroxyéthyl)amino]propoxy}quinazolin-4-yl)amino]-1*H*-pyrazol-3-yl}-*N*-(3-fluorophényl)acétamide

defosbarasertib — 2-{5-[(7-{3-[etil(2-hidroxietil)amino]propoxi}quinazolin-4-il)amino]-1*H*-pirazol-3-il}-*N*-(3-fluorofenil)acetamida



delandistrogenum moxeparvovecum #

delandistrogene moxeparvovec	A non-replicating adeno-associated virus (AAV) vector encoding human micro-dystrophin. A recombinant, non-replicating, adeno-associated virus (AAV) serotype rh74 vector (AAVrh74) encoding codon-optimized human micro-dystrophin (a shortened functional version of human dystrophin), under control of a hybrid MHCK7 promoter consisting of enhancer/promoter regions of murine muscle creatine kinase (CK) and alpha-myosin heavy-chain genes, followed by a chimeric intron [including the SV40 late 16S/19S splice signals and a small 5′ UTR] and a small synthetic polyadenylation (polyA) signal sequence, flanked by adeno-associated virus 2 (AAV2) inverted terminal repeats (ITRs).
délandistrogène moxéparvovec	Un vecteur adéno-associé (AAV) non-répliquant codant la micro-dystrophine humaine. Un vecteur adéno-associé de sérotype rh74 (AAVrh74) recombinant, non-répliquant codant la micro-dystrophine humaine aux codons optimisés (une version fonctionnelle raccourcie de la dystrophine humaine), sous le contrôle d'un promoteur hybride MHCK7 consistant en régions activatrices/promotrices de la créatine kinase (CK) de muscle murin et des gènes de la chaîne lourde de l'alpha-myosine, suivi d'un intron chimérique [incluant les signaux d'épissage SV40 tardifs 16S/19S et une UTR courte en 5'] et d'une petite séquence signal synthétique de polyadénylation (polyA), flanquée de répétitions terminales inversées (ITRs) du virus adéno-associé 2 (AAV2).
delandistrogén moxeparvovec	Un vector de virus adeno-asociado (AAV) no replicativo que codifica para la micro distrofina humana. Un vector de virus adeno-asociado (AAV) recombinante de serotipo rh74 (AAVrh74), no replicativo que codifica para la micro distrofina humana (una versión funcional acortada de la distrofina humana), con codones optimizados, bajo el control de un promotor híbrido MHCK7 consistente en regiones potenciadoras/promotoras de los genes de la creatinina quinasa (CK) de músculo y de la cadena pesada de la miosina alfa murinas, seguido de un intrón quimérico [incluyendo las señales de procesamiento 16S/19S del SV40 tardío y una pequeña región 5' UTR] y una pequeña secuencia señal de poliadenilación (polyA) sintética, flanqueado por las repeticiones terminales invertidas (ITRs) del virus adeno-asociado 2 (AAV2).

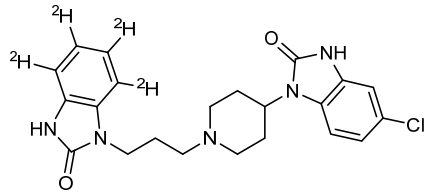
deudomperidonum

deudomperidone — 5-chloro-1-(1-{3-[2-oxo-2,3-dihydro-1*H*-(4,5,6,7-$^{2}H_4$)benzimidazol-1-yl]propyl}piperidin-4-yl)-1,3-dihydro-2*H*-benzimidazol-2-one

deudompéridone — 5-chloro-1-(1-{3-[2-oxo-2,3-dihydro-1*H*-(4,5,6,7-$^{2}H_4$)benzimidazol-1-yl]propyl}pipéridin-4-yl)-1,3-dihydro-2*H*-benzimidazol-2-one

deudomperidona — 5-cloro-1-(1-{3-[2-oxo-2,3-dihidro-1*H*-(4,5,6,7-$^{2}H_4$)benzimidazol-1-il]propil}piperidin-4-il)-1,3-dihidro-2*H*-benzimidazol-2-ona

$C_{22}H_{20}{}^{2}H_4ClN_5O_2$

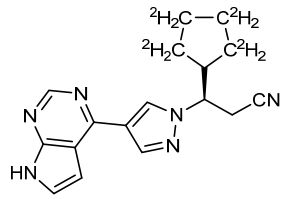


deuruxolitinibum

deuruxolitinib — (3*R*)-3-(2,2,3,3,3,4,4,5,5-$^{2}H_8$)cyclopentyl-3-[4-(7*H*-pyrrolo[2,3-*d*]pyrimidin-4-yl)-1*H*-pyrazol-1-yl]propanenitrile

deuruxolitinib — (3*R*)-3-(2,2,3,3,3,4,4,5,5-$^{2}H_8$)ciclopentil-3-[4-(7*H*-pirrolo[2,3-*d*]pirimidin-4-il)-1*H*-pirazol-1-il]propanonitrilo

$C_{17}H_{10}{}^{2}H_8N_6$

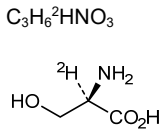


deutarserinum

deutarserine — D-(2-^{2}H)serine; (2*R*)-2-amino-3-hydroxy(2-^{2}H)propanoic acid

deutarsérine — D-(2-^{2}H)sérine; acide (2*R*)-2-amino-3-hydroxy(2-^{2}H)propanoïque

deutarserina — D-(2-^{2}H)serina; ácido (2*R*)-2-amino-3-hidroxi(2-^{2}H)proapoico



domvanalimabum #

domvanalimab	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 (1-448) [VH (*Homo sapiens* IGHV3-48*01 (90.8%) -(IGHD) -IGHJ4*01 (92.3%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -*Homo sapiens* IGHG1*01, G1m17,1, G1v14 CH2 A1.3, A1.2 (CH1 K120 (216) (120-217), hinge 1-15 (218-232), CH2 L1.3>A (236), L1.2>A (237) (233-342), CH3 D12 (358), L14 (360) (343-447), CHS K>del (448)) (120-448)], (222-214')-disulfide with kappa light chain humanized (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-16*01 (89.5%) -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 a Chinese hamster ovary (CHO)-K1 cell line, glycoform alfa
domvanalimab	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 transmembranaire, VSTM3)], anticorps monoclonal humanisé; chaîne lourde gamma1 humanisée (1-448) [VH (*Homo sapiens* IGHV3-48*01 (90.8%) -(IGHD) - IGHJ4*01 (92.3%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -*Homo sapiens* IGHG1*01, G1m17,1, G1v14 CH2 A1.3, A1.2 (CH1 K120 (216) (120-217), charnière 1-15 (218-232), CH2 L1.3>A (236), L1.2>A (237) (233-342), CH3 D12 (358), L14 (360) (343-447), CHS K>del (448)) (120-448)], (222-214')-disulfure avec la chaîne légère kappa humanisée (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-16*01 (89.5%) -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) lignée cellulaire CHO-K1, glycoforme alfa
domvanalimab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* TIGIT (inmunoreceptor de los linfocitos T con dominio Ig e 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 (1-448) [VH (*Homo sapiens* IGHV3-48*01 (90.8%) -(IGHD) - IGHJ4*01 (92.3%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -*Homo sapiens* IGHG1*01, G1m17,1, G1v14 CH2 A1.3, A1.2 (CH1 K120 (216) (120-217), bisagra 1-15 (218-232), CH2 L1.3>A (236), L1.2>A (237) (233-342), CH3 D12 (358), L14 (360) (343-447), CHS K>del (448)) (120-448)], (222-214')-disulfuro con la cadena ligera kappa humanizada (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-16*01 (89.5%) -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) línea celular CHO-K1, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGGSLRL SCAASGFTFS NFGMHWVRQA PGKGLEWVAF  50
ISSGSSSIYY ADTVKGRFTI SRDNAKNSLY LQMNSLRAED TAVYYCARMR 100
LDYYAMDYWG QGTMVTVSSA STKGPSVFPL APSSKSTSGG TAALGCLVKD 150
YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY 200
ICNVNHKPSN TKVDKKVEPK SCDKTHTCPP CPAPEAAGGP SVFLFPPKPK 250
DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VDGVEVHNAK TKPREEQYNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKAL PAPIEKTISK AKGQPREPQV 350
YTLPPSRDEL TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL 400
DSDGSFFLYS KLTVDKSRWQ QGNVFSCSVM HEALHNHYTQ KSLSLSPG   448
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Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS LSASVGDRVT ITCRASKSIS KYLAWYQQKP GKAPKLLIYS  50
GSTLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ HNEYPWTFGG 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
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Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 146-202 263-323 369-427
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.

donidalorsenum
donidalorsen

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]hex-yl}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)-*P*-thioguanylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methylcytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)adenylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-*P*-thioadenylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-deoxy-5-methyl-*P*-thiocytidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-deoxy-5-methyl-*P*-thiocytidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-deoxy-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)adenylyl-(3'→5')-2'-*O*-(2-methoxyethyl)adenylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-*P*-thioadenylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)adenosine

donidalorsen

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)-*P*-thioguanylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthylcytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)adénylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-*P*-thioadénylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-désoxy-5-méthyl-*P*-thiocytidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-désoxy-5-méthyl-*P*-thiocytidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-2'-désoxy-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)adénylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)adénylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-*P*-thioadénylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)adénosine

donidalorsén

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-hydroxi-1,10,14,21-tetraoxo-2,18-dioxa-9,15,22-triaza-1λ^5-fosfaoctacosan-1-il)-5-metil-2'-*O*-(2-metoxietil)-*P*-tio-uridilil-(3'→5')-2'-*O*-(2-metoxietil)-*P*-tioguanilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)citidilil-(3'→5')-2'-*O*-(2-metoxietil)adenilil-(3'→5')-2'-*O*-(2-metoxi-etil)-*P*-tioadenilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-5-metil-*P*-tiocitidilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-5-metil-*P*-tiocitidilil-(3'→5')-*P*-tiotimidilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-2'-desoxi-5-metil-*P*-tiocitidilil-(3'→5')-2'-*O*-(2-metoxietil)adenilil-(3'→5')-2'-*O*-(2-metoxietil)adenilil-(3'→5')-2'-*O*-(2-metoxietil)-*P*-tioadenilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)-*P*-tiocitidilil-(3'→5')-2'-*O*-(2-metoxietil)adenosina

$C_{296}H_{435}N_{83}O_{151}P_{20}S_{15}$

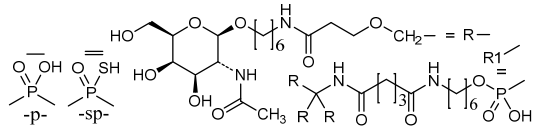
(3'-5') R1-U=G=C-A-A=d(G=T=C=T=C=T=T=G=G=C=)A-A-A=C=A

Legend:

G & T : 2'-deoxynucleotide C : 2'-deoxy-5-methylcytidine

A & G : 2'-*O*-(2-methoxyethyl)nucleotide

C & U : 2'-*O*-(2-methoxyethyl)-5-methylnucleotide



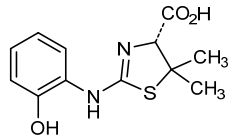
ebaresdaxum

ebaresdax

(4*R*)-2-(2-hydroxyanilino)-5,5-dimethyl-4,5-dihydro-1,3-thiazole-4-carboxylic acid

ébaresdax	acide (4*R*)-2-(2-hydroxyanilino)-5,5-diméthyl-4,5-dihydro-1,3-thiazole-4-carboxylique
ebaresdax	ácido (4*R*)-2-(2-hidroxianilino)-5,5-dimetil-4,5-dihidro-1,3-tiazol-4-carboxílico

$C_{12}H_{14}N_2O_3S$



ebdarokimabum #

ebdarokimab	immunoglobulin G1-kappa, anti-[*Homo sapiens* IL12B (interleukin 12B, CLMF, IL-12B, NKSF, CLMF2)], humanized monoclonal antibody; gamma1 heavy chain humanized(1-449) [VH (*Homo sapiens* IGHV5-51*01 (84.7%) -(IGHD) -IGHJ3*02 (92.9%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -*Homo sapiens* IGHG1*03v G1m3>G1m17, nG1m1 (CH1 R120>K (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* IGKV3D-11*02 (86.7%) -IGKJ5*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
ebdarokimab	immunoglobuline G1-kappa, anti-[*Homo sapiens* IL12B (interleukine 12B, CLMF, IL-12B, NKSF, CLMF2)], anticorps monoclonal humanisé; chaîne lourde gamma1 humanisée (1-449) [VH (*Homo sapiens* IGHV5-51*01 (84.7%) -(IGHD) -IGHJ3*01 (92.9%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -*Homo sapiens* IGHG1*03v G1m3>G1m17, nG1m1 (CH1 R120>K (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* IGKV3D-11*02 (86.7%) -IGKJ5*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
ebdarokimab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* IL12B (interleukina 12B, CLMF, IL-12B, NKSF, CLMF2)], anticuerpo monoclonal humanizado;

cadena pesada gamma1 humanizada (1-449) [VH (*Homo sapiens* IGHV5-51*01 (84.7%) -(IGHD) -IGHJ3*01 (92.9%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -*Homo sapiens* IGHG1*03v G1m3>G1m17, nG1m1 (CH1 R120>K (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* IGKV3D-11*02 (86.7%) -IGKJ5*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

```
EVQLVQSGAE VKKPGESLKI SCQSSGYTFT SYWIGWVRQM PGQGLEWIGI  50
MSPVDSDIRY NPMFRGQVTM SVDKSSSTAY LQWSSLKASD TAMYYCARRR 100
PGQGYFDFWG QGTMVTVSSA 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
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Light chain / Chaîne légère / Cadena ligera

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EIVLTQSPAT LSASPGERAT ISCRASQSVG TWVAWYQQKP GQAPRSLIYA  50
ASNLQSGIPA RFSGSGSGTD FTLTISSLEP EDFAVYYCQQ YNIYPYTFGQ 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) 22-96 146-202 263-323 369-427
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 / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
449, 449"

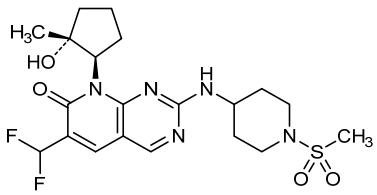
ebvaciclibum

ebvaciclib — 6-(difluoromethyl)-8-[(1*R*,2*R*)-2-hydroxy-2-methylcyclopentyl]-2-{[1-(methanesulfonyl)piperidin-4-yl]amino}pyrido[2,3-*d*]pyrimidin-7(8*H*)-one

ebvaciclib — 6-(difluorométhyl)-8-[(1*R*,2*R*)-2-hydroxy-2-méthylcyclopentyl]-2-{[1-(méthanesulfonyl)pipéridin-4-yl]amino}pyrido[2,3-*d*]pyrimidin-7(8*H*)-one

ebvaciclib — 6-(difluorometil)-8-[(1*R*,2*R*)-2-hidroxi-2-metilciclopentil]-2-{[1-(metanosulfonil)piperidin-4-il]amino}pirido[2,3-*d*]pirimidin-7(8*H*)-ona

$C_{20}H_{27}F_2N_5O_4S$



ecubectedinum

ecubectedin

(1'*R*,3'*S*,6*R*,6a*R*,7*R*,13*S*,14*S*,16*R*)-8,14-dihydroxy-3'-(hydroxymethyl)-9-methoxy-4,10,23-trimethyl-19-oxo-2',3',4',6,6a,7,9',13,14,16-decahydro-2*H*,12*H*-spiro[7,13-azano-6,16-(sulfanopropanooxymethano)[1,3]dioxolo[7,8]isoquino[3,2-*b*][3]benzazocine-20,1'-pyrido[3,4-*b*]indol]-5-yl acetate

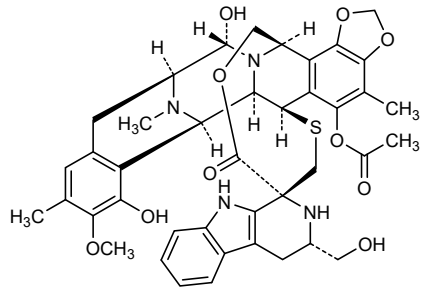
écubectédine

acétate de (1'*R*,3'*S*,6*R*,6a*R*,7*R*,13*S*,14*S*,16*R*)-8,14-dihydroxy-3'-(hydroxyméthyl)-9-méthoxy-4,10,23-triméthyl-19-oxo-2',3',4',6,6a,7,9',13,14,16-décahydro-2*H*,12*H*-spiro[7,13-azano-6,16-(sulfanopropanooxyméthano)[1,3]dioxolo[7,8]isoquino[3,2-*b*][3]benzazocine-20,1'-pyrido[3,4-*b*]indol]-5-yle

ecubectedina

acetato de (1'*R*,3'*S*,6*R*,6a*R*,7*R*,13*S*,14*S*,16*R*)-8,14-dihidroxi-3'-(hidroximetil)-4,10,23-trimetil-9-metoxi-19-oxo-2',3',4',6,6a,7,9',13,14,16-decahidro-2*H*,12*H*-spiro[7,13-azano-6,16-(sulfanopropanooximetano)[1,3]dioxolo[7,8]isoquino[3,2-*b*][3]benzazocina-20,1'-pirido[3,4-*b*]indol]-5-ilo

$C_{41}H_{44}N_4O_{10}S$



edaxeterkibum

edaxeterkib

6-[(3*R*)-1-benzylpiperidin-3-yl]-3-(2-methoxypyrimidin-5-yl)-1,5,6,8-tetrahydro-7*H*-pyrazolo[4,3-*g*]quinazolin-7-one

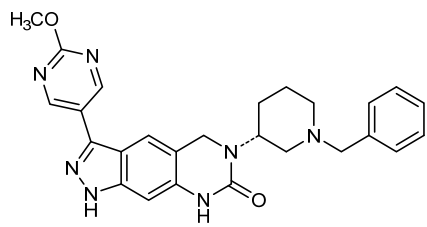
édaxéterkib

6-[(3*R*)-1-benzylpipéridin-3-yl]-3-(2-méthoxypyrimidin-5-yl)-1,5,6,8-tétrahydro-7*H*-pyrazolo[4,3-*g*]quinazolin-7-one

edaxeterkib

6-[(3*R*)-1-bencilpiperidin-3-il]-3-(2-metoxipirimidin-5-il)-1,5,6,8-tetrahidro-7*H*-pirazolo[4,3-*g*]quinazolin-7-ona

$C_{26}H_{27}N_7O_2$



eflimrufuspum alfa

eflimrufusp alfa	human vascular endothelial growth factor receptor 1 (VEGFR-1) immunoglobulin-like domain 2 containing fragment (132-232, 1-101 in the current sequence), fused via human vascular endothelial growth factor receptor 2 (VEGFR-2) immunoglobulin-like domain 3 containing fragment (227-327, 102-202 in the current sequence) to human fibroblast growth factor receptor 1 (FGFR-1) immunoglobulin-like domains 2 and 3 containing fragment (150-361, 203-414 in the current sequence), fused to human immunoglobulin G1 Fc fragment (415-641), dimer, glycosylated, produced in Chinese hamster ovary (CHO) cells; vascular endothelial growth factor receptor 1 (*Homo sapiens* VEGFR-1) (132-232)-peptide (1-101), containing the immunoglobulin-like domain 2, fused with vascular endothelial growth factor receptor 2 (*Homo sapiens* VEGFR-2) (227-327)-peptide (102-202), containing the immunoglobulin-like domain 3, with fibroblast growth factor receptor 1 (*Homo sapiens* FGFR-1) (150-361)-peptide (203-414), containing the immunoglobulin-like domains 2 and 3 (211-299 and 308-410), and with a C-terminal *Homo sapiens* immunoglobulin G1 227-peptide Fc fragment (415-641), [*Homo sapiens* IGHG1*01; hinge 415-424; CH2: 425-534; CH3: 535-639; CHS: 640-641]; dimer (420-420':423-423')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa
éflimrufusp alfa	domaine 2 analogue à l'immunoglobuline du récepteur 1 du facteur de croissance de l'endothélium vasculaire humain (VEGFR-1) contenant le fragment (132-232, 1-101 dans la séquence actuelle), fusionné via le domaine 3 analogue à l'immunoglobuline du récepteur 2 du facteur de croissance de l'endothélium vasculaire humain (VEGFR-2) contenant le fragment (227-327, 102-202 dans la séquence actuelle) aux domaines 2 et 3 analogues à l'immunoglobuline du récepteur 1 du facteur de croissance des fibroblastes humain 21 (FGFR-1) contenant le fragment (150-361, 203-414 dans la séquence actuelle), fusionné au fragment Fc (415-641) de l'immunoglobuline G1 humaine, dimère, glycosylé, produit dans des cellules ovariennes de hamster chinois (CHO); peptide 132-232 du récepteur 1 du facteur de croissance de l'endothélium vasculaire (VEGFR-1 d'*Homo sapiens*) (1-101), contenant le domaine 2 analogue à l'immunoglobuline, fusionné avec le peptide-(227-327) du récepteur 2 du facteur de croissance de l'endothélium vasculaire (VEGFR-2 d'*Homo sapiens*) (102-202), contenant le domaine 3 analogue à l'immunoglobuline, avec le peptide-(150-361) du récepteur 1 du facteur de croissance des fibroblastes (FGFR-1 d'*Homo sapiens*) (203-414), contenant les domaines 2 et 3 analogues à l'immunoglobuline (211-299 et 308-410), et avec le fragment Fc du peptide-227 C-terminal de l'immunoglobulines G1 d'*Homo sapiens* (415-641), [*Homo sapiens* IGHG1*01; charnière 415-424; CH2: 425-534; CH3: 535-639; CHS: 640-641]; dimère (420-420':423-423')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

eflimrufusp alfa

el receptor 1 del factor de crecimiento endotelial vascular humano (VEGFR-1) dominio 2 de inmunoglobulina conteniendo fragmento (132-232, 1-101 en la secuencia actual), fusionado a tráves del receptor 2 del factor de crecimiento endotelial vascular humano (VEGFR-2) dominio 3 de la inmunoglobulina conteniendo el fragmento (227-327, 102-202 en la secuencia actual) al receptor 1 del factor de crecimiento de fibroblastos humano (FGFR-1) dominio 2 y 3 de la inmunoglobulina conteniendo el fragmento (150-361, 203-414 en la secuencia actual), fusionado al fragmento de la inmunoglobulina humana G1 Fc (415-641), dímero, glicosilado, producido en células ováricas de hámster chino (CHO);
péptido 132-232 del receptor 1 del factor de crecimiento del endotelio vascular (VEGFR-1 de *Homo sapiens*) (1-101), que contiene el dominio 2 del tipo inmunoglobulina, fusionado con el péptido 227-327 del receptor 2 del factor de crecimiento del endotelio vascular (VEGFR-2 de *Homo sapiens*) (102-202), que contiene el dominio 3 del tipo inmunoglobulina, con el péptido 150-361 del receptor 1 del factor de crecimiento de fibroblastos (FGFR-1 de *Homo sapiens*) (203-414), que contiene los dominios 2 y 3 de tipo inmunoglobulina (211-299 y 308-410), y con el fragmento Fc 227-peptÍdico C-terminal de inmunoglobulinas G1 de *Homo sapiens* (415-641), [*Homo sapiens* IGHG1*01; bisagra 415-424; CH2: 425-534; CH3: 535-639; CHS: 640-641]; dímero (420-420':423-423')-bisdisulfuro, producido en células ováricas de hámster chino (CHO), glicoforma alfa

Sequence / Séquence / Secuencia

```
GRPFVEMYSE IPEIIHMTEG RELVIPCRVT SPNITVTLKK FPLDTLIPDG    50
KRIIWDSRKG FIISNATYKE IGLLTCEATV NGHLYKTNYL THRQTNTIID   100
VVLSPSHGIE LSVGEKLVLN CTARTELNVG IDFNWEYPSS KHQHKKLVNR   150
DLKTQSGSEM KKFLSTLTID GVTRSDQGLY TCAASSGLMT KKNSTFVRVH   200
EKPVAPYWTS PEKMEKKLHA VPAAKTVKFK CPSSGTPNPT LRWLKNGKEF   250
KPDHRIGGYK VRYATWSIIM DSVVPSDKGN YTCIVENEYG SINHTYQLDV   300
VERSPHRPIL QAGLPANKTV ALGSNVEFMC KVYSDPQPHI QWLKHIEVNG   350
SKIGPDNLPY VQILKTAGVN TTDKEMEVLH LRNVSFEDAG EYTCLAGNSI   400
GLSHHSAWLT VLEADKTHTC PPCPAPELLG GPSVFLFPPK PKDTLMISRT   450
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL   500
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD   550
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL   600
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K            641
```

VEGFR-1 Ig-like 2 / *VEGFR-2 Ig-like 3* / **FGFR-1 Ig-like 2+3** / IgG1 Fc

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-VEGFR1:	27-76	Intra-VEGFR2:	121-182
	27'-76'		121'-182'
Intra-FGFR1:	231-283, 330-394	Intra-Fc:	455-515, 561-619
	231'-283', 330'-394'		455'-515', 561'-619'
Inter-Fc:	420-420', 423-423'		

Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación
N33, N65, N120, N193, N280, N293, N317, N349, N370, N383, N491, N33', N65', N120', N193', N280', N293', N317', N349', N370', N383', N491'

C-terminal lysine clipping / Coupure de la lysine C-terminale / Supresión de lisina C-terminal
K641, K641'

efruxiferminum #
efruxifermin

human L-methionyl immunoglobulin G1 Fc fragment (1-228) fused via peptidyl linker ^{229}GGGGSGGGGSGGGGS^{243} to human fibroblast growth factor 21 (FGF-21) fragment (29-209, 244-424 in the current sequence) variant (L^{98}>R^{341}, P^{171}>G^{414}, A^{180}>E^{423}), dimer, produced in *Escherichia coli;*

	L-methionyl-immunoglobulin G1 (*Homo sapiens*) 33γ1-chain C-terminal 227-peptide Fc fragment (1-228) [*Homo sapiens* IGHG1*1; hinge 1-11; CH2 12-121; CH3 122-226; CHS 227-228] fused with the peptide linker $(G_4S)_3$ (229-243) and [$L^{98}>R^{341}$, $P^{171}>G^{414}$, $A^{180}>E^{423}$]-fibroblast growth factor 21 (*Homo sapiens* FGF-21) (244-424), dimer (7-7':10-10')-bisdisulfide, non-glycosylated, produced in *Escherichia coli*
éfruxifermine	fragment Fc L-méthionyl (1-228) de l'immunoglobuline G1 humaine fusionné via un linker peptidique ^{229}GGGGSGGGGSGGGGS^{243} au fragment (29-209, 244-424 dans la séquence actuelle) du facteur de croissance des fibroblastes 21 (FGF-21), variant ($L^{98}>R^{341}$, $P^{171}>G^{414}$, $A^{180}>E^{423}$), dimère, produit par *Escherichia coli*; L-méthionyl-fragment Fc (1-228) de l'immunoglobuline G1 (227-peptide C-terminal de la chaîne γ1 d'*Homo sapiens*) [*Homo sapiens* IGHG1*1; charnière 1-11; CH2 12-121; CH3 122-226; CHS 227-228] fusionné avec le linker peptidique $(G_4S)_3$ (229-243) et [$L^{98}>R^{341}$, $P^{171}>G^{414}$, $A^{180}>E^{423}$]-facteur 21 de croissance des fibroblastes (FGF-21 d'*Homo sapiens*) (244-424), dimère (7-7':10-10')-bisdisulfure, non-glycosylé, produit par *Escherichia coli*
efruxifermina	fragmento Fc L-metionil (1-228) de la inmunoglobulina G1 humana fusionada a través de un enlace peptidil ^{229}GGGGSGGGGSGGGGS^{243} al factor fibroblasto humano 21 (FGF-21) fragmento (29-209, 244-424 en la secuencia actual) variante ($L^{98}>R^{341}$, $P^{171}>G^{414}$, $A^{180}>E^{423}$), dímero, producido en *Escherichia coli;* L-metionil-fragmento Fc de inmunoglobulina G1 (227-péptido C-terminal de la cadena γ1 de *Homo sapiens*) (1-228) [*Homo sapiens* IGHG1*1; bisagra 1-11; CH2 12-121; CH3 122-226; CHS 227-228] fusionado con el péptido conector $(G_4S)_3$ (229-243) y [$L^{98}>R^{341}$, $P^{171}>G^{414}$, $A^{180}>E^{423}$]-factor 21 de crecimiento fibroblástico (FGF-21 de *Homo sapiens*) (244-424), dímero (7-7':10-10')-bisdisulfuro, no glicosilado, producido por *Escherichia coli*

Sequence / Séquence / Secuencia

```
MDKTHTCPPC PAPELLGGPS VFLFPPKPKD TLMISRTPEV TCVVVDVSHE    50
DPEVKFNWYV DGVEVHNAKT KPREEQYNST YRVVSVLTVL HQDWLNGKEY   100
KCKVSNKALP APIEKTISKA KGQPREPQVY TLPPSRDELT KNQVSLTCLV   150
KGFYPSDIAV EWESNGQPEN NYKTTPPVLD SDGSFFLYSK LTVDKSRWQQ   200
GNVFSCSVMH EALHNHYTQK SLSLSPGKGG GGSGGGGSGG GGSHPIPDSS   250
PLLQFGGQVR QRYLYTDDAQ QTEAHLEIRE DGTVGGAADQ SPESLLQLKA   300
LKPGVIQILG VKTSRFLCQR PDGALYGSLH FDPEACSFRE RLLEDGYNVY   350
QSEAHGLPLH LPGNKSPHRD PAPRGPARFL PLPGLPPAPP EPPGILAPQP   400
PDVGSSDPLS MVGGSQGRSP SYES                               424
```

Mutation sites / Sites de mutation / Posiciones de mutación
L341>R, P414>G, A423>E
L341'>R, P414'>G, A423'>E

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-Fc:	42-102, 148-206	Intra-FGF21:	318-336
	42'-102', 148'-206'		318'-336'
Inter-Fc	7-7', 10-10'		

Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación
none / aucun / ninguna

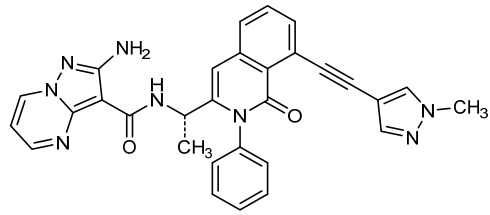
eganelisibum

eganelisib — 2-amino-*N*-[(1*S*)-1-{8-[(1-methyl-1*H*-pyrazol-4-yl)ethynyl]-1-oxo-2-phenyl-1,2-dihydroisoquinolin-3-yl}ethyl]pyrazolo[1,5-*a*]pyrimidine-3-carboxamide

éganélisib — 2-amino-*N*-[(1*S*)-1-{8-[(1-méthyl-1*H*-pyrazol-4-yl)éthynyl]-1-oxo-2-phényl-1,2-dihydroisoquinoléin-3-yl}éthyl]pyrazolo[1,5-*a*]pyrimidine-3-carboxamide

eganelisib — 2-amino-*N*-[(1*S*)-1-{2-fenil-8-[(1-metil-1*H*-pirazol-4-il)etinil]-1-oxo-1,2-dihidroisoquinolein-3-il}etil]pirazolo[1,5-*a*]pirimidina-3-carboxamida

$C_{30}H_{24}N_8O_2$



elasomeranum #

elasomeran — 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 ID MN908947.3) spike (S) glycoprotein, further optimized by two additional stop codons, flanked by an artificial 5' untranslated region (UTR) and a 3' UTR derived from the human alpha globin gene (HBA1) and terminated by a 3' poly(A) tail; contains N^1-methylpseudouridine instead of uridine (*all*-U>m$^1\Psi$).

élasoméran — ARN messager (ARNm), protégé d' une coiffe en 5', codant la séquence entière d' un variant de la glycoprotéine de spicule (S) du SARS-CoV-2 (coronavirus 2 du syndrome respiratoire aigu sévère; GenBank ID MN908947.3) à la conformation stabilisée par pré-fusion (K986P et V987P) et aux codons optimisés, optimisation renforcée par l'ajout de deux codons stop, flanqué d'une région non traduite (UTR) en 5' artificielle et d' une UTR en 3' dérivée du gène de l'alpha-globine humaine (HBA1) et terminé par une queue poly(A) en 3'; contient de la N^1-méthylpseudouridine au lieu de l'uridine (*all*-U>m$^1\Psi$).

elasomerán — ARN mensajero (ARNm), protegido en 5', que codifica para una variante estabilizada en conformación pre-fusión (K986P and V987P) de la glicoproteína de la espícula (S) del SARS-Cov-2 (coronavirus 2 del síndrome respiratorio agudo severo; GenBank ID MN908947.3) completa, con codones optimizados, con dos codones de terminación adicionales, flanqueado por una región 5' no traducida (UTR) artificial y una UTR en 3' derivada del gen de de la globina alfa humana (HBA1) y terminado por una cola poly(A) en 3'; contiene N^1-metilpseudouridina en lugar de uridina (*all*-U>m$^1\Psi$).

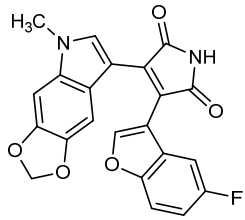
elraglusibum

elraglusib — 3-(5-fluoro-1-benzofuran-3-yl)-4-(5-methyl-5*H*-[1,3]dioxolo[4,5-*f*]indol-7-yl)-1*H*-pyrrole-2,5-dione

elraglusib — 3-(5-fluoro-1-benzofuran-3-yl)-4-(5-méthyl-5*H*-[1,3]dioxolo[4,5-*f*]indol-7-yl)-1*H*-pyrrole-2,5-dione

elraglusib — 3-(5-fluoro-1-benzofuran-3-il)-4-(5-metil-5*H*-[1,3]dioxolo[4,5-*f*]indol-7-il)-1*H*-pirrol-2,5-diona

$C_{22}H_{13}FN_2O_5$



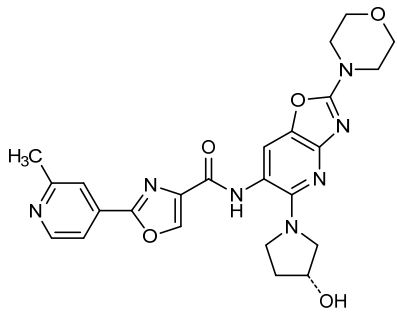
emavusertibum

emavusertib — *N*-{5-[(3*R*)-3-hydroxypyrrolidin-1-yl]-2-(morpholin-4-yl)[1,3]oxazolo[4,5-*b*]pyridin-6-yl}-2-(2-methylpyridin-4-yl)-1,3-oxazole-4-carboxamide

émavusertib — *N*-{5-[(3*R*)-3-hydroxypyrrolidin-1-yl]-2-(morpholin-4-yl)[1,3]oxazolo[4,5-*b*]pyridin-6-yl}-2-(2-méthylpyridin-4-yl)-1,3-oxazole-4-carboxamide

emavusertib — *N*-{5-[(3*R*)-3-hidroxipirrolidin-1-il]-2-(morfolin-4-il)[1,3]oxazolo[4,5-*b*]piridin-6-il}-2-(2-metilpiridin-4-il)-1,3-oxazol-4-carboxamida

$C_{24}H_{25}N_7O_5$



emvododstatum

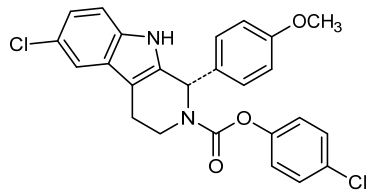
emvododstat — 4-chlorophenyl (1*S*)-6-chloro-1-(4-methoxyphenyl)-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate

emvododstat — (1*S*)-6-chloro-1-(4-méthoxyphényl)-1,3,4,9-tétrahydro-2*H*-pyrido[3,4-*b*]indole-2-carboxylate de 4-chlorophényle

emvododstat

(1*S*)-6-cloro-1-(4-metoxifenil)-1,3,4,9-tetrahidro-2*H*-pirido[3,4-*b*]indol-2-carboxilato de 4-clorofenilo

$C_{25}H_{20}Cl_2N_2O_3$



encoberminogenum rezmadenovecum #

encoberminogene rezmadenovec

A replication-deficient recombinant adenovirus, serotype 5, encoding multiple human vascular endothelial growth factor (VEGF) isoforms.
A replication-deficient recombinant adenovirus, serotype 5 (Ad5), encoding multiple human vascular endothelial growth factor (VEGF) isoforms (VEGF121, VEGF165 and VEGF189) under the control of a cytomegalovirus immediate early promoter/enhancer (CMV) and the simian virus 40 (SV40) polyA sequence. Alternative splicing provides mRNA that encodes the three major isoforms of VEGF: VEGF121 (exons 1-5 and 8), VEGF165 (exons 1-5, 7 and 8) and VEGF189 (exons 1-5, 6A, 7 and 8). The VEGF transgene is inserted into the region from which the adenovirus early gene *E1A* is deleted and *E1B* is partially deleted; the *E3* gene is deleted between late gene *L5* and the early gene *E4*.

encoberminogène rezmadénovec

Un adénovirus recombinant déficient à la réplication, de sérotype 5, codant de multiples isoformes du facteur de croissance de l'endothélium vasculaire humain (VEGF).
Un adénovirus recombinant déficient à la réplication, de sérotype 5 (Ad5), codant de multiples isoformes (VEGF121, VEGF165 et VEGF189) du facteur de croissance de l'endothélium vasculaire humain (VEGF) sous le contrôle d'un promoteur/activateur précoce immédiat du cytomégalovirus (CMV) et d'une séquence polyA du virus simien (SV40). L'épissage alternatif génère un ARNm qui code trois isoformes majeures du VEGF : VEGF121 (exons 1-5 et 8), VEGF165 (exons 1-5, 7 et 8) et VEGF189 (exons 1-5, 6A, 7 et 8). Le transgène VEGF est inséré dans la région de laquelle le gène précoce de l'adénovirus *E1A* est supprimé et où *E1B* est partiellement supprimé; le gène E3 est supprimé entre le gène tardif *L5* et le gène précoce *E4*.

encoberminogén rezmadenovec

Un adenovirus recombinante, deficiente en replicación, serotipo 5, que codifica para múltiples isoformas del factor de crecimiento del endotelio vascular humano (VEGF).

Un adenovirus recombinante, deficiente en replicación, serotipo 5 (Ad5), que codifica para múltiples isoformas del factor de crecimiento del endotelio vascular humano (VEGF) (VEGF121, VEGF165 y VEGF189) bajo el control de un promotor/potenciador inmediato temprano del citomegalovirus (CMV) y una secuencia polyA del virus 40 de simios (SV40). El procesamiento alternativo proporciona mRNA que codifica para las tres principales isoformas de VEGF: VEGF121 (exones 1-5 y 8), VEGF165 (exones 1-5, 7 y 8) y VEGF189 (exones 1-5, 6A, 7 y 8). El transgén VEGF está insertado en la región en la que el gen temprano *E1A* del adenovirus está delecionado y *E1B* está parcialmente delecionado; el gen *E3* está delecionado entre el gen tardío *L5* y el gen temprano *E4*.

ensovibepum #

ensovibep

fusion protein consisting of two identical engineered ankyrin repeats-containing binding protein domains anti-(human albumin) (1-126 fused via peptidyl linker ^{127}GSPTPTPTTPTPTPTTPTPTPT^{148} to 149-274), fused via peptidyl linker ^{275}GSPTPTPTTPTPTPTTPTPTPT^{296} to three engineered ankyrin repeats-containing binding protein domains anti-(three different epitopes of the SARS-CoV-2 spike glycoprotein) (297-455 fused via peptidyl linker ^{456}GSPTPTPTTPTPTPTTPTPTPT^{477} to 478-636 in turn fused via peptidyl linker ^{637}GSPTPTPTTPTPTPTTPTPTPT^{658} to 659-817), produced in *Escherichia coli;*
fusion protein comprising five engineered protein-binding ankyrin repeat protein domains: two identical human serum albumin (HSA)-binding 126-peptides 1-126 and 149-274 plus three different 159-peptides 297-455, 478-636 and 659-817 that bind to three different epitopes of the spike glycoprotein (S protein, S1S2 protein) of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), connected by four $GS(PT)_3T(PT)_3T(PT)_3$ 22-peptide linkers 127-148, 275-296, 456-477 and 637-658, produced in *Escherichia coli*

ensovibep

protéine de fusion consistant de deux répétitions ankyrine identiques issues de l'ingénierie-contenant des domaines de protéines de liaison anti-(albumine humaine) (1-126 fusionné via un linker peptidique ^{127}GSPTPTPTTPTPTPTTPTPTPT^{148} au 149-274), fusionné via un linker peptidique ^{275}GSPTPTPTTPTPTPTTPTPTPT^{296} à trois répétitions ankyrine issues de l'ingénierie-contenant des domaines de protéines de liaison anti-(trois épitopes différents de la glycoprotéine de spicule) (297-455 fusionné via un linker peptidique ^{456}GSPTPTPTTPTPTPTTPTPTPT^{477} au 478-636 fusionné à son tour via un linker peptidique ^{637}GSPTPTPTTPTPTPTTPTPTPT^{658} au 659-817), produit chez *Escherichia coli*;
protéine de fusion consistant de cinq protéines issues de l'ingénierie-liant des domaines protéiques de répétitions ankyrine: deux albumines sériques humaines identiques (HAS)-liant 126-peptides 1-126 et 149-274 plus trois différents 159-peptides 297-455, 478-636 et 659-817 liés aux trois épitopes différents de la glycoprotéine de spicule (protéine S, protéine S1S2) du SARS-CoV-2 (coronavirus 2 du syndrome respiratoire aigu sévère), connectés par quatre $GS(PT)_3T(PT)_3T(PT)_3$ 22-linkers peptidiques 127-148, 275-296, 456-477 et 637-658, produit chez *Escherichia coli*

ensovibep

proteína de fusión consistente en dos dominios anti-(albúmina humana) diseñados de forma idéntica conteniendo repeticiones de anquirina (1-126 fusionada a través de un enlace peptidil ^{127}GSPTPTPTTPTPTPTTPTPTPT^{148} a 149-274), fusionado a través de un enlace peptidil ^{275}GSPTPTPTTPTPTPTTPTPTPT^{296} a tres dominios anti-(tres epítopos diferentes de SARS-CoV-2 glicoproteína espícula) diseñados conteniendo repeticiones de anquirina (297-455 fusionados a través del enlace pepitdil ^{456}GSPTPTPTTPTPTPTTPTPTPT^{477} a 478-636 por turno fusionado a través de un enlace peptidil ^{637}GSPTPTPTTPTPTPTTPTPTPT^{658} to 659-817), producido en *Escherichia coli*;
proteína de fusión que comprende cinco dominios diseñados conteniendo repeticiones de union a proteína anquirina: dos albúminas séricas idénticas humanas aglutinantes-(HSA) 126-péptidos 1-126 y 149-274 y además 159-péptidos 297-455, 478-636 y 659-817 que se une a 3 epítopos distintos de la glicoproteína espícula (S proteína, S1S2 proteína) de SARS-CoV-2 (síndrome severo agudo respiratorio del coronavirus 2) conectado por cuatro enlaces tipo péptido 127-148, 275-296, 456-477 y 637-658, producido en *Escherichia coli*

Sequence / Séquence / Secuencia

M 0

```
GSDLGKKLLE AARAGQDDEV RELLKAGADV NAKDYFSHTP LHLAARNGHL   50
KIVEVLLKAG ADVNAKDFAG KTPLHLAANE GHLEIVEVLL KAGADVNAQD  100
IFGKTPADIA ADAGHEDIAE VLQKAAGSPT PTPTTPTPTP TTPTPTPTGS  150
DLGKKLLEAA RAGQDDEVRE LLKAGADVNA KDYFSHTPLH LAARNGHLKI  200
VEVLLKAGAD VNAKDFAGKT PLHLAANEGH LEIVEVLLKA GADVNAQDIF  250
GKTPADIAAD AGHEDIAEVL QKAAGSPTPT PTTPTPTPTT PTPTPTGSDL  300
GKKLLQAARA GQLDEVRELL KAGADVNAKD REGITPLHLA AQHGHLEIVE  350
VLLKAGADVN AKDVWGRTPL HLAAWQGHLE IVEVLLKAGA DVNAKDLAGA  400
TPLHVAALYG HLEIVEVLLK AGADVNAQDK SGKTPADLAA RAGHQDIAEV  450
LQKAAGSPTP TPTTPTPTPT TPTPTPTGSD LGKKLLQAAR AGQLDEVREL  500
LKAGADVNAK DREGKTPLHV AAQEGHLEIV EVLLKAGADV NAKDVWGRTP  550
LHLAAWIGHL EIVEVLLKAG ADVNAKDVSG ATPLHAAALH GHLEIVEVLL  600
NAGADVNAQD KSGKTPADLA ARAGHQDIAE VLQKAAGSPT PTPTTPTPTP  650
TTPTPTPTGS DLGKKLLQAA RAGQLDEVRE LLKAGADVNA KDQEGITPLH  700
VAAHQGHLEI VEVLLKAGAD VNAKDVWGRT PLHLAAWRGH LEIVEVLLKA  750
GADVNAKDHA GATPLHAAAL SGHLEIVEVL LKAGADVNAQ DKSGKTPADL  800
AARAGHQDIA EVLQKAA                                      817
```

italicized *underlined* *letters*: 22-peptide linkers $GS(PT)_3T(PT)_3T(PT)_3$

Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación:
none / aucune / ninguna

M: Met^0 is clipped

enuvaptanum

enuvaptan

3-({3-(4-chlorophenyl)-5-oxo-4-[(2S)-3,3,3-trifluoro-2-hydroxypropyl]-4,5-dihydro-1*H*-1,2,4-triazol-1-yl}methyl)-1-[3-(trifluoromethyl)pyridin-2-yl]-1*H*-1,2,4-triazole-5-carboxamide

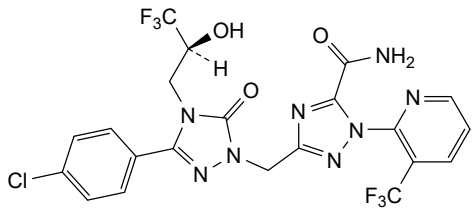
énuvaptan

3-({3-(4-chlorophényl)-5-oxo-4-[(2S)-3,3,3-trifluoro-2-hydroxypropyl]-4,5-dihydro-1*H*-1,2,4-triazol-1-yl}méthyl)-1-[3-(trifluorométhyl)pyridin-2-yl]-1*H*-1,2,4-triazole-5-carboxamide

enuvaptán

3-({3-(4-clorofenil)-5-oxo-4-[(2S)-3,3,3-trifluoro-2-hidroxipropil]-4,5-dihidro-1*H*-1,2,4-triazol-1-il}metil)-1-[3-(trifluorometil)piridin-2-il]-1*H*-1,2,4-triazol-5-carboxamida

$C_{21}H_{15}ClF_6N_8O_3$



eramkafuspum alfa #

eramkafusp alfa

chimeric immunoglobulin G1-kappa anti-(human B-lymphocyte antigen CD20) *(rituximab (77)(39)),* fused at the C-terminus of both heavy chains (1-451) via peptidyl linker ^{452}SGGGGS^{457} to human interferon α-2b (IFNα-2b) fragment (24-188, 458-622 in the current sequence) variant (^{23}K>R^{480}), dimer, glycosylated, produced in Chinese hamster ovary (CHO) cells;
immunoglobulin G1-kappa, anti-[*Homo sapiens* CD20 antigen (B-lymphocyte antigen CD20)], humanized monoclonal antibody *(rituximab (77)(39))*, gamma1 heavy chain humanized (1-451) [*Mus musculus* IGHV1-12*01; *Mus musculus* IGHJ1*01; *Homo sapiens* IGHG1*01; VH: 1-121; CH1: 122-219; hinge 220-234; CH2: 235-344; CH3: 345-449; CHS: 450-451; CDRKabatH1: SYNMH (31-35); CDRKabatH2: AIYPGNGDTSYNQKFKG (50-66); CDRKabatH3: STYYGGDWYFNV (99-110)], fused via a SG_4S linker (452-457) with interferon α-2b (*Homo sapiens*) [K^{23}>R^{480}]-variant (458-622), (224-213')-disulfide with kappa light chain humanized (1'-213') [*Mus musculus* IGKJ1*01; *Homo sapiens* IGKC*01; VL: 1-111; CL: 112-218; CDRKabatL1: RASSSVSYIH (24-33); CDRKabatL2: ATSNLAS (49-55); CDRKabatL3: QQWTSNPPT (88-96)]; dimer (230-230":233-233")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

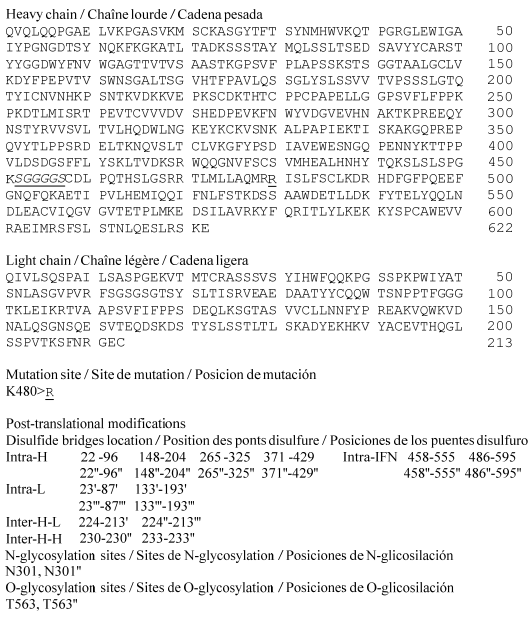
éramkafusp alfa

immunoglobuline chimérique G1-kappa anti-(antigène CD20 du lymphocyte B humain) (rituximab (77)(39)), fusionnée à la partie C-terminale des deux chaînes lourdes (1-451) via le linker peptidique 452SGGGGS457 du fragment (24-188, 458-622 de la séquence actuelle) de l'interféron α-2b (IFNα-2b) variant (23K>R480), dimère, glycosylée, produite dans des cellules ovariennes de hamster chinois (CHO);

immunoglobuline G1-kappa, anti-[antigène CD20 *Homo sapiens* des lymphocytes B), anticorps monoclonal humanisé *(rituximab (77)(39))*, chaîne lourde gamma1 humanisée (1-451) [*Mus musculus* IGHV1-12*01; *Mus musculus* IGHJ1*01; *Homo sapiens* IGHG1*01; VH: 1-121; CH1: 122-219; charnière 220-234; CH2: 235-344; CH3: 345-449; CHS: 450-451; CDRKabatH1: SYNMH (31-35); CDRKabatH2: AIYPGNGDTSYNQKFKG (50-66); CDRKabatH3: STYYGGDWYFNV (99-110)], fusionnée via le linker SG_4S (452-457) avec l'interféron α-2b (*Homo sapiens*) variant $K^{23}>R^{480}$ (458-622), (224-213')-disulfure avec la chaîne légère kappa humanisée (1'-213') [*Mus musculus* IGKJ1*01; *Homo sapiens* IGKC*01; VL: 1-111; CL: 112-218; CDRKabatL1: RASSSVSYIH (24-33); CDRKabatL2: ATSNLAS (49-55); CDRKabatL3: QQWTSNPPT (88-96)]; dimère (230-230":233-233")-bisdisulfure, produite dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

eramkafusp alfa

inmunoglobulina quimérica G1-kappa anti-(antígeno de linfocitos B CD20 humano) *(rituximab (77)(39))*, fusionado en la C-terminal de ambas cadenas pesadas (1-451) a través de un enlace peptidil $^{452}SGGGGS^{457}$ al fragmento del interferón α-2b (IFNα-2b) humano (24-188, 458-622 en la secuencia actual) variante ($^{23}K>R^{480}$), dímero, glicosilado, producido en células ováricas de hámster chino (CHO);
inmunoglobulina G1-kappa, anti-(*Homo sapiens* antígeno CD20 de los linfocitos B), anticuerpo monoclonal humanizado *(rituximab (77)(39))*, cadena pesada gamma1 humanizada (1-451) [*Mus musculus* IGHV1-12*01; *Mus musculus* IGHJ1*01; *Homo sapiens* IGHG1*01; VH: 1-121; CH1: 122-219; bisagra 220-234; CH2: 235-344; CH3: 345-449; CHS: 450-451; CDRKabatH1: SYNMH (31-35); CDRKabatH2: AIYPGNGDTSYNQKFKG (50-66); CDRKabatH3: STYYGGDWYFNV (99-110)], fusionado a través de un péptido conector SG_4S (452-457) con interferón α-2b (*Homo sapiens*) variante $K^{23}>R^{480}$ (458-622), (224-213')-disulfuro con la cadena ligera kappa humanizada (1'-213') [*Mus musculus* IGKJ1*01; *Homo sapiens* IGKC*01; VL: 1-111; CL: 112-218; CDRKabatL1: RASSSVSYIH (24-33); CDRKabatL2: ATSNLAS (49-55); CDRKabatL3: QQWTSNPPT (88-96)]; dímero (230-230":233-233")-bisdisulfuro, producido en células ováricas de hámster chino (CHO), glicoforma alfa



Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLQQPGAE LVKPGASVKM SCKASGYTFT SYNMHWVKQT PGRGLEWIGA    50
IYPGNGDTSY NQKFKGKATL TADKSSSTAY MQLSSLTSED SAVYYCARST   100
YYGGDWYFNV WGAGTTVTVS AASTKGPSVF 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
QVYTLPPSRD ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP   400
VLDSDGSFFL YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG   450
KSGGGGSCDL PQTHSLGSRR TLMLLAQMRR ISLFSCLKDR HDFGFPQEEF   500
GNQFQKAETI PVLHEMIQQI FNLFSTKDSS AAWDETLLDK FYTELYQQLN   550
DLEACVIQGV GVTETPLMKE DSILAVRKYF QRITLYLKEK KYSPCAWEVV   600
RAEIMRSFSL STNLQESLRS KE                                 622
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Light chain / Chaîne légère / Cadena ligera

```
QIVLSQSPAI LSASPGEKVT MTCRASSSVS YIHWFQQKPG SSPKPWIYAT    50
SNLASGVPVR FSGSGSGTSY SLTISRVEAE DAATYYCQQW TSNPPTFGGG   100
TKLEIKRTVA APSVFIFPPS DEQLKSGTAS VVCLLNNFYP REAKVQWKVD   150
NALQSGNSQE SVTEQDSKDS TYSLSSTLTL SKADYEKHKV YACEVTHQGL   200
SSPVTKSFNR GEC                                           213
```

Mutation site / Site de mutation / Posicion de mutación
K480>R

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro

Intra-H	22 -96	148-204	265 -325	371 -429	Intra-IFN	458-555	486-595
	22"-96"	148"-204"	265"-325"	371"-429"		458"-555"	486"-595"
Intra-L	23'-87'	133'-193'					
	23'"-87'"	133'"-193'"					
Inter-H-L	224-213'	224"-213'"					
Inter-H-H	230-230"	233-233"					

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
N301, N301"
O-glycosylation sites / Sites de O-glycosylation / Posiciones de O-glicosilación
T563, T563"

erfonrilimabum #

erfonrilimab	immunoglobulin G1 VH-VH-h-CH2-CH3 dimer, anti-[*Homo sapiens* CD274 (programmed death ligand 1, PDL1, PD-L1, B7 homolog 1, B7H1)] and anti-[*Homo sapiens* CTLA4 (cytotoxic T-lymphocyte-associated protein 4, CD152)], chimeric and humanized monoclonal antibody, bispecific; gamma1 VH-VH-h-CH2-CH3 chain, chimeric and humanized (1-493) [VH anti-CD274 Vicpac/Homsap (*Vicugna pacos* IGHV3-3*01 (80.6%) -(IGHD) -IGHJ5*01 (92.3)/*Homo sapiens* IGHV3-64*04 (78.4%) -(IGHD) -IGHJ1*01 (92.9%)) CDR-IMGT [8.8.21] (26-33.51-58.97-117) (1-128)] -3-mer glycyl-alanyl-prolyl linker (129-131) -[VH anti-CTLA4 humanized (*Homo sapiens* IGHV3-NL1*01 (86.6%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.21] (157-164.182-189.228-248) (132-259)] -2-mer glycyl-seryl linker (260-261) -[*Homo sapiens* IGHG1*01, G1m1 D12, L14, G1v37 h S5, hinge-CH2-CH3 (100%) (hinge 1-15 C5>S (266) (262-276), CH2 (277-386), CH3 D12 (402), L14 (404) (387-491), CHS (492-493)) (262-493)], dimer (272-272'':275-275'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa
erfonrilimab	immunoglobuline G1 VH-VH-h-CH2-CH3 dimère, anti-[*Homo sapiens* CD274 (ligand 1 de mort programmée, PDL1, PD-L1, homologue 1 de B7, B7H1)] et anti-[*Homo sapiens* CTLA4 (protéine 4 associée aux lymphocytes T cytotoxiques, CD152)], anticorps monoclonal chimérique et humanisé, bispécifique; gamma1 VH-VH-h-CH2-CH3 chaîne, chimérique et humanisée (1-493) [VH anti-CD274 Vicpac/Homsap (*Vicugna pacos* IGHV3-3*01 (80.6%) -(IGHD) -IGHJ5*01 (92.3)/*Homo sapiens* IGHV3-64*04 (78.4%) -(IGHD) -IGHJ1*01 (92.9%)) CDR-IMGT [8.8.21] (26-33.51-58.97-117) (1-128)] -3-mer glycyl-alanyl-prolyl linker (129-131) -[VH anti-CTLA4 humanisé (*Homo sapiens* IGHV3-NL1*01 (86.6%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.21] (157-164.182-189.228-248) (132-259)] -2-mer glycyl-séryl linker (260-261) -[*Homo sapiens* IGHG1*01, G1m1 D12, L14, G1v37 h S5, charnière-CH2-CH3 (100%) (charnière 1-15 C5>S (266) (262-276), CH2 (277-386), CH3 D12 (402), L14 (404) (387-491), CHS (492-493)) (262-493)], dimère (272-272'':275-275'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa
erfonrilimab	inmunoglobulina G1 VH-VH-h-CH2-CH3 dímero, anti-[*Homo sapiens* CD274 (ligando 1 de muerte programada, PDL1, PD-L1, homólogo 1 de B7, B7H1)] y anti-[*Homo sapiens* CTLA4 (proteína 4 asociada con los linfocitos T citotóxicos, CD152)], anticuerpo monoclonal quimérico y humanizado, biespecífico; gamma1 VH-VH-h-CH2-CH3 cadena, quimérica y humanizada (1-493) [VH anti-CD274 Vicpac/Homsap (*Vicugna pacos* IGHV3-3*01 (80.6%) -(IGHD) -IGHJ5*01 (92.3)/*Homo sapiens* IGHV3-64*04 (78.4%) -(IGHD) -IGHJ1*01 (92.9%)) CDR-IMGT [8.8.21] (26-33.51-58.97-117) (1-128)] -3-mer glicil-alanil-prolil linker (129-131) -[VH anti-CTLA4 humanizado (*Homo sapiens* IGHV3-NL1*01 (86.6%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.21] (157-164.182-189.228-248) (132-259)] -2-mer glicil-seril linker (260-261) -[*Homo sapiens* IGHG1*01, G1m1 D12, L14, G1v37 h S5, bisagra-CH2-CH3 (100%) (bisagra 1-15 C5>S (266) (262-276), CH2 (277-386), CH3 D12 (402), L14 (404) (387-491), CHS (492-493)) (262-493)], dímero (272-272'':275-275'')-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVESGGG LVQPGGSLRL SCAASGKMSS RRCMAWFRQA PGKERERVAK  50
LLTTSGSTYL ADSVKGRFTI SRDNSKNTVY LQMNSLRAED TAVYYCAADS 100
FEDPTCTLVT SSGAFQYWGQ GTLVTVSSGA PQVQLVESGG GLVQPGGSLR 150
LSCAASGYIY SAYCMGWFRQ APGKGLEGVA AIYIGGGSTY YADSVKGRFT 200
ISRDNSKNTL YLQMNSLRAE DTAVYYCAAD VIPTETCLGG SWSGPFGYWG 250
QGTLVTVSSG SEPKSSDKTH TCPPCPAPEL LGGPSVFLFP PKPKDTLMIS 300
RTPEVTCVVV DVSHEDPEVK FNWYVDGVEV HNAKTKPREE QYNSTYRVVS 350
VLTVLHQDWL NGKEYKCKVS NKALPAPIEK TISKAKGQPR EPQVYTLPPS 400
RDELTKNQVS LTCLVKGFYP SDIAVEWESN GQPENNYKTT PPVLDSDGSF 450
FLYSKLTVDK SRWQQGNVFS CSVMHEALHN HYTQKSLSLS PGK        493
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 153-227 307-367 413-471
22"-96" 153"-227" 307"-367" 413"-471"
Intra-H VH (C38-C111.3) 33-106 164-237
33"-106" 164-237"
Inter-H-H (h 11, h 14) 272-272" 275-275"

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:
343, 343"
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:
493, 493"

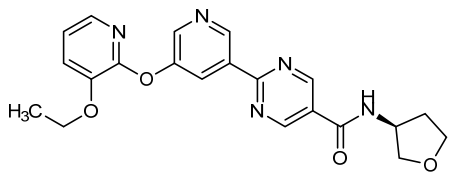
ervogastatum

ervogastat — 2-{5-[(3-ethoxypyridin-2-yl)oxy]pyridin-3-yl}-*N*-[(3*S*)-oxolan-3-yl]pyrimidine-5-carboxamide

ervogastat — 2-{5-[(3-éthoxypyridin-2-yl)oxy]pyridin-3-yl}-*N*-[(3*S*)-oxolan-3-yl]pyrimidine-5-carboxamide

ervogastat — 2-{5-[(3-etoxipiridin-2-il)oxi]piridin-3-yl}-*N*-[(3*S*)-oxolan-3-il]pirimidina-5-carboxamida

$C_{21}H_{21}N_5O_4$



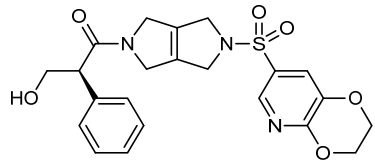
etavopivatum

etavopivat — (2*S*)-1-[5-(2,3-dihydro[1,4]dioxino[2,3-*b*]pyridine-7-sulfonyl)-3,4,5,6-tetrahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl]-3-hydroxy-2-phenylpropan-1-one

étavopivat — (2*S*)-1-[5-(2,3-dihydro[1,4]dioxino[2,3-*b*]pyridine-7-sulfonyl)-3,4,5,6-tétrahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl]-3-hydroxy-2-phénylpropan-1-one

etavopivat — (2*S*)-1-[5-(2,3-dihidro[1,4]dioxino[2,3-*b*]piridina-7-sulfonil)-3,4,5,6-tetrahidropirrolo[3,4-*c*]pirrol-2(1*H*)-il]-2-fenil-3-hidroxipropan-1-ona

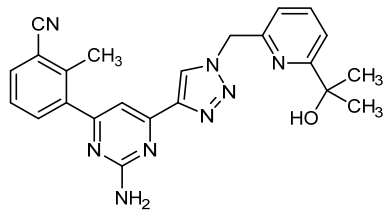
$C_{22}H_{23}N_3O_6S$



etrumadenantum

etrumadenant	3-[2-amino-6-(1-{[6-(2-hydroxypropan-2-yl)pyridin-2-yl]methyl}-1*H*-1,2,3-triazol-4-yl)pyrimidin-4-yl]-2-methylbenzonitrile
étrumadénant	3-[2-amino-6-(1-{[6-(2-hydroxypropan-2-yl)pyridin-2-yl]méthyl}-1*H*-1,2,3-triazol-4-yl)pyrimidin-4-yl]-2-méthylbenzonitrile
etrumadenant	3-[2-amino-6-(1-{[6-(2-hidroxipropan-2-il)piridin-2-il]metil}-1*H*-1,2,3-triazol-4-il)pirimidin-4-il]-2-metilbenzonitrilo

$C_{23}H_{22}N_8O$



exagamglogenum autotemcelum #

exagamglogene autotemcel	Autologous CD34+ cells isolated from mobilised peripheral blood by positive selection, modified by CRISPR/Cas9 (clustered regularly interspaced short palindromic repeats/CRISPR-associated protein 9) mediated gene editing consisting of a guide RNA (gRNA) introduced transiently as ribonucleoprotein (RNP) complex, targeting the erythroid lineage-specific enhancer region of *BCL11A* (B-cell lymphoma/leukemia 11A). The site-specific cleavage by Cas9 forms a double strand break (DSB), which is subsequently repaired by nonhomologous end-joining (NHEJ), leading to the transcriptional repression of *BCL11A*, a repressor of γ-globin gene transcription.
exagamglogène autotemcel	Cellules CD34+ autologues isolées du sang périphérique mobilisé par sélection positive, modifiées par CRISPR/Cas9 (courtes répétitions palindromiques groupées et régulièrement espacées / protéine 9 associée à CRISPR) induisant une édition génétique consistant de deux ARN guides (gRNA) introduisant transitoirement un complexe ribonucléoprotéique,

	ciblant la région activatrice spécifique du lignage des érythroïdes de *BCL11A* (lymphome des cellules B/ leucémie 11A). Le clivage site-spécifique par Cas9 forme une cassure double brin (DSB), qui est ensuite réparée par la jonction d'extrémités non homologues (NHEJ), menant à la répression transcriptionnelle de BCL11A, un répresseur de la transcription du gène γ-globine.
exagamglogén autotemcel	Células CD34+ autólogas aisladas de células movilizadas en sangre periférica mediante selección positiva, modificadas por CRISPR/Cas9 (repeticiones palindrómicas cortas agrupadas y regularmente espaciadas/proteína asociada a CRISPR 9) mediante edición geníca consistente en un RNA guía (gRNA) introducido transitoriamente como un complejo de ribonucleoproteína (RNP), dirigido a la región potenciadora específica de linaje eritroide de BCL11A (linfoma/leucemia de linfocitos B11A). El corte específico de sitio por Cas9 forma una rotura de la doble hélice (DSB) que es subsiguientemente reparada mediante unión de extremos no homóloga (NHEJ), lo que conduce a la represión transcripcional de BCL11A, un represor de la transcripción del gen de la γ-globina.

fesomersenum

fesomersen	*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]hex-yl}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)-*P*-thioadenylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methylcytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)guanylyl-(3'→5')-2'-*O*-(2-methoxyethyl)guanylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methylcytidylyl-(3'→5')-2'-deoxy-*P*-thioadenylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(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-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-deoxy-*P*-thioadenylyl-(3'→5')-2'-deoxy-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)adenylyl-(3'→5')-2'-*O*-(2-methoxyethyl)guanylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyluridine
fésomersen	*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)-*P*-thioadénylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthylcytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)guanylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)guanylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-

5-méthylcytidylyl-(3'→5')-2'-désoxy-*P*-thioadénylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(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-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-désoxy-*P*-thioadénylyl-(3'→5')-2'-désoxy-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)adénylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)guanylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyluridine

fesomersén

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)-*P*-tioadenilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)citidilil-(3'→5')-2'-*O*-(2-metoxietil)guanilil-(3'→5')-2'-*O*-(2-metoxietil)guanilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)citidilil-(3'→5')-2'-desoxi-*P*-tioadenilil-(3'→5')-*P*-tiotimidilil-(3'→5')-*P*-tiotimidilil-(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-5-metil-*P*-tiocitidilil-(3'→5')-2'-desoxi-*P*-tioadenilil-(3'→5')-2'-desoxi-5-metil-*P*-tiocitidilil-(3'→5')-2'-*O*-(2-metoxietil)adenilil-(3'→5')-2'-*O*-(2-metoxietil)guanilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)-*P*-tiouridilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)-*P*-tiouridilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)uridina

$C_{296}H_{434}N_{82}O_{156}P_{20}S_{13}$

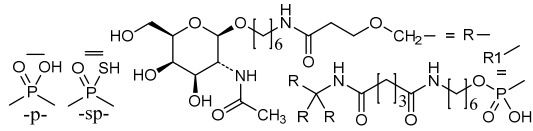
(3'-5') R1-A=C-G-G-C-d(A=T=T=G=G=T=G=C=A=C=)A-G-U=U=U

Legend:

A , G & T : 2'-deoxynucleotide C : 2'-deoxy-5-methylcytidine

A & G : 2'-*O*-(2-methoxyethyl)nucleotide

C & U : 2'-*O*-(2-methoxyethyl)-5-methylnucleotide



finotonlimabum #

finotonlimab

immunoglobulin G4-kappa, anti-[*Homo sapiens* PDCD1 (programmed cell death 1, PD-1, PD1, CD279)], monoclonal antibody;

	gamma4 heavy chain (1-445) [VH (*Mus musculus* IGHV5-9-2*01 (88.8%) -(IGHD) -IGHJ4*01 (90.9%)/*Homo sapiens* IGHV3-23*04 (86.7%) -(IGHD) -IGHJ3*01 (90.9%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118)-*Homo sapiens* IGHG4*01, G4v5 h P10 (CH1 (119-216), hinge 1-12 S10>P (226) (217-228), CH2 (229-338), CH3 (339-443), CHS (444-445)) (119-445)], (132-218')-disulfide with kappa light chain (1'-218') [V-KAPPA (*Homo sapiens* IGKV3D-11*02 (81.9%) -IGKJ1*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 (224-224":227-227")-bisdisulfide, produced in a Chinese hamster ovary (CHO)-DG44 cell line, glycoform alfa
finotonlimab	immunoglobuline G4-kappa, anti-[*Homo sapiens* PDCD1 (protéine 1 de mort cellulaire programmée, PD-1, PD1, CD279)], anticorps monoclonal; chaîne lourde gamma4 (1-445) [VH (*Mus musculus* IGHV5-9-2*01 (88.8%) -(IGHD) -IGHJ4*01 (90.9%)/*Homo sapiens* IGHV3-23*04 (86.7%) -(IGHD) -IGHJ3*01 (90.9%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118)-*Homo sapiens* IGHG4*01, G4v5 h P10 (CH1 (119-216), charnière 1-12 S10>P (226) (217-228), CH2 (229-338), CH3 (339-443), CHS (444-445)) (119-445)], (132-218')-disulfure avec la chaîne légère kappa humanisée(1'-218') [V-KAPPA (*Homo sapiens* IGKV3D-11*02 (81.9%) -IGKJ1*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 (224-224":227-227")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-DG44, glycoforme alfa
finotonlimab	inmunoglobulina G4-kappa, anti-[*Homo sapiens* PDCD1 (proteína 1 de muerte celular programada, PD-1, PD1, CD279)], anticuerpo monoclonal; cadena pesada gamma4 (1-445) [VH (*Mus musculus* IGHV5-9-2*01 (88.8%) -(IGHD) -IGHJ4*01 (90.9%)/*Homo sapiens* IGHV3-23*04 (86.7%) -(IGHD) -IGHJ3*01 (90.9%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118)-*Homo sapiens* IGHG4*01, G4v5 h P10 (CH1 (119-216), bisagra 1-12 S10>P (226) (217-228), CH2 (229-338), CH3 (339-443), CHS (444-445)) (119-445)], (132-218')-disulfuro con la cadena ligera kappa (1'-218') [V-KAPPA humanizado (*Homo sapiens* IGKV3D-11*02 (81.9%) -IGKJ1*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 (224-224":227-227")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-DG44, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVKPGGSLRL SCAASGFTFS SYGMSWVRQA PGKRLEWVAT  50
ISGGGRDTYY SDSVKGRFTI SRDNAKNNLY LQMNSLRAED TAVYYCSRQY 100
GTVWFFNWGQ 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
```

Light chain / Chaîne légère / Cadena ligera

```
EIVLTQSPAT LSLSPGERAT LSCRASESVD SYGNSFMHWY QQKPGQPPRL 50
LIYAASNQGS GVPARFSGSG SGTDFTLTIS SLEPEDFAMY FCQQSKEVPW 100
TFGQGTKVEI 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) 22-96 145-201 259-319 365-423
22"-96" 145"-201" 259"-319" 365"-423"
Intra-L (C23-C104) 23'-92' 138'-198'
23'"-92'" 138'"-198'"
Inter-H-L (CH1 10-CL 126) 132-218' 132"-218'"
Inter-H-H (h 8, h 11) 224-224" 227-227"

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 / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
445, 445"

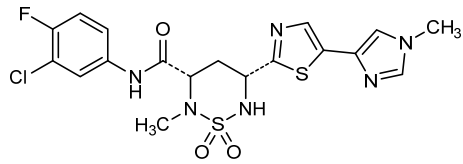
firzacorvirum

firzacorvir — (3*S*,5*R*)-*N*-(3-chloro-4-fluorophenyl)-2-methyl-5-[5-(1-methyl-1*H*-imidazol-4-yl)-1,3-thiazol-2-yl]-1,1-dioxo-1λ^6,2,6-thiadiazinane-3-carboxamide

firzacorvir — (3*S*,5*R*)-*N*-(3-chloro-4-fluorophényl)-2-méthyl-5-[5-(1-méthyl-1*H*-imidazol-4-yl)-1,3-thiazol-2-yl]-1,1-dioxo-1λ^6,2,6-thiadiazinane-3-carboxamide

firzacorvir — (3*S*,5*R*)-*N*-(3-cloro-4-fluorofenil)-2-metil-5-[5-(1-metil-1*H*-imidazol-4-il)-1,3-tiazol-2-il]-1,1-dioxo-1λ^6,2,6-tiadiazinano-3-carboxamida

$C_{18}H_{18}ClFN_6O_3S_2$



foscenvivintum

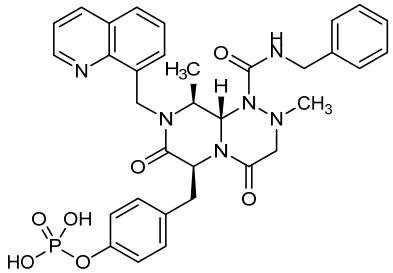
foscenvivint — 4-({(6*S*,9*S*,9a*S*)-1-(benzylcarbamoyl)-2,9-dimethyl-4,7-dioxo-8-[(quinolin-8-yl)methyl]octahydro-2*H*-pyrazino[2,1-*c*][1,2,4]triazin-6-yl}methyl)phenyl dihydrogen phosphate

foscenvivint — dihydrogénophosphate de 4-({(6*S*,9*S*,9a*S*)-1-(benzylcarbamoyl)-2,9-diméthyl-4,7-dioxo-8-[(quinoléin-8-yl)méthyl]octahydro-2*H*-pyrazino[2,1-*c*][1,2,4]triazin-6-yl}méthyl)phényle

foscenvivint

dihidrogenofosfato de 4-({(6*S*,9*S*,9a*S*)-1-(bencilcarbamoil)-2,9-dimetil-4,7-dioxo-8-[(quinolein-8-il)metil]octahidro-2*H*-pirazino[2,1-*c*][1,2,4]triazin-6-il}metil)fenilo

$C_{33}H_{35}N_6O_7P$



govorestatum

govorestat

(4-oxo-3-{[5-(trifluoromethyl)-1,3-benzothiazol-2-yl]methyl}-3,4-dihydrothieno[3,4-*d*]pyridazin-1-yl)acetic acid

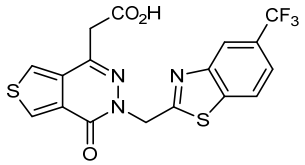
govorestat

acide (4-oxo-3-{[5-(trifluorométhyl)-1,3-benzothiazol-2-yl]méthyl}-3,4-dihydrothiéno[3,4-*d*]pyridazin-1-yl)acétique

govorestat

ácido (4-oxo-3-{[5-(trifluorometil)-1,3-benzotiazol-2-il]metil}-3,4-dihidrotieno[3,4-*d*]piridazin-1-il)acético

$C_{17}H_{10}F_3N_3O_3S_2$



guretolimodum

guretolimod

[({4-[(2-amino-4-{[(3*S*)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]-3-methoxyphenyl}methyl)(2,2,2-trifluoroethyl)amino]acetic acid

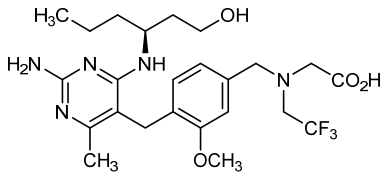
gurétolimod

acide [({4-[(2-amino-4-{[(3*S*)-1-hydroxyhexan-3-yl]amino}-6-méthylpyrimidin-5-yl)méthyl]-3-méthoxyphényl}méthyl)(2,2,2-trifluoroéthyl)amino]acétique

guretolimod

ácido [({4-[(2-amino-4-{[(3*S*)-1-hidroxihexan-3-il]amino}-6-metilpirimidin-5-il)metil]-3-metoxifenil}metil)(2,2,2-trifluoroetil)amino]acético

$C_{24}H_{34}F_3N_5O_4$



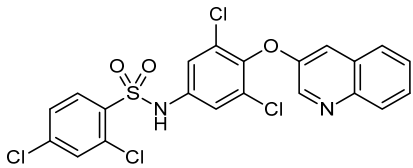
ibrigamparum

ibrigampar — 2,4-dichloro-*N*-{3,5-dichloro-4-[(quinolin-3-yl)oxy]phenyl}benzene-1-sulfonamide

ibrigampar — 2,4-dichloro-*N*-{3,5-dichloro-4-[(quinoléin-3-yl)oxy]phényl}benzène-1-sulfonamide

ibrigampar — 2,4-dicloro-*N*-{3,5-dicloro-4-[(quinolein-3-il)oxi]fenil}benceno-1-sulfonamida

$C_{21}H_{12}Cl_4N_2O_3S$



ilofotasum alfa #

ilofotase alfa — human intestinal-type alkaline phosphatase (IAP) variant (H^{279}>L, L^{328}>V, P^{478}>L), engineered by substituting its crown domain (366-430) with the human placental-type alkaline phosphatase (placental alkaline phosphatase 1, PLAP-1) crown domain (364-428, 366-430 in the current sequence), C-terminal linked glycosylphosphatidylinositol anchor removed, dimer, glycosylated, produced in Chinese hamster ovary (CHO) cells;
human intestinal-type alkaline phosphatase (ALPI, intestinal alkaline phosphatase, IAP) variant [H^{279}>L, L^{328}>V, P^{478}>L] (1-484) with its crown domain (65-peptide 366-430) being replaced by the human placental-type alkaline phosphatase (ALPP, alkaline phosphatase Regan isozyme, placental alkaline phosphatase 1, PLAP-1) crown domain (65-peptide 364-428) (366-430), dimer (481-481')-disulfide, without glycosylphosphatidylinositol (GPI) anchors at Asp-484 and Asp-484' (secretable, soluble enzyme), produced in Chinese hamster ovary (CHO) cells, glycoform alfa

ilofotase alfa — variant (H279>L, L328>V, P478>L) de la phosphatase alcaline humaine de type intestinal (IAP), conçu en substituant son domaine couronne (366-430) avec le domaine couronne (364-428, 366-430 dans la séquence actuelle) de la phosphatase alcaline humaine de type placentaire (phosphatase alcaline placentaire 1, PLAP-1), élimination de l'ancrage glycosylphosphatidylinositol lié à la partie C-terminale, dimère, glycosylé, produit dans des cellules ovariennes de hamster chinois (CHO);

phosphatase alcaline humaine de type intestinal (ALPI, phosphatase alcaline intestinale, IAP) variant [H279>L, L328>V, P478>L] (1-484), dont le domaine couronne (65-peptide 366-430) étant remplacé par le domaine couronne (65-peptide 364-428) de la phosphatase alcaline humaine de type placentaire (ALPP, isoenzyme Regan de la phosphatase alcaline, phosphatase alcaline placentaire 1, PLAP-1) (366-430), dimère (481-481')-disulfure, sans ancrage glycosylphosphatidylinositol (GPI) à Asp-484 et Asp-484' (sécrétable, enzyme soluble), produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

ilofotasa alfa

fosfatasa alcalina de tipo intestinal humana (IAP) variante (H^{279}>L, L^{328}>V, P^{478}>L), diseñada por sustitución de su propio dominio de corona (366-430) con la fosfatasa alcalina de tipo placentaria humana (fosfatasa alcalina placentaria 1, PLAP-1) dominio de corona (364-428, 366-430 en la secuencia actual), C-terminal unido al glicosilfosfatidilinositol anclaje eliminado, dímero, glicosilado, producido en células ováricas de hámster chino (CHO);
fosfatasa alcalina humana del tipo intestinal (ALPI, fosfatasa alcalina intestinal, IAP) variante [H^{279}>L, L^{328}>V, P^{478}>L](1-484) con su dominio corona (65-péptido 366-430) siendo reemplazado por el dominio corona (65-péptido 364-428) de la fosfatasa alcalina humana del tipo placentario (ALPP, isoenzima Regan de fosfatasa alcalina, fosfatasa alcalina placentaria 1, PLAP-1) (366-430), dímero (481-481')-disulfuro, sin anclajes de amidas de glicosilfosfatidilinositol (GPI) en Asp-484 y Asp-484' (soluble y secretable), producido en células ováricas de hámster chino (CHO), glicoforma alfa

Sequence / Séquence / Secuencia

```
VIPAEEENPA FWNRQAAEAL DAAKKLQPIQ KVAKNLILFL GDGLGVPTVT    50
ATRILKGQKN GKLGPETPLA MDRFPYLALS KTYNVDRQVP DSAATATAYL   100
CGVKANFQTI GLSAAARFNQ CNTTRGNEVI SVMNRAKQAG KSVGVVTTTR   150
VQHASPAGTY AHTVNRNWYS DADMPASARQ EGCQDIATQL ISNMDIDVIL   200
GGGRKYMFPM GTPDPEYPAD ASQNGIRLDG KNLVQEWLAK HQGAWYVWNR   250
TELMQASLDQ SVTHLMGLFE PGDTKYEILR DPTLDPSLME MTEAALRLLS   300
RNPRGFYLFV EGGRIDHGHH EGVAYQAVTE AVMFDDAIER AGQLTSEEDT   350
LTLVTADHSH VFSFGGYPLR GSSIFGLAPG KARDRKAYTV LLYGNGPGYV   400
LKDGARPDVT ESESGSPEYR QQSAVPLDEE THGGEDVAVF ARGPQAHLVH   450
GVQEQSFVAH VMAFAACLEP YTACDLALPA CTTD                    484
```

Mutation sites / Sites de mutation / Posiciones de mutación
H279>L, L328>V, P478>L, crown domain replacement *G366-E430*
H279'>L, L328'>V, P478'>L, crown domain replacement *G366'-E430'*

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posición del puentes disulfuro
intra-monomer 121-183 467-474 121'-183' 467'-474' (Cys-SH: 101, 101')
inter-monomer 481-481'
Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación
N122, N249, N122', N249'

iltamiocelum

iltamiocel

Autologous human skeletal muscle progenitor cells derived from muscle biopsy (*vastus lateralis*). The progenitor cells are isolated by enzymatic digestion and expanded in culture in growth media containing human recombinant basic fibroblast growth factor (rbFGF), human recombinant endothelial growth factor (rEGF) and fetal bovine serum (FBS). Cell function and phenotype are maintained through control of culture confluence. The cells are positive for the myogenic cell marker desmin (on average 89%), and other muscle specific genes. The final substance contains also non-myogenic cell populations, such as fibroblasts. The cells have been demonstrated to have myogenic cell differentiation capacity.

iltamiocel	Cellules progénitrices autologues humaines du muscle squelettique dérivées d'une biopsie de muscle (*vastus lateralis*). Les cellules progénitrices ont été isolées par digestion enzymatique et placées en culture d'expansion dans un milieu de croissance contenant le facteur de croissance basique recombinant des fibroblastes humain (rbFGF), le facteur de croissance recombinant de l'endothélium humain (rEGF) et le sérum bovin fœtal (FBS). Le phénotype et la fonction cellulaire ont été maintenus en contrôlant la confluence de la culture. Les cellules sont positives pour le marqueur cellulaire myogénique desmine (en moyenne 89%), et d'autres gènes spécifiques des muscles. La substance finale contient aussi des populations cellulaires non-myogéniques tels que les fibroblastes. Il a été démontré que les cellules ont une capacité de différenciation en cellules myogéniques.
iltamiocel	Células progenitoras de músculo esquelético humano autólogas derivadas de biopsia muscular (*vastus lateralis*). Las células progenitoras se aíslan mediante digestión enzimática y se expanden en cultivo con medio de crecimiento que contiene factor de crecimiento de fibroblastos básico humano recombinante (rbFGF), factor de crecimiento endotelial humano recombinante (rEGF) y suero bovino fetal (FBS). La función y el fenotipo celular se mantienen mediante el control de la confluencia del cultivo. Las células son positivas para el marcador de células miogénicas desmina (89% de media), y otros genes específicos de músculo. La substancia final contiene también poblaciones de células no miogénicas, tales como fibroblastos. Se ha demostrado que las células tienen capacidad de diferenciación de células miogénicas.
imsidolimabum #	
imsidolimab	immunoglobulin G4-kappa, anti-[*Homo sapiens* IL36R (interleukin 36 receptor)], monoclonal antibody; gamma4 heavy chain (1-447) [VH (*Homo sapiens* IGHV1-46*01 (84.7%) -(IGHD) -IGHJ1*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120)-*Homo sapiens* IGHG4*01 (100%), G4v5 h P10 (CH1 (121-218), hinge 1-12 S10>P (228) (219-230), CH2 (231-340), CH3 (341-445), CHS (446-447) (121-447)], (134-219')-disulfide with kappa light chain (1'-219') [V-KAPPA Musmus/Homsap (*Mus musculus* IGKV2-109*01 (85%) -IGKJ1*01 (90.9%)/*Homo sapiens* IGKV2D-29*01 (84%) -IGKJ4*01 (100%)) 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 (226-226'':229-229'')-bisdisulfide, produced in a Chinese hamster ovary (CHO)-S cell line, glycoform alfa
imsidolimab	immunoglobuline G4-kappa, anti-[*Homo sapiens* IL36R (récepteur de l'interleukine 36)], anticorps monoclonal;

chaîne lourde gamma4 (1-447) [VH (*Homo sapiens* IGHV1-46*01 (84.7%) -(IGHD) -IGHJ1*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120)-*Homo sapiens* IGHG4*01 (100%), G4v5 h P10 (CH1 (121-218), charnière 1-12 S10>P (228) (219-230), CH2 (231-340), CH3 (341-445), CHS (446-447) (121-447)], (134-219')-disulfure avec la chaîne légère kappa (1'-219') [V-KAPPA Musmus/Homsap (*Mus musculus* IGKV2-109*01 (85%) -IGKJ1*01 (90.9%)/*Homo sapiens* IGKV2D-29*01 (84%) -IGKJ4*01 (100%)) 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 (226-226'':229-229'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-S, glycoforme alfa

imsidolimab

inmunoglobulina G4-kappa, anti-[*Homo sapiens* IL36R (receptor de la interleukina 36)], anticuerpo monoclonal; cadena pesada gamma4 (1-447) [VH (*Homo sapiens* IGHV1-46*01 (84.7%) -(IGHD) -IGHJ1*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120)-*Homo sapiens* IGHG4*01 (100%), G4v5 h P10 (CH1 (121-218), bisagra 1-12 S10>P (228) (219-230), CH2 (231-340), CH3 (341-445), CHS (446-447) (121-447)], (134-219')-disulfuro con la cadena ligera kappa (1'-219') [V-KAPPA Musmus/Homsap (*Mus musculus* IGKV2-109*01 (85%) -IGKJ1*01 (90.9%)/*Homo sapiens* IGKV2D-29*01 (84%) -IGKJ4*01 (100%)) 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 (226-226'':229-229'')-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-S, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGASVKV SCKASGYTFT NYWMNWVRQA PRQGLEWMGM  50
FHPTGDVTRL NQKFKDRVTM TRDTSTSTVY MELSSLRSED TAVYYCARTT 100
SMIIGGFAYW GQGTLVTVSS ASTKGPSVFP LAPCSRSTSE STAALGCLVK 150
DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGTKT 200
YTCNVDHKPS NTKVDKRVES KYGPPCPPCP APEFLGGPSV FLFPPKPKDT 250
LMISRTPEVT CVVVDVSQED PEVQFNWYVD GVEVHNAKTK PREEQFNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKGLPS SIEKTISKAK GQPREPQVYT 350
LPPSQEEMTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTPPVLDS 400
DGSFFLYSRL TVDKSRWQEG NVFSCSVMHE ALHNHYTQKS LSLSLGK    447
```

Light chain / Chaîne légère / Cadena ligera

```
DIVMTQTPLS LSVTPGQPAS ISCRSSKSLL HRNAITYFYW YLHKPGQPPQ  50
LLIYQMSNLA SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCAQNLELP 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) 22-96 147-203 261-321 367-425
22"-96" 147"-203 261"-321" 367"-425"
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 8, h 11) 226-226" 229-229"

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:
297, 297"
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, 447"

inetagugenum geperpavecum #

inetagugene geperpavec	A replication-defective Herpes simplex virus encoding human transglutaminase 1 (TGM1). A recombinant replication-deficient, non-integrating Herpes simplex virus type 1 (HSV-1) (strain KOS) vector encoding two copies of codon-optimised human transglutaminase 1 [TGM1, (EC:2.3.2.13)], also known as protein-glutamine gamma-glutamyltransferase K (TGK) with both copies being expressed under the control of a human cytomegalovirus (hCMV) immediate early promoter and bovine growth hormone polyadenylation signal (bGH polyA). The vector was generated by deleting both copies of the viral immediate early (IE) gene ICP4 and inserting a copy of the TGM1 gene into each ICP4 locus. The vector is also deleted for the IE gene ICP22.
inétagugène géperpavec	Un virus Herpès simplex incompétent à la réplication codant la transglutaminase 1 humaine (TGM1). Un vecteur recombinant du virus Herpès simplex de type 1 (HSV-1) (lignée KOS) incompétent à la réplication, non intégrant, codant deux copies de la transglutaminase 1 humaine [TGM1, (EC:2.3.2.13)] aux codons optimisés aussi connue comme la gamma-glutamyltransférase protéine-glutamine K (TGK) avec deux copies étant exprimées sous le contrôle du promoteur précoce immédiat du cytomégalovirus humain (CMV) et du signal de polyadénylation de l'hormone de croissance bovine (bGH polyA). Le vecteur a été généré en supprimant les deux copies du ICP4, gène viral précoce immédiat (IE) et en insérant une copie du gène TGM1 dans chaque locus ICP4. Le vecteur a aussi été supprimé du ICP22, gène IE.
inetagugén geperpavec	Un virus Herpes simplex deficiente en replicación que codifica para la transglutaminasa humana 1 (TGM1). Un vector del virus Herpes simplex tipo 1 (HSV-1) (cepa KOS) recombinante, deficiente en replicación, no integrativo, que codifica dos copias de la transglutaminasa humana 1[TGM1, (EC:2.3.2.13)] , también conocida como proteína-glutamina gamma-glutamiltransferasa K (TGK), con codones optimizados, y ambas copias siendo expresadas bajo el control del promotor inmediato temprano del citomegalovirus humano (hCMV) y la señal de poliaadenilación de la hormona del crecimiento bovina (bGH polyA).El vector se generó mediante la deleción de ambas copias del gen inmediato temprano (IE) viral ICP4 y la inserción de una copia del gen TGM1 en cada locus ICP4. El vector tiene también delecionado el gen IE ICP22.

isaralgagenum civaparvovecum #

isaralgagene civaparvovec	A non-replicating adeno-associated viral vector encoding codon-optimised human alpha-galactosidase A (GLA). A recombinant, non-replicating adeno-associated viral vector serotype 6 (AAV6) encoding codon-optimised human alpha-galactosidase A (GLA) under control of liver-specific regulatory elements [comprising enhancer and hepatic control region from the human apolipoprotein E (ApoE) gene, the human α-1-antitrypsin (hAAT) promoter, a chimeric human β-globin/IgG (HBB-IGG) intron, as well as a WPREmut6 region] and a bovine growth hormone (bGH) poly A sequence, flanked by adeno-associated virus 2 (AAV2) inverted terminal repeats.

isaralgagène civaparvovec

Un vecteur viral adéno-associé non-répliquant codant la galactosidase alpha A humaine (GLA) aux codons optimisés.
Un vecteur viral adéno-associé non-répliquant, recombinant, de sérotype 6 (AAV6) codant la galactosidase alpha A humaine (GLA) aux codons optimisés sous le contrôle d'éléments régulateurs spécifiques du foie [comprenant un activateur et une région de contrôle hépatique provenant du gène de l'apolipoprotéine E humaine (ApoE), le promoteur de l'alpha-1-antitrypsine humaine (hAAT), un intron chimérique de la β-globine/IgG humaine (HBB-IGG), ainsi qu'une région WPREmut6] et d'une séquence polyA de l'hormone de croissance bovine (bGH), flanquée de répétitions terminales inversées du virus adéno-associé 2 (AAV2).

isaralgagén civaparvovec

Un vector viral adeno-asociado, deficiente en replicación, que codifica para la alfa galactosidasa A (GLA) humana, con codones optimizados.
Un vector viral adeno-asociado de serotipo 6 (AAV6) recombinante, no replicativo, que codifica para la alfa galactosidasa A (GLA) humana, con codones optimizados, bajo el control de elementos reguladores específicos de hígado [comprende el potenciador y la región de control hepático del gen de la apolipoproteína (ApoE) humana, el promotor de la α-1-antitripsina humana (hAAT), un intrón quimérico de β-globina humana/IgG (HBB-IGG), así como una región WPREmut6] y una secuencia polyA de la hormona decrecimiento bovina (bGH), flanqueado por la repeticiones terminales invertidas del virus adeno-asociado 2 (AAV2).

isuzinaxibum

isuzinaxib

3-phenyl-4-propyl-1-(pyridin-2-yl)-1*H*-pyrazol-5-ol

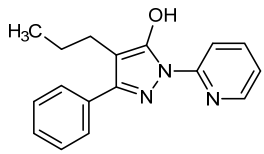
isuzinaxib

3-phényl-4-propyl-1-(pyridin-2-yl)-1*H*-pyrazol-5-ol

isuzinaxib

3-fenil-4-propil-1-(piridin-2-il)-1*H*-pirazol-5-ol

$C_{17}H_{17}N_3O$



labuvirtidum

labuvirtide

$N^{\alpha.1}$-acetyl-$N^{6.13}$-[(2-{2-[3-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)propan-amido]ethoxy}ethoxy)acetyl]-[M^{118}>E^{2}, S^{129}>K^{13}, S^{133}>E^{17}]-(117-150)-peptide (1-34)-34-amide (non-glycosylated) of the transmembrane glycoprotein 41 (gp41) of the human immunodeficiency virus type 1 (HIV-1):

N-acetyl-L-tryptophyl-L-α-glutamyl-L-α-glutamyl-L-tryptophyl-L-α-aspartyl-L-arginyl-L-α-glutamyl-L-isoleucyl-L-asparaginyl-L-asparaginyl-L-tyrosyl-L-threonyl-N^6-[(2-{2-[3-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)propanamido]-ethoxy}ethoxy)acetyl]-L-lysyl-L-leucyl-L-isoleucyl-L-histidyl-L-α-glutamyl-L-leucyl-L-isoleucyl-L-α-glutamyl-L-α-glutamyl-L-seryl-L-glutaminyl-L-asparaginyl-L-glutaminyl-L-glutaminyl-L-α-glutamyl-L-lysyl-L-asparaginyl-L-α-glutamyl-L-glutaminyl-L-α-glutamyl-L-leucyl-L-leucinamide

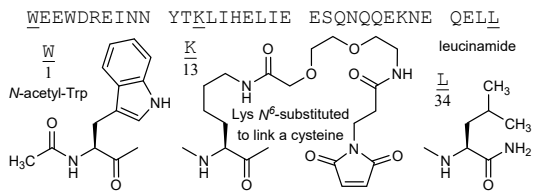
labuvirtide

$N^{\alpha.1}$-acétyl-$N^{6.13}$-[(2-{2-[3-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)propan-amido]éthoxy}éthoxy)acétyl]-[M^{118}>E^2, S^{129}>K^{13}, S^{133}>E^{17}]-peptide 117-150 (1-34)-34-amide (non glycosylé) de la glycoprotéine transmembra-naire 41 (gp41) du virus de l'immunodéficience humaine de type 1 (VIH-1, HIV-1):
N-acétyl-L-tryptophyl-L-α-glutamyl-L-α-glutamyl-L-tryptophyl-L-α-aspartyl-L-arginyl-L-α-glutamyl-L-isoleucyl-L-asparaginyl-L-asparaginyl-L-tyrosyl-L-thréonyl-N^6-[(2-{2-[3-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)propanamido]-éthoxy}éthoxy)acétyl]-L-lysyl-L-leucyl-L-isoleucyl-L-histidyl-L-α-glutamyl-L-leucyl-L-isoleucyl-L-α-glutamyl-L-α-glutamyl-L-séryl-L-glutaminyl-L-asparaginyl-L-glutaminyl-L-glutaminyl-L-α-glutamyl-L-lysyl-L-asparaginyl-L-α-glutamyl-L-glutaminyl-L-α-glutamyl-L-leucyl-L-leucinamide

labuvirtida

$N^{\alpha.1}$-acetil-$N^{6.13}$-[(2-{2-[3-(2,5-dioxo-2,5-dihidro-1*H*-pirrol-1-il)propan-amido]etoxi}etoxi)acetil]-[M^{118}>E^2, S^{129}>K^{13}, S^{133}>E^{17}]-péptido 117-150 (1-34)-34-amida (no glicosilado) de la glicoproteína transmembranaria 41 (gp41) del virus de inmunodeficiencia humana del tipo 1 (VIH-1, HIV-1):
N-acetil-L-triptofil-L-α-glutamil-L-α-glutamil-L-triptofil-L-α-aspartil-L-arginil-L-α-glutamil-L-isoleucil-L-asparaginil-L-asparaginil-L-tirosil-L-treonil-N^6-[(2-{2-[3-(2,5-dioxo-2,5-dihidro-1*H*-pirrol-1-il)propanamido]etoxi}etoxi)acetil]-L-lisil-L-leucil-L-isoleucil-L-histidil-L-α-glutamil-L-leucil-L-isoleucil-L-α-glutamil-L-α-glutamil-L-seril-L-glutaminil-L-asparaginil-L-glutaminil-L-glutaminil-L-α-glutamil-L-lisil-L-asparaginil-L-α-glutamil-L-glutaminil-L-α-glutamil-L-leucil-L-leucinamida

$C_{204}H_{306}N_{54}O_{72}$



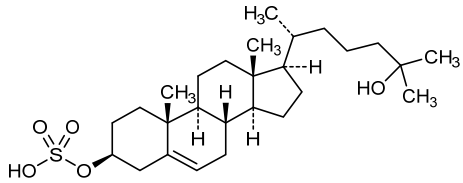
larsucosterolum

larsucosterol — 25-hydroxycholest-5-en-3β-yl hydrogen sulfate

larsucostérol — hydrogénosulfate de 25-hydroxycholest-5-én-3β-yle

larsucosterol — hidrogenosulfato de 25-hidroxicolest-5-en-3β-ilo

$C_{27}H_{46}O_5S$



latozinemabum #

latozinemab — immunoglobulin G1-kappa, anti-[*Homo sapiens* SORT1 (sortilin 1, Gp95, NT3)], *Homo sapiens* monoclonal antibody;
gamma1 heavy chain *Homo sapiens* (1-452) [VH (*Homo sapiens* IGHV4-38-2*01 (99.0%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [9.7.15] (26-34.52-58.97-111) (1-122) -*Homo sapiens* IGHG1*01 G1m17,1, G1v40 CH2 A1.3, A1.2, S116 (CH1 K120 (219) (123-220), hinge 1-15 (221-235), CH2 L1.3>A (239), L1.2>A (240), P116>S (336) (236-345), CH3 D12 (361), L14 (363) (346-450), CHS (451-452)) (123-452)], (225-219')-disulfide with kappa light chain *Homo sapiens* (1'-219') [V-KAPPA (*Homo sapiens* IGKV2-28*01 (93.0%) -IGKJ4*01 (100%)) 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 (231-231":234-234")-bisdisulfide, produced in Chinese hamster ovary (CHO)-K1SV cell line lacking the glutamine synthetase gene (GSKO), glycoform alfa

latozinémab — immunoglobuline G1-kappa, anti-[*Homo sapiens* SORT1 (sortiline 1, Gp95, NT3)], anticorps monoclonal *Homo sapiens*;
chaîne lourde gamma1 *Homo sapiens* (1-452) [VH (*Homo sapiens* IGHV4-38-2*01 (99.0%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [9.7.15] (26-34.52-58.97-111) (1-122) -*Homo sapiens* IGHG1*01 G1m17,1, G1v40 CH2 A1.3, A1.2, S116 (CH1 K120 (219) (123-220), charnière 1-15 (221-235), CH2 L1.3>A (239), L1.2>A (240), P116>S (336) (236-345), CH3 D12 (361), L14 (363) (346-450), CHS (451-452)) (123-452)], (225-219')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-219') [V-KAPPA (*Homo sapiens* IGKV2-28*01 (93.0%) -IGKJ4*01 (100%)) 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 (231-231":234-234")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-K1SV ne présentant pas le gène de la glutamine synthétase (GSKO), glycoforme alfa

latozinemab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* SORT1 (sortilina 1, Gp95, NT3)], anticuerpo monoclonal *Homo sapiens*;
cadena pesada gamma1 *Homo sapiens* (1-452) [VH (*Homo sapiens* IGHV4-38-2*01 (99.0%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [9.7.15] (26-34.52-58.97-111) (1-122) -*Homo sapiens* IGHG1*01 G1m17,1, G1v40 CH2 A1.3, A1.2, S116 (CH1 K120 (219) (123-220), bisagra 1-15 (221-235), CH2 L1.3>A (239), L1.2>A (240), P116>S (336) (236-345), CH3 D12 (361), L14 (363) (346-450), CHS (451-452)) (123-452)], (225-219')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-219') [V-KAPPA (*Homo sapiens* IGKV2-28*01 (93.0%) -IGKJ4*01 (100%)) 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 (231-231":234-234")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-K1SV en ausencia del gen glutamina sintetasa (GSKO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLQESGPG LVKPSETLSL TCAVSGYSIS SGYYWGWIRQ PPGKGLEWIG  50
TIYHSGSTYY NPSLKSRVTI SVDTSKNQFS LKLSSVTAAD TAVYYCARQG 100
SIKQGYYGMD VWGQGTTVTV SSASTKGPSV FPLAPSSKST SGGTAALGCL 150
VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ SSGLYSLSSV VTVPSSSLGT 200
QTYICNVNHK PSNTKVDKKV EPKSCDKTHT CPPCPAPEAA GGPSVFLFPP 250
KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NWYVDGVEVH NAKTKPREEQ 300
YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPASIEKT ISKAKGQPRE 350
PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP 400
PVLDSDGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP 450
GK                                                      452
```

Light chain / Chaîne légère / Cadena ligera

```
DIVMTQSPLS LPVTPGEPAS ISCRSSQSLL RSTGYNYLDW YLQKPGQSPQ  50
LLIYLGSNRA SGVPDRFSGS GSGTDFTLKI SRAEAEDVGV YYCMQQQEAP 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) 22-96 149-205 266-326 372-430
22"-96" 149"-205" 266"-326" 372"-430"
Intra-L (C23-C104) 23'-93' 139'-199'
23'"-93'" 139'"-199'"
Inter-H-L (h 5-CL 126) 225-219' 225"-219'"
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:
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 / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
452, 452"

ledelabricinum alfa #
ledelabricin alfa

human proteoglycan 4 (PRG4, lubricin, cartilage superficial zone proteoglycan, SZP, megakaryocyte-stimulating factor) isoform A, (S^{722}>C)-variant, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

lédélabricine alfa

protéoglycane 4 humain (PRG4, lubricine, protéoglycane de la zone superficielle du cartilage, SZP, facteur de stimulation des mégakaryocytes) isoforme A, (S^{722}>C)-variant, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

ledelabricina alfa

proteoglicano 4 humano (PRG4, lubricina, proteoglicano de la zona superficial del cartílago, SZP, factor de estimulación de los megacariocitos) isoforma A, (S^{722}>C)-variante, producido en las células ováricas de hamster chino (CHO), glicoforma alfa

Sequence / Séquence / Secuencia:

```
QDLSSCAGRC GEGYSRDATC NCDYNCQHYM ECCPDFKRVC TAELSCKGRC   50
FESFERGREC DCDAQCKKYD KCCPDYESFC AEVHNPTSPP SSKKAPPPSG  100
ASQTIKSTTK RSPKPPNKKK TKKVIESEEI TEEHSVSENQ ESSSSSSSS   150
SSSTIRKIKS SKNSAANREL QKKLKVKDNK KNRTKKKPTP KPPVVDEAGS  200
GLDNGDFKVT TPDTSTTQHN KVSTSPKITT AKPINPRPSL PPNSDTSKET  250
SLTVNKETTV ETKETTTTNK QTSTDGKEKT TSAKETQSIE KTSAKDLAPT  300
SKVLAKPTPK AETTTKGPAL TTPKEPTPTT PKEPASTTPK EPTPTTIKSA  350
PTTPKEPAPT TTKSAPTTPK EPAPTTTKEP APTTPKEPAP TTTKEPAPTT  400
TKSAPTTPKE PAPTTPKKPA PTTPKEPAPT TPKEPTPTTP KEPAPTTKEP  450
APTTPKEPAP TAPKKPAPTT PKEPAPTTPK EPAPTTTKEP SPTTPKEPAP  500
TTTKSAPTTT KEPAPTTTKS APTTPKEPSP TTTKEPAPTT PKEPAPTTPK  550
KPAPTTPKEP APTTPKEPAP TTTKKPAPTT PKEPAPTTPK ETAPTTPKKL  600
TPTTPEKLAP TTPEKPAPTT PEELAPTTPE EPTPTTPEEP APTTPKAAAP  650
NTPKEPAPTT PKEPAPTTPK EPAPTTPKET APTTPKGTAP TTLKEPAPTT  700
PKKPAPKELA PTTTKEPTST TCDKPAPTTP KGTAPTTPKE PAPTTPKEPA  750
PTTPKGTAPT TLKEPAPTTP KKPAPKELAP TTTKGPTSTT SDKPAPTTPK  800
ETAPTTPKEP APTTPKKPAP TTPETPPPTT SEVSTPTTTK EPTTIHKSPD  850
ESTPELSAEP TPKALENSPK EPGVPTTKTP AATKPEMTTT AKDKTTERDL  900
RTTPETTTAA PKMTKETATT TEKTTESKIT ATTTQVTSTT TQDTTPFKIT  950
TLKTTTLAPK VTTTKKTITT TEIMNKPEET AKPKDRATNS KATTPKPQKP 1000
TKAPKKPTST KKPKTMPRVR KPKTTPTPRK MTSTMPELNP TSRIAEAMLQ 1050
TTTRPNQTPN SKLVEVNPKS EDAGGAEGET PHMLLRPHVF MPEVTPDMDY 1100
LPRVPNQGII INPMLSDETN ICNGKPVDGL TTLRNGTLVA FRGHYFWMLS 1150
PFSPPSPARR ITEVWGIPSP IDTVFTRCNC EGKTFFFKDS QYWRFTNDIK 1200
DAGYPKPIFK GFGGLTGQIV AALSTAKYKN WPESVYFFKR GGSIQQYIYK 1250
QEPVQKCPGR RPALNYPVYG ETTQVRRRRF ERAIGPSQTH TIRIQYSPAR 1300
LAYQDKGVLH NEVKVSILWR GLPNVVTSAI SLPNIRKPDG YDYYAFSKDQ 1350
YYNIDVPSRT ARAITTRSGQ TLSKVWYNCP                        1380
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
6, 10, 20, 22, 26, 32, 33, 40, 46, 50, 60, 62, 66, 72, 73, 80, 1122, 1379
(linked pairs variable or undetermined)
Cys-SH: 722, 1257; unknown status: 1178, 1180

Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación
N182, N1056, N1120, N1135
Fucosylated complex bi-antennary CHO-type glycans / Glycanes de type CHO bi-antennaires complexes fucosylés / Glicanos de tipo CHO biantenarios complejos fucosilados

Potential O-glycosylation sites
26 Ser, 174 Thr:
Sialylated and/or sulfated core 1 (Galβ1-3GalNAcβ1) CHO type O-glycans
Ser: 99, 102, 107, 112, 223, 225, 273, 282, 288, 293, 301, 336, 349, 364, 403, 491, 505, 529, 788, 848, 852, 857, 868, 938, 990, 1009;
Thr: 104, 108, 109, 216, 224, 229, 253, 258, 259, 265, 266, 267, 268, 272, 274, 280, 281, 286, 292, 300, 308, 321, 322, 327, 329, 330, 337, 338, 343, 345, 346, 352, 353, 360, 361, 362, 367, 368, 375, 376, 377, 383, 384, 391, 392, 393, 399, 400, 401, 406, 407, 414, 415, 422, 423, 430, 431, 436, 438, 439, 446, 447, 453, 454, 461, 469, 470, 477, 478, 485, 486, 487, 493, 494, 501, 502, 503, 508, 509, 510, 516, 517, 518, 523, 524, 531, 532, 533, 539, 540, 547, 548, 555, 556, 563, 564, 571, 572, 573, 579, 580, 587, 588, 592, 595, 603, 652, 659, 660, 667, 668, 675, 676, 680, 683, 688, 691, 692, 699, 700, 712, 733, 736, 737, 744, 745, 752, 753, 757, 760, 761, 768, 769, 781, 787, 789, 805, 813, 814, 843, 844, 853, 861, 876, 906, 907, 917, 919, 920, 921, 930, 932, 933, 934, 937, 939, 940, 941, 944, 951, 954, 955, 956, 962, 963, 964, 988, 1008, 1010, 1015, 1024, 1025, 1027, 1137

Gln1>Glp (pyroglutamyl, 5-oxoprolyl)

lemzoparlimabum #

lemzoparlimab	immunoglobulin G4-kappa, anti-[*Homo sapiens* CD47 (integrin associated protein, IAP, MER6, OA3)], monoclonal antibody; gamma4 heavy chain (1-445) [VH (*Homo sapiens* IGHV3-15*07 (93.9%) -(IGHD) -IGHJ3*02 (100%)) CDR-IMGT [8.10.9] (26-33.51-60.99-107) (1-118)-*Homo sapiens* IGHG4*01 (100%), G4v5 h P10 (CH1 (119-216), hinge 1-12 S10>P (226) (217-228), CH2 (229-338), CH3 (339-443), CHS (444-445)) (119-445)], (132-220')-disulfide with kappa light chain (1'-220') [V-KAPPA (*Homo sapiens* IGKV4-1*01 (89.1%) -IGKJ2*01 (90%) Q120>G (106)) 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 (224-224'':227-227'')-bisdisulfide, produced in a Chinese hamster ovary (CHO)-K1 cell line, glycoform alfa
lemzoparlimab	immunoglobuline G4-kappa, anti-[*Homo sapiens* CD47 (protéine associée à l'intégrine, IAP, MER6, OA3)], anticorps monoclonal; chaîne lourde gamma4 (1-445) [VH (*Homo sapiens* IGHV3-15*07 (93.9%) -(IGHD) -IGHJ3*02 (100%)) CDR-IMGT [8.10.9] (26-33.51-60.99-107) (1-118)-*Homo sapiens* IGHG4*01 (100%), G4v5 h P10 (CH1 (119-216), charnière 1-12 S10>P (226) (217-228), CH2 (229-338), CH3 (339-443), CHS (444-445)) (119-445)], (132-220')-disulfure avec la chaîne légère kappa (1'-220') [V-KAPPA (*Homo sapiens* IGKV4-1*01 (89.1%) -IGKJ2*01 (90%) Q120>G (106)) 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 (224-224'':227-227'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-K1, glycoforme alfa
lemzoparlimab	inmunoglobulina G4-kappa, anti-[*Homo sapiens* CD47 (proteína asociada a la integrina, IAP, MER6, OA3)], anticuerpo monoclonal; cadena pesada gamma4 (1-445) [VH (*Homo sapiens* IGHV3-15*07 (93.9%) -(IGHD) -IGHJ3*02 (100%)) CDR-IMGT [8.10.9] (26-33.51-60.99-107) (1-118)-*Homo sapiens* IGHG4*01 (100%), G4v5 h P10 (CH1 (119-216), bisagra 1-12 S10>P (226) (217-228), CH2 (229-338), CH3 (339-443), CHS (444-445)) (119-445)], (132-220')-disulfuro con la cadena ligera kappa (1'-220') [V-KAPPA (*Homo sapiens* IGKV4-1*01 (89.1%) -IGKJ2*01 (90%) Q120>G (106)) 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 (224-224'':227-227'')-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-K1, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVKPGGSLRL SCAASGLTFE RAWMNWVRQA PGKGLEWVGR  50
IKRKTDGETT DYAAPVKGRF SISRDDSKNT LYLQMNSLKT EDTAVYYCAG 100
SNRAFDIWGQ GTMVTVSSAS 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
```

Light chain / Chaîne légère / Cadena ligera

```
DIVMTQSPDS LAVSLGERAT INCKSSQSVL YAGNNRNYLA WYQQKPGQPP  50
KLLINQASTR ASGVPDRFSG SGSGTEFTLI ISSLQAEDVA IYYCQQYYTP 100
PLAFGGGTKL 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)	22-98	145-201	259-319	365-423
	22"-98"	145"-201"	259"-319"	365"-423"
Intra-L (C23-C104)	23'-94'	140'-200'		
	23'"-94'"	140'"-200'"		
Inter-H-L (CH1 10-CL 126)	132-220'	132"-220'"		
Inter-H-H (h 8, h 11)	224-224"	227-227"		

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 / Coupure de la lysine C-terminale / Recorte de lisina C-terminal

H CHS K2:
445, 445"

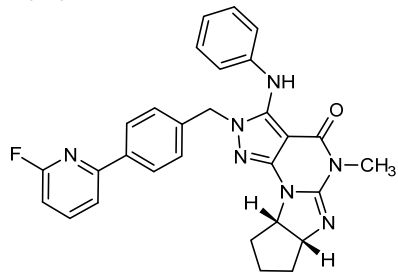
lenrispodunum

lenrispodun — (6a*R*,9a*S*)-3-anilino-2-{[4-(6-fluoropyridin-2-yl)phenyl]methyl}-5-methyl-5,6a,7,8,9,9a-hexahydrocyclopenta[4,5]imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(2*H*)-one

lenrispodun — (6a*R*,9a*S*)-3-anilino-2-{[4-(6-fluoropyridin-2-yl)phényl]méthyl}-5-méthyl-5,6a,7,8,9,9a-hexahydrocyclopenta[4,5]imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(2*H*)-one

lenrispodun — (6a*R*,9a*S*)-3-anilino-2-{[4-(6-fluoropiridin-2-yl)fenil]metil}-5-metil-5,6a,7,8,9,9a-hexahidrociclopenta[4,5]imidazo[1,2-*a*]pirazolo[4,3-*e*]pirimidin-4(2*H*)-ona

$C_{29}H_{26}FN_7O$



libvatrepum

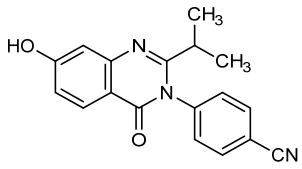
libvatrep — 4-[7-hydroxy-4-oxo-2-(propan-2-yl)quinazolin-3(4*H*)-yl]benzonitrile

libvatrep — 4-[7-hydroxy-4-oxo-2-(propan-2-yl)quinazolin-3(4*H*)-yl]benzonitrile

libvatrep

4-[7-hidroxi-4-oxo-2-(propan-2-il)quinazolin-3(4*H*)-il]benzonitrilo

$C_{18}H_{15}N_3O_2$



licaminlimabum #

licaminlimab

immunoglobulin scFv, anti-[*Homo sapiens* TNF (tumor necrosis factor, TNFSF2, DIF, TNF-alpha)], humanized monoclonal antibody single chain;
IG scFv humanized single chain (V-KAPPA-VH) (1-254) [V-KAPPA (*Homo sapiens* IGKV1-5*03 (79.2%) -(IGHD) - IGKJ2*02 (77.8%)) CDR-IMGT [8.3.11] (28-35.53-55.92-102) (1-112)] -21-mer glycyl-tetrakis(tetraglycyl-seryl) linker (113-133) -[VH (*Homo sapiens* IGHV3-66*01 (76%) - IGHJ6*01 (92.3%)) CDR-IMGT [8.8.14] (159-166.184-191.230-243) (134-254)], produced in the bacteria *Escherichia coli* (*E. coli*), non-glycosylated

licaminlimab

immunoglobuline scFv, anti-[*Homo sapiens* TNF (facteur de nécrose tumorale, TNFSF2, DIF, TNF-alpha)], anticorps monoclonal humanisé à chaîne unique;
IG scFv chaîne unique humanisée (V-KAPPA-VH) (1-254) [V-KAPPA (*Homo sapiens* IGKV1-5*03 (79.2%) -(IGHD) - IGKJ2*02 (77.8%)) CDR-IMGT [8.3.11] (28-35.53-55.92-102) (1-112)] -21-mer glycyl-tétrakis(tétraglycyl-séryl) linker (113-133) -[VH (*Homo sapiens* IGHV3-66*01 (76%) - IGHJ6*01 (92.3%)) CDR-IMGT [8.8.14] (159-166.184-191.230-243) (134-254)], produit dans la bactérie *Escherichia coli* (*E. coli*), non-glycosylé

licaminlimab

inmunoglobulina scFv, anti-[*Homo sapiens* TNF (factor de necrosis tumoral, TNFSF2, DIF, TNF-alfa)], anticuerpo monoclonal humanizado con cadena única;
IG scFv cadena única humanizada (V-KAPPA-VH) (1-254) [V-KAPPA (*Homo sapiens* IGKV1-5*03 (79.2%) -(IGHD) - IGKJ2*02 (77.8%)) CDR-IMGT [8.3.11] (28-35.53-55.92-102) (1-112)] -21-mer glicil-tetrakis(tetraglicil-seril) linker (113-133) -[VH (*Homo sapiens* IGHV3-66*01 (76%) - IGHJ6*01 (92.3%)) CDR-IMGT [8.8.14] (159-166.184-191.230-243) (134-254)], producido en la bacteria *Escherichia coli* (*E. coli*), no glicosilado

scFv chain / Chaîne scFv / Cadena scFv

```
MEIVMTQSPS TLSASVGDRV IITCQSSQSV YGNIWMAWYQ QKPGRAPKLL  50
IYQASKLASG VPSRFSGSGS GAEFTLTISS LQPDDFATYY CQGNFNTGDR 100
YAFGQGTKLT VLGGGGGSGG GGSGGGGSGG GGSEVQLVES GGGSVQPGGS 150
LRLSCTASGF TISRSYWICW VRQAPGKGLE WVGCIYGDND ITPLYANWAK 200
GRFTISRDTS KNTVYLQMNS LRAEDTATYY CARLGYADYA YDLWGQGTTV 250
TVSS                                                    254
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-scFv (C23-C104) 24-91 155-231 169-184

No N-glycosylation sites / pas de sites de N-glycosylation / ningún posición de N-glicosilación

lirentelimabum #

lirentelimab	immunoglobulin G1-kappa, anti-[*Homo sapiens* SIGLEC8 (sialic acid binding Ig-like lectin 8, SIGLEC-8, SAF2, SIGLEC8L)], humanized monoclonal antibody; gamma1 heavy chain humanized (1-450) [VH (*Homo sapiens* IGHV3-66*01 (79.4%) -(IGHD) -IGHJ5*01 (90.9%)) CDR-IMGT [8.7.14] (26-33.51-57.96-109) (1-120) -*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 (449-450)) (121-450)], (223-213')-disulfide with kappa light chain humanized (1'-213') [V-KAPPA (*Homo sapiens* IGKV3-11*01 (86.3%) -IGKJ3*01 (91.7%)) CDR-IMGT [5.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (152), V101 (190) (108'-213')]; dimer (229-229":232-232")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa
lirentélimab	immunoglobuline G1-kappa, anti-[*Homo sapiens* SIGLEC8 (lectine 8 de type Ig-like liant l'acide sialique, SIGLEC-8, SAF2, SIGLEC8L)], anticorps monoclonal humanisé; chaîne lourde gamma1 humanisée (1-450) [VH (*Homo sapiens* IGHV3-66*01 (79.4%) -(IGHD) -IGHJ5*01 (90.9%)) CDR-IMGT [8.7.14] (26-33.51-57.96-109) (1-120) -*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 (449-450)) (121-450)], (223-213')-disulfure avec la chaîne légère kappa humanisée (1'-213') [V-KAPPA (*Homo sapiens* IGKV3-11*01 (86.3%) -IGKJ3*01 (91.7%)) CDR-IMGT [5.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (152), V101 (190) (108'-213')]; dimère (229-229":232-232")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa
lirentelimab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* SIGLEC8 (lectina 8 de tipo Ig-like de unión al ácido siálico, SIGLEC-8, SAF2, SIGLEC8L)], anticuerpo monoclonal humanizado; cadena pesada gamma1 humanizada (1-450) [VH (*Homo sapiens* IGHV3-66*01 (79.4%) -(IGHD) -IGHJ5*01 (90.9%)) CDR-IMGT [8.7.14] (26-33.51-57.96-109) (1-120) -*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 (449-450)) (121-450)], (223-213')-disulfuro con la cadena ligera kappa humanizada (1'-213') [V-KAPPA (*Homo sapiens* IGKV3-11*01 (86.3%) -IGKJ3*01 (91.7%)) CDR-IMGT [5.3.9] (27-32.50-52.89-97) (1'-107') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (152), V101 (190) (108'-213')]; dímero (229-229":232-232")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGGSLRL SCAASGFSLT IYGAHWVRQA PGKGLEWVGV  50
IWAGGSTNYN SALMSRFTIS KDNSKNTVYL QMNSLRAEDT AVYYCARDGS 100
SPYYYSMEYW GQGTTVTVSS 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 QKSLSLSPGK 450
```

Light chain / Chaîne légère / Cadena ligera

```
EIVLTQSPAT LSLSPGERAT LSCSATSSVS YMHWFQQKPG QAPRLLIYST  50
SNLASGIPAR FSGSGSGTDF TLTISSLEPE DFAVYYCQQR SSYPFTFGPG 100
TKLDIKRTVA 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) 22-95 147-203 264-324 370-428
22"-95" 147"-203" 264"-324" 370"-428"
Intra-L (C23-C104) 23'-87' 133'-193'
23'"-87'" 133'"-193'"
Inter-H-L (h 5-CL 126) 223-213' 223"-213'"
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"
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:
450, 450"

locnartecanum
locnartecan

(4*S*)-4,11-diethyl-4-hydroxy-3,14-dioxo-3,4,12,14-tetrahydro-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinolin-9-yl 4-[2-(5-{3-[2,4-dihydroxy-5-(propan-2-yl)phenyl]-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl}-1*H*-indol-1-yl)ethyl]piperidine-1-carboxylate

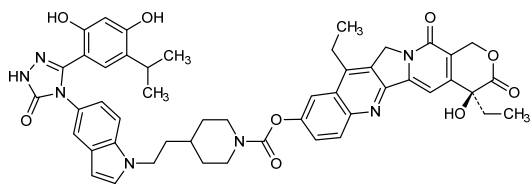
locnartécan

4-[2-(5-{3-[2,4-dihydroxy-5-(propan-2-yl)phényl]-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl}-1*H*-indol-1-yl)éthyl]pipéridine-1-carboxylate de (4*S*)-4,11-diéthyl-4-hydroxy-3,14-dioxo-3,4,12,14-tétrahydro-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinoléin-9-yle

locnartecán

4-[2-(5-{3-[2,4-dihidroxi-5-(propan-2-il)fenil]-5-oxo-1,5-dihidro-4*H*-1,2,4-triazol-4-il}-1*H*-indol-1-il)etil]piperidina-1-carboxilato de (4*S*)-4,11-dietil-4-hidroxi-3,14-dioxo-3,4,12,14-tetrahidro-1*H*-pirano[3',4':6,7]indolizino[1,2-*b*]quinolein-9-ilo

$C_{49}H_{49}N_7O_9$



lonigutamabum #
lonigutamab

immunoglobulin G1-kappa, anti-[*Homo sapiens* IGF1R (insulin like growth factor 1 receptor, IGF1-R, IGF-1R, CD221)], humanized monoclonal antibody;

	gamma1 heavy chain humanized (1-449) [VH humanized (*Homo sapiens* IGHV1-46*01 (92.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*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)], (223-214')-disulfide with kappa light chain humanized (1'-214') [V-KAPPA humanized (*Homo sapiens* IGKV1-39*01 (86.3%) -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)-K1SV cell line lacking the glutamine synthetase gene (GSKO), glycoform alfa
lonigutamab	immunoglobuline G1-kappa, anti-[*Homo sapiens* IGF1R (récepteur du facteur de croissance 1 analogue à l'insuline, IGF1-R, IGF-1R, CD221)], anticorps monoclonal humanisé; chaîne lourde gamma1 humanisée (1-449) [VH humanisé (*Homo sapiens* IGHV1-46*01 (92.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (217) (121-218), charnière 11-15 (219-233), CH2 (234-343), CH3 E12 (359), M14 (361) (344-448), CHS K>del (449)) (121-449)], (223-214')-disulfure avec la chaîne légère kappa humanisée (1'-214') [V-KAPPA humanisé (*Homo sapiens* IGKV1-39*01 (86.3%) -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) lignée cellulaire CHO-K1SV ne présentant pas le gène de la glutamine synthétase (GSKO), glycoforme alfa
lonigutamab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* IGF1R (receptor del factor de crecimiento 1 análogo a la insulina, IGF1-R, IGF-1R, CD221)], anticuerpo monoclonal humanizado; cadena pesada gamma1 humanizada (1-449) [VH humanizado (*Homo sapiens* IGHV1-46*01 (92.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (217) (121-218), bisagra 11-15 (219-233), CH2 (234-343), CH3 E12 (359), M14 (361) (344-448), CHS K>del (449)) (121-449)], (223-214')-disulfuro con la cadena ligera kappa humanizada (1'-214') [V-KAPPA humanizado (*Homo sapiens* IGKV1-39*01 (86.3%) -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) línea celular CHO-K1SV en ausencia del gen glutamina sintetasa (GSKO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGASVKV SCKASGYTFT SYYIHWVRQA PGQGLEWMGW  50
IWPGDGSTKY AQKFQGRVTM TRDTSTSTVY MELSSLRSED TAVYFCASPM 100
ITPNYAMDYW GQGTLVTVSS ASTKGPSVFP LAPSSKSTSG GTAALGCLVK 150
DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT 200
YICNVNHKPS NTKVDKRVEP KSCDKTHTCP PCPAPELLGG PSVFLFPPKP 250
KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ 350
VYTLPPSREE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPG  449
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS LSASVGDRVT ITCRASQDIS KYLNWYQQKP GKAPKLLIYY  50
TSRLQSGVPS RFSGRGSGTD YSLTISSLQP EDFATYFCQQ GSTLPYTFGG 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 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:
300, 300"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

Ionigutamabum ugodotinum #

Ionigutamab ugodotin	immunoglobulin G1-kappa, anti-[*Homo sapiens* IGF1R (insulin like growth factor 1 receptor, IGF1-R, IGF-1R, CD221)], humanized monoclonal antibody conjugated to a dolastatin derivative (ugodotin groups); gamma1 heavy chain humanized (1-449) [VH humanized (*Homo sapiens* IGHV1-46*01 (92.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*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)], (223-214')-disulfide with kappa light chain humanized (1'-214') [V-KAPPA humanized (*Homo sapiens* IGKV1-39*01 (86.3%) -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)-K1SV cell line lacking the glutamine synthetase gene (GSKO), glycoform alfa; conjugated at the cysteines 223, 214', 223" and 214"' with four (3*S*,6*R*,7*R*,8^{2}*S*,11*R*,12*S*,15*S*,18*S*,30^{3}*RS*)-12-[(2*S*)-butan-2-yl]-3-carboxy-7,11-dimethoxy-6,13,19,23-tetramethyl-5,9,14,17,24,30^{2},30^{5}-heptaoxo-15,18-di(propan-2-yl)-4,13,16,19,23-pentaaza-8(2,1),30(1)-dipyrrolidina-1(1),22(1,4)-dibenzenatriacontaphan-30^{3}-yl (ugodotin) groups
Ionigutamab ugodotine	immunoglobuline G1-kappa, anti-[*Homo sapiens* IGF1R (récepteur du facteur de croissance 1 analogue à l'insuline, IGF1-R, IGF-1R, CD221)], anticorps monoclonal humanisé conjugué à un dérivé de dolastatine (groupes ugodotine);

	chaîne lourde gamma1 humanisée (1-449) [VH humanisé (*Homo sapiens* IGHV1-46*01 (92.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*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)], (223-214')-disulfure avec la chaîne légère kappa humanisée (1'-214') [V-KAPPA humanisé (*Homo sapiens* IGKV1-39*01 (86.3%) -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) lignée cellulaire CHO-K1SV ne présentant pas le gène de la glutamine synthétase (GSKO), glycoforme alfa; conjugué aux cystéines 223, 214', 223'' et 214''' avec quatre groupes (3*S*,6*R*,7*R*,8^{2}*S*,11*R*,12*S*,15*S*,18*S*,30^{3}*RS*)-12-[(2*S*)-butan-2-yl]-3-carboxy-7,11-diméthoxy-6,13,19,23-tétraméthyl-5,9,14,17,24,30^{2},30^{5}-heptaoxo-15,18-di(propan-2-yl)-4,13,16,19,23-pentaaza-8(2,1),30(1)-dipyrrolidina-1(1),22(1,4)-dibenzénatriacontaphan-30^{3}-yle (ugodotine)
lonigutamab ugodotina	inmunoglobulina G1-kappa, anti-[*Homo sapiens* IGF1R (receptor del factor de crecimiento 1 análogo a la insulina, IGF1-R, IGF-1R, CD221)], anticuerpo monoclonal humanizado conjugado a un derivado de dolastatina (grupos ugodotina); cadena pesada gamma1 humanizada (1-449) [VH humanizado (*Homo sapiens* IGHV1-46*01 (92.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*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)], (223-214')-disulfuro con la cadena ligera kappa humanizada (1'-214') [V-KAPPA humanizado (*Homo sapiens* IGKV1-39*01 (86.3%) -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) línea celular CHO-K1SV en ausencia del gen glutamina sintetasa (GSKO), forma glicosilada alfa; conjugado a cisteínas 223, 214', 223'' y 214''' con quatro grupos (3*S*,6*R*,7*R*,8^{2}*S*,11*R*,12*S*,15*S*,18*S*,30^{3}*RS*)-12-[(2*S*)-butan-2-il]-3-carboxi-6,13,19,23-tetrametil-7,11-dimetoxi-5,9,14,17,24,30^{2},30^{5}-heptaoxo-15,18-di(propan-2-il)-4,13,16,19,23-pentaaza-8(2,1),30(1)-dipirrolidina-1(1),22(1,4)-dibencenatriacontafan-30^{3}-il (ugodotina)

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGASVKV SCKASGYTFT SYYIHWVRQA PGQGLEWMGW  50
IWPGDGSTKY AQKFQGRVTM TRDTSTSTVY MELSSLRSED TAVYFCASPM 100
ITPNYAMDYW GQGTLVTVSS ASTKGPSVFP LAPSSKSTSG GTAALGCLVK 150
DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT 200
YICNVNHKPS NTKVDKRVEP KSCDKTHTCP PCPAPELLGG PSVFLFPPKP 250
KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ 350
VYTLPPSREE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPG  449
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS LSASVGDRVT ITCRASQDIS KYLNWYQQKP GKAPKLLIYY  50
TSRLQSGVPS RFSGRGSGTD YSLTISSLQP EDFATYFCQQ GSTLPYTFGG 100
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                        214
```

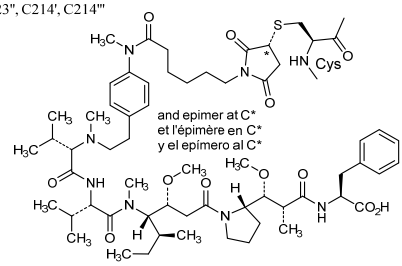
Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 147-203 264-324 370-428
22"-96" 147"-203" 264"-324" 370"-428"
Intra-L (C23-C104) 23'-88' 134'-194'
23'"-88'" 134'"-194'"
Inter-H-L (h 5-CL 126)* 223-214' 223"-214'"
Inter-H-H (h 11, h 14)* 229-229" 232-232"

*At least two of the four inter-chain disulfide bridges are not present, an average of 4 cysteinyl being conjugated each via a thioether bond to a drug linker. *Au moins deux des quatre ponts disulfures inter-chaînes ne sont pas présents, 4 cystéinyl en moyenne étant chacun conjugué via une liaison thioéther à un linker-principe actif. *Al menos dos de los cuatro puentes disulfuro inter-catenarios no estan presentes, una media de 4 cisteinil está conjugada a conectores de principio activo.

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:
300, 300"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

Conjugation sites / Sites de conjugaison / Posiciones de coniugación:
C223, C223", C214', C214'"



lusvertikimabum #
lusvertikimab

immunoglobulin G4-kappa, anti-[*Homo sapiens* IL7R (interleukin 7 receptor, CD127, IL7RA)], humanized monoclonal antibody; gamma4 heavy chain humanized (1-449) [VH (*Homo sapiens* IGHV3-11*01 (90.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122)-*Homo sapiens* IGHG4*01 (100%), G4v5 h P10 (CH1 (123-220), hinge 1-12 S10>P (230) (221-232), CH2 (233-342), CH3 (343-447), CHS (448-449)) (123-449)], (136-214')-disulfide with kappa light chain humanized (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-NL1*01 (86.3%) -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 (228-228":231-231")-bisdisulfide, produced in a Chinese hamster ovary (CHO)-K1 cell line, glycoform alfa

lusvertikimab

immunoglobuline G4-kappa, anti-[*Homo sapiens* IL7R (récepteur de l'interleukine 7, CD127, IL7RA)], anticorps monoclonal humanisé;
chaîne lourde gamma4 humanisée (1-449) [VH (*Homo sapiens* IGHV3-11*01 (90.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122)-*Homo sapiens* IGHG4*01 (100%), G4v5 h P10 (CH1 (123-220), charnière 1-12 S10>P (230) (221-232), CH2 (233-342), CH3 (343-447), CHS (448-449)) (123-449)], (136-214')-disulfure avec la chaîne légère kappa humanisée (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-NL1*01 (86.3%) -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 (228-228'':231-231'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-K1, glycoforme alfa

lusvertikimab

inmunoglobulina G4-kappa, anti-[*Homo sapiens* IL7R (receptor de la interleukina 7, CD127, IL7RA)], anticuerpo monoclonal humanizado;
cadena pesada gamma4 humanizada (1-449) [VH (*Homo sapiens* IGHV3-11*01 (90.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.15] (26-33.51-58.97-111) (1-122)-*Homo sapiens* IGHG4*01 (100%), G4v5 h P10 (CH1 (123-220), bisagra 1-12 S10>P (230) (221-232), CH2 (233-342), CH3 (343-447), CHS (448-449)) (123-449)], (136-214')-disulfuro con la cadena ligera kappa humanizada (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-NL1*01 (86.3%) -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 (228-228'':231-231'')-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-K1, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVESGGG LVKPGGSLRL SCAVSGFTLS DYYMAWIRQA PGKGLEWVST  50
ISASGLRTYY PDSVKGRFTI SRDNAKNSLY LQMNSLRAED TAVYYCARPL 100
SAHYGFNYFD YWGQGTLVTV SSASTKGPSV FPLAPCSRST SESTAALGCL 150
VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ SSGLYSLSSV VTVPSSSLGT 200
KTYTCNVDHK PSNTKVDKRV ESKYGPPCPP CPAPEFLGGP SVFLFPPKPK 250
DTLMISRTPE VTCVVVDVSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV 350
YTLPPSQEEM TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL 400
DSDGSFFLYS RLTVDKSRWQ EGNVFSCSVM HEALHNHYTQ KSLSLSPGK  449
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS LSASVGDRVT ITCRTSEDIY QGLAWYQQKP GKAPKLLLYS  50
ANTLHIGVPS RFSGSGSGTD YTLTISSLQP EDFATYYCQQ YYDYPLAFGG 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	149-205	263-323	369-427
	22"-96"	149"-205"	263"-323"	369"-427"
Intra-L (C23-C104)	23'-88'	134'-194'		
	23'"-88'"	134'"-194'"		
Inter-H-L (CH1 10-CL 126)	136-214'	136"-214'"		
Inter-H-H (h 8, h 11)	228-228"	231-231"		

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:
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"

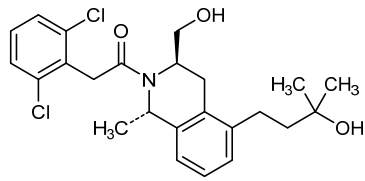
mevidalenum

mevidalen — 2-(2,6-dichlorophenyl)-1-[(1*S*,3*R*)-3-(hydroxymethyl)-5-(3-hydroxy-3-methylbutyl)-1-methyl-3,4-dihydroisoquinolin-2(1*H*)-yl]ethan-1-one

mévidalène — 2-(2,6-dichlorophényl)-1-[(1*S*,3*R*)-3-(hydroxyméthyl)-5-(3-hydroxy-3-méthylbutyl)-1-méthyl-3,4-dihydroisoquinoléin-2(1*H*)-yl]éthan-1-one

mevidaleno — 2-(2,6-diclorofenil)-1-[(1*S*,3*R*)-3-(hidroximetil)-5-(3-hidroxi-3-metilbutil)-1-metil-3,4-dihidroisoquinolein-2(1*H*)-il]etan-1-ona

$C_{24}H_{29}Cl_2NO_3$



mibavademabum #

mibavademab — immunoglobulin G4-kappa, anti-[*Homo sapiens* LEPR (leptin receptor, OBR, CD295)], monoclonal antibody; gamma4 heavy chain (1-446) [VH (*Homo sapiens* IGHV3-30*15 (86.7%) -(IGHD) -IGHJ2*01 (100%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119)-*Homo sapiens* IGHG4*01 (100%), G4v5 h P10 (CH1 (120-217), hinge 1-12 S10>P (227) (218-229), CH2 (230-339), CH3 (340-444), CHS (445-446)) (120-446)], (133-215')-disulfide with kappa light chain (1'-215') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (100%) -IGKJ5*01 (100%)) 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 (225-225'':228-228'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

mibavadémab — immunoglobuline G4-kappa, anti-[*Homo sapiens* LEPR (récepteur de la leptine, OBR, CD295)], anticorps monoclonal;
chaîne lourde gamma4 (1-446) [VH (*Homo sapiens* IGHV3-30*15 (86.7%) -(IGHD) -IGHJ2*01 (100%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119)-*Homo sapiens* IGHG4*01 (100%), G4v5 h P10 (CH1 (120-217), charnière 1-12 S10>P (227) (218-229), CH2 (230-339), CH3 (340-444), CHS (445-446)) (120-446)], (133-215')-disulfure avec la chaîne légère kappa (1'-215') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (100%) -IGKJ5*01 (100%)) 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 (225-225'':228-228'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

mibavademab

inmunoglobulina G4-kappa, anti-[*Homo sapiens* LEPR (receptor de la leptina, OBR, CD295)], anticuerpo monoclonal;
cadena pesada gamma4 (1-446) [VH (*Homo sapiens* IGHV3-30*15 (86.7%) -(IGHD) -IGHJ2*01 (100%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119)-*Homo sapiens* IGHG4*01 (100%), G4v5 h P10 (CH1 (120-217), bisagra 1-12 S10>P (227) (218-229), CH2 (230-339), CH3 (340-444), CHS (445-446)) (120-446)], (133-215')-disulfuro con la cadena ligera kappa (1'-215') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (100%) -IGKJ5*01 (100%)) 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 (225-225'':228-228'')-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVESGGS VVQPGRSLRL SCAASGFTFS TYAMYWVRQT PGKGLEWVAV  50
LYSDGSNKYY IDSVKGRFTI SRDTSTNTLY LQMSSLRADD SALYYCARLN 100
WDYWYFDLWG RGTLVTVSSA 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

```
DIQMTQSPSS LSASVGDRVT ITCRASQSIS SYLNWYQQKP GKAPKLLIYA  50
ASSLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ SYSTPPITFG 100
QGTRLEIKRT 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) 22-96 146-202 260-320 366-424
22"-96" 146"-202" 260"-320" 366"-424"
Intra-L (C23-C104) 23'-88' 135'-195'
23'"-88'" 135'"-195'"
Inter-H-L (CH1 10-CL 126) 133-215' 133"-215'"
Inter-H-H (h 8, h 11) 225-225" 228-228"

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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
446, 446"

mipicoledinum

mipicoledine

cholest-5-en-3β-yl 3,5-dichloro-2-methoxy-6-(trichloromethyl)pyridin-4-yl carbonate

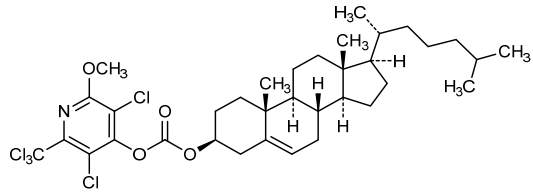
mipicolédine

carbonate de cholest-5-én-3β-yle et de 3,5-dichloro-2-méthoxy-6-(trichlorométhyl)pyridin-4-yle

mipicoledina

carbonato de colest-5-en-3β-ilo y de 3,5-dicloro-2-metoxi-6-(triclorometil)piridin-4-ilo

$C_{35}H_{48}Cl_5NO_4$



nadecnemabum #

nadecnemab	immunoglobulin G4-kappa, anti-[*Homo sapiens* GFRA3 (glial cell derived neurotrophic factor family receptor alpha 3, GFRa-3)], *Homo sapiens* monoclonal antibody; gamma4 heavy chain *Homo sapiens* (1-451) [VH (*Homo sapiens* IGHV3-23*04 (95.9%) -(IGHD) - IGHJ6*01 (94.4%)) CDR-IMGT [8.8.17] (26-33.51-58.97-113) (1-124)-*Homo sapiens* IGHG4*01 (100%), G4v5 h P10 (CH1 (125-222), hinge 1-12 S10>P (232) (223-234), CH2 (235-344), CH3 (345-449), CHS (450-451)) (125-451)], (138-214')-disulfide with kappa light chain *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (98.9%) -IGKJ3*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 (230-230'':233-233'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa
nadecnémab	immunoglobuline G4-kappa, anti-[*Homo sapiens* GFRA3 (récepteur-3 alfa de la famille du facteur neurotrophe dérivé de la glie, GFRa-3)], anticorps monoclonal *Homo sapiens*; chaîne lourde gamma4 *Homo sapiens* (1-451) [VH (*Homo sapiens* IGHV3-23*04 (95.9%) -(IGHD) - IGHJ6*01 (94.4%)) CDR-IMGT [8.8.17] (26-33.51-58.97-113) (1-124)-*Homo sapiens* IGHG4*01 (100%), G4v5 h P10 (CH1 (125-222), charnière 1-12 S10>P (232) (223-234), CH2 (235-344), CH3 (345-449), CHS (450-451)) (125-451)], (138-214')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (98.9%) - IGKJ3*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 (230-230'':233-233'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa
nadecnemab	inmunoglobulina G4-kappa, anti-[*Homo sapiens* GFRA3 (receptor-3 alfa de la familia del factor neurotrófico derivado de la glia, GFRa-3)], anticuerpo monoclonal *Homo sapiens*;

cadena pesada gamma4 *Homo sapiens* (1-451) [VH (*Homo sapiens* IGHV3-23*04 (95.9%) -(IGHD) - IGHJ6*01 (94.4%)) CDR-IMGT [8.8.17] (26-33.51-58.97-113) (1-124)-*Homo sapiens* IGHG4*01 (100%), G4v5 h P10 (CH1 (125-222), bisagra 1-12 S10>P (232) (223-234), CH2 (235-344), CH3 (345-449), CHS (450-451)) (125-451)], (138-214')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (98.9%) - IGKJ3*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 (230-230":233-233")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSV  50
ISGSGGSTYY ADAVKGRFTI SRDNSKHTLY LQMNSLRAED TAVYYCTKPS 100
SYSSSNFYYG MDVWGQGTTV TVSSASTKGP SVFPLAPCSR STSESTAALG 150
CLVKDYFPEP VTVSWNSGAL TSGVHTFPAV LQSSGLYSLS SVVTVPSSSL 200
GTKTYTCNVD HKPSNTKVDK RVESKYGPPC PPCPAPEEFLG GPSVFLFPPK 250
PKDTLMISRT PEVTCVVVDV SQEDPEVQFN WYVDGVEVHN AKTKPREQF 300
NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK GLPSSIEKTI SKAKGQPREP 350
QVYTLPPSQE EMTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP 400
VLDSDGSFFL YSRLTVDKSR WQEGNVFSCS VMHEALHNHY TQKSLSLSLG 450
K                                                       451
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Light chain / Chaîne légère / Cadena ligera

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DIQMTQSPSS VSASVGDRVT ITCRASQGIS SWLAWYQQKP GKAPKLLIYA  50
ASSLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ TNSFPFPFGP 100
GTKVDIKRTV 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) 22-96 151-207 265-325 371-429
22"-96" 151"-207" 265"-325" 371"-429"
Intra-L (C23-C104) 23'-88' 134'-194'
23'"-88'" 134'"-194'"
Inter-H-L (CH1 10-CL 126) 138-214' 138"-214'"
Inter-H-H (h 8, h 11) 230-230" 233-233"

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

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

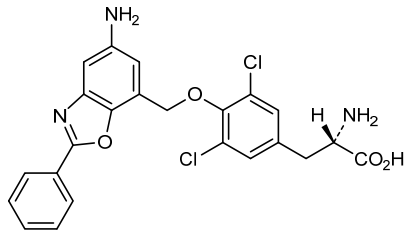
C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal

H CHS K2:
451, 451"

nanvuranlatum

nanvuranlat	*O*-[(5-amino-2-phenyl-1,3-benzoxazol-7-yl)methyl]-3,5-dichloro-L-tyrosine
nanvuranlat	*O*-[(5-amino-2-phényl-1,3-benzoxazol-7-yl)méthyl]-3,5-dichloro-L-tyrosine
nanvuranlat	*O*-[(5-amino-2-fenil-1,3-benzoxazol-7-il)metil]-3,5-dicloro-L-tirosina

$C_{23}H_{19}Cl_2N_3O_4$



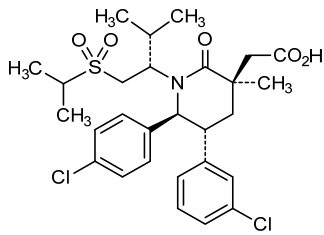
navtemadlinum

navtemadlin — {(3*R*,5*R*,6*S*)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-3-methyl-1-[(2*S*)-3-methyl-1-(propane-2-sulfonyl)butan-2-yl]-2-oxopiperidin-3-yl}acetic acid

navtémadline — acide {(3*R*,5*R*,6*S*)-5-(3-chlorophényl)-6-(4-chlorophényl)-3-méthyl-1-[(2*S*)-3-méthyl-1-(propane-2-sulfonyl)butan-2-yl]-2-oxopipéridin-3-yl}acétique

navtemadlina — ácido {(3*R*,5*R*,6*S*)-5-(3-clorofenil)-6-(4-clorofenil)-3-metil-1-[(2*S*)-3-metil-1-(propano-2-sulfonil)butan-2-il]-2-oxopiperidin-3-il}acético

$C_{28}H_{35}Cl_2NO_5S$



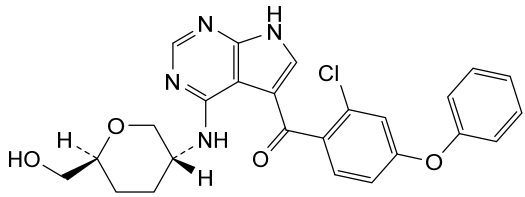
nemtabrutinibum

nemtabrutinib — (1^3R,1^6S)-5^2-chloro-1^6-(hydroxymethyl)-3^7H-6-oxa-2-aza-3(4,5)-pyrrolo[2,3-*d*]pyrimidina-1(3)-oxana-5(1,4),7(1)-dibenzenaheptaphan-4-one

nemtabrutinib — (1^3R,1^6S)-5^2-chloro-1^6-(hydroxyméthyl)-3^7H-6-oxa-2-aza-3(4,5)-pyrrolo[2,3-*d*]pyrimidina-1(3)-oxana-5(1,4),7(1)-dibenzénaheptaphan-4-one

nemtabrutinib — (1^3R,1^6S)-5^2-cloro-1^6-(hidroximetil)-3^7H-6-oxa-2-aza-3(4,5)-pirrolo[2,3-*d*]pirimidina-1(3)-oxana-5(1,4),7(1)-dibencenaheptafan-4-ona

$C_{25}H_{23}ClN_4O_4$



nendratareotidum

nendratareotide

S^2,S^7-cyclo(D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyl-L-cysteinamide)

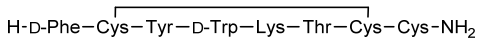
nendrataréotide

S^2,S^7-cyclo(D-phénylalanyl-L-cystéinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-thréonyl-L-cystéinyl-L-cystéinamide)

nendratareotida

S^2,S^7-ciclo(D-fenilalanil-L-cisteinil-L-tirosil-D-triptofil-L-lisil-L-treonil-L-cisteinil-L-cisteinamide)

$C_{48}H_{63}N_{11}O_{10}S_3$



nendratareotidum uzatansinum

nendratareotide uzatansine

S^2,S^7-cyclo{D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyl-3-[(3-{[(2*S*)-1-{[(1^4*S*,1^6*S*,2*R*,3^2*S*,3^3*S*,4*S*,10*E*,12*E*,14*R*)-8^6-chloro-1^4-hydroxy-8^5,14-dimethoxy-2,3^3,7,10-tetramethyl-1^2,6-dioxo-7-aza-1(6,4)-[1,3]oxazinana-3(2,3)-oxirana-8(1,3)-benzenacyclotetradecaphane-10,12-dien-4-yl]oxy}-1-oxopropan-2-yl](methyl)amino}-3-oxopropyl)disulfanyl]-L-alaninamide}

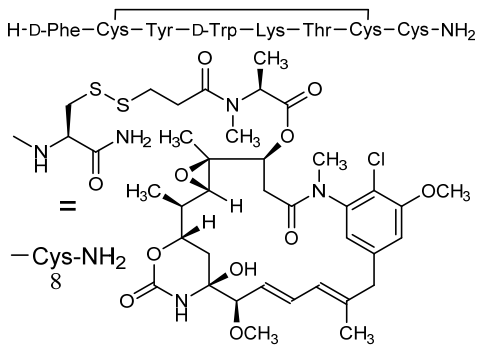
nendrataréotide uzatansine

S^2,S^7-cyclo{D-phénylalanyl-L-cystéinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-thréonyl-L-cystéinyl-3-[(3-{[(2*S*)-1-{[(1^4*S*,1^6*S*,2*R*,3^2*S*,3^3*S*,4*S*,10*E*,12*E*,14*R*)-8^6-chloro-1^4-hydroxy-8^5,14-diméthoxy-2,3^3,7,10-tétraméthyl-1^2,6-dioxo-7-aza-1(6,4)-[1,3]oxazinana-3(2,3)-oxirana-8(1,3)-benzénacyclotétradeca-phane-10,12-dién-4-yl]oxy}-1-oxopropan-2-yl](méthyl)amino}-3-oxopropyl)disulfanyl]-L-alaninamide}

nendratareotida uzatansina

S^2,S^7-ciclo{D-fenilalanil-L-cisteinil-L-tirosil-D-triptofil-L-lisil-L-treonil-L-cisteinil-3-[(3-{[(2*S*)-1-{[(1^4*S*,1^6*S*,2*R*,3^2*S*,3^3*S*,4*S*,10*E*,12*E*,14*R*)-8^6-cloro-1^4-hidroxi-2,3^3,7,10-tetrametil-8^5,14-dimetoxi-1^2,6-dioxo-7-aza-1(6,4)-[1,3]oxazinana-3(2,3)-oxirana-8(1,3)-bencenaciclotetradeca-fano-10,12-dien-4-il]oxi}-1-oxopropan-2-il](metil)amino}-3-oxopropil)disulfanil]-L-alaninamida}

$C_{83}H_{109}ClN_{14}O_{20}S_4$



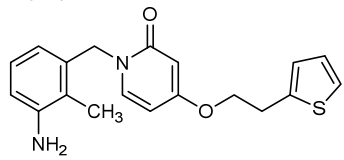
nilofabicinum

nilofabicin — 1-[(3-amino-2-methylphenyl)methyl]-4-[2-(thiophen-2-yl)ethoxy]pyridin-2(1*H*)-one

nilofabicine — 1-[(3-amino-2-méthylphényl)méthyl]-4-[2-(thiophén-2-yl)éthoxy]pyridin-2(1*H*)-one

nilofabicina — 1-[(3-amino-2-metilfenil)metil]-4-[2-(tiofen-2-il)etoxi]piridin-2(1*H*)-ona

$C_{19}H_{20}N_2O_2S$



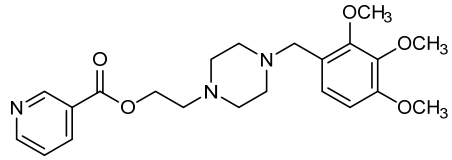
ninerafaxstatum

ninerafaxstat — 2-{4-[(2,3,4-trimethoxyphenyl)methyl]piperazin-1-yl}ethyl pyridine-3-carboxylate

ninérafaxstat — pyridine-3-carboxylate de 2-{4-[(2,3,4-triméthoxyphényl)méthyl]pipérazin-1-yl}éthyle

ninerafaxstat — piridina-3-carboxilato de 2-{4-[(2,3,4-trimetoxifenil)metil]piperazin-1-il}etilo

$C_{22}H_{29}N_3O_5$



nivadstrocelum

nivadstrocel — Allogeneic mesenchymal stromal cells derived from subcutaneous adipose tissue collected by liposuction. The cells are isolated from the adipose tissue by enzymatic digestion and are expanded in a three-dimensional hydrogel matrix with scaffold structure. The cells express cell surface markers CD105 and CD90 (≥95%), lack cell surface expression (<2% positive) of CD45, CD34, and do not express T cell co-stimulatory molecules CD40, CD80 or CD86 and major histocompatibility complex (MHC) class II (HLA-DR). The cells also secrete various growth factors (e.g. insulin-like growth factor (IGF), hepatocyte growth factor (HGF) and vascular endothelial growth factor (VEGF)) and express extracellular matrix proteins, in particular collagen type VII.

nivadstrocel — Cellules stromales mésenchymateuses allogéniques dérivées du tissu adipeux sous-cutané recueillies par liposuccion. Les cellules ont été isolées du tissu

adipeux par digestion enzymatique et ont été expansées dans une matrice d'hydrogel tridimensionnelle avec une structure d'échafaudage. Les cellules expriment les marqueurs cellulaires de surface CD105 et CD90 (≥95%), présentent une absence d'expression à la surface cellulaire (<2% positive) de CD45, CD34, et n'expriment pas les molécules co-stimulatrices des lymphocytes T CD40, CD80 ou CD86 ainsi que le complexe majeur d'histocompatibilité (MHC) de classe II (HLA-DR). Les cellules sécrètent aussi différents facteurs de croissance (p. ex. le facteur de croissance analogue à l'insuline (IGF), le facteur de croissance des hépatocytes (HGF) et le facteur de croissance de l'endothélium vasculaire (VEGF)) et expriment des protéines de la matrice extracellulaire, en particulier le collagène de type VII.

nivadstrocel — Células estromales mesenquimales alogénicas derivadas de tejido adiposo subcutáneo obtenido por liposucción. Las células se aíslan del tejido adiposo mediante digestión enzimática y se expanden en una matriz tridimensional de hidrogel con estructura de andamiaje. Las células expresan los marcadores de superficie CD105 y CD90 ((≥95%), carecen de expresión en la superficie celular (<2% positivo) de CD45, CD34 y no expresan las moléculas coestimuladoras de linfocitos T CD40, CD80 o CD86 ni complejo principal de histocompatibilidad (MHC) clase II (HLA-DR). Las células también secretan varios factores de crecimiento (por ejemplo el factor de crecimiento similar a insulina (IGF), el factor de crecimiento de hepatocitos (HGF) y el factor de crecimiento del endotelio vascular (VEGF)) y expresan proteínas de la matiz extracelular, en particular colágeno tipo VII.

nivatrotamabum #

nivatrotamab — immunoglobulin G1-kappa anti-[*Homo sapiens* GD2 (ganglioside GD2)], each kappa chain being fused to a scFv anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], monoclonal antibody, bispecific;
gamma1 heavy chain anti-GD2 (1-449) [VH (*Mus musculus* IGHV2-9*02 (79.2%) -(IGHD) -IGHJ3*01 (91.7%) A128>S (119)/*Homo sapiens* IGHV3-33*01 (72.2%) -(IGHD) -IGHJ4*01 (92.3%)) CDR-IMGT [8.7.13] (26-33.51-57.96-108) (1-119) -*Homo sapiens* IGHG1*08p (100%), G1m3,1, G1v29 CH2 A84.4, G1v20 CH2 A105 (CH1 R120 (216) (120-217), hinge 1-15 (218-232), CH2 N84.4>A (299), K105>A (324) (233-342), CH3 D12 (358), L14 (360) (343-447), CHS (448-449)) (120-449)], (222-211')-disulfide with kappa light chain anti-GD2 fused to scFv anti-CD3E (1'-484') [kappa light chain anti-GD2 (1'-211') [V-KAPPA anti-GD2 (*Mus musculus* IGKV6-32*02 (84.9%) -(IGHD) -IGKJ2*03 (90.0%) S120>Q (97)/*Homo sapiens* IGKV3-15*01 (78.9%) -IGKJ2*03 (100%)) CDR-IMGT [6.3.6] (27-32.50-52.89-94) (1'-104') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (150), V101 (188) (105'-211')]-17-mer threonyl-seryl-tris(tetraglycyl-seryl) linker (212'-228') -scFv heavy-kappa anti-CD3E (229'-484') [VH anti-CD3E G49>C (272), C114>S (333) (*Homo sapiens* IGHV3-30*10 (70.4%) -(IGHD) -IGHJ4*01 (85.7%) L123>P (342)) CDR-IMGT [8.8.12] (254-261.279-286.325-336) (229'-347') -30-mer hexakis(tetraglycyl-seryl) linker (348'-377') -V-KAPPA anti-CD3E (*Homo sapiens* IGKV1-33*01 (81.1%) -IGKJ2*02 (80.0%) Q120>C (476), E125>Q (481)) CDR-IMGT [5.3.9] (404-408.426-428.465-473) (378'-484')]]; dimer (228-228":231-231")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, non-glycosylated

nivatrotamab	immunoglobuline G1-kappa anti-[*Homo sapiens* GD2 (ganglioside GD2)], chaque chaîne kappa étant fusionnée à un scFv anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], anticorps monoclonal, bispécifique; chaîne lourde gamma1 anti-GD2 (1-449) [VH (*Mus musculus* IGHV2-9*02 (79.2%) -(IGHD) -IGHJ3*01 (91.7%) A128>S (119)/*Homo sapiens* IGHV3-33*01 (72.2%) -(IGHD) -IGHJ4*01 (92.3%)) CDR-IMGT [8.7.13] (26-33.51-57.96-108) (1-119) -*Homo sapiens* IGHG1*08p (100%), G1m3,1, G1v29 CH2 A84.4, G1v20 CH2 A105 (CH1 R120 (216) (120-217), charnière 1-15 (218-232), CH2 N84.4>A (299), K105>A (324) (233-342), CH3 D12 (358), L14 (360) (343-447), CHS (448-449)) (120-449)], (222-211')-disulfure avec la chaîne légère kappa anti-GD2 fusionnée au scFv anti-CD3E (1'-484') [chaîne légère kappa anti-GD2 (1'-211' [V-KAPPA anti-GD2 (*Mus musculus* IGKV6-32*02 (84.9%) -(IGHD) -IGKJ2*03 (90.0%) S120>Q (97)/*Homo sapiens* IGKV3-15*01 (78.9%) -IGKJ2*03 (100%)) CDR-IMGT [6.3.6] (27-32.50-52.89-94) (1'-104') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (150), V101 (188) (105'-211')]-17-mer thréonyl-séryl-tris(tétraglycyl-séryl) linker (212'-228') -scFv lourd-kappa anti-CD3E (229'-484') [VH anti-CD3E G49>C (272), C114>S (333) (*Homo sapiens* IGHV3-30*10 (70.4%) -(IGHD) -IGHJ4*01 (85.7%) L123>P (342)) CDR-IMGT [8.8.12] (254-261.279-286.325-336) (229'-347') -30-mer hexakis(tétraglycyl-séryl linker (348'-377') -V-KAPPA anti-CD3E (*Homo sapiens* IGKV1-33*01 (81.1%) -IGKJ2*02 (80.0%) Q120>C (476), E125>Q (481)) CDR-IMGT [5.3.9] (404-408.426-428.465-473) (378'-484')]]; dimère (228-228":231-231")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), non-glycosylé
nivatrotamab	inmunoglobulina G1-kappa anti-[*Homo sapiens* GD2 (ganglиósido GD2)], cada cadena kappa estando fusionada a un scFv anti-[*Homo sapiens* CD3E (CD3 épsilon, Leu-4)], anticuerpo monoclonal, biespecífico; cadena pesada gamma1 anti-GD2 (1-449) [VH (*Mus musculus* IGHV2-9*02 (79.2%) -(IGHD) -IGHJ3*01 (91.7%) A128>S (119)/*Homo sapiens* IGHV3-33*01 (72.2%) -(IGHD) -IGHJ4*01 (92.3%)) CDR-IMGT [8.7.13] (26-33.51-57.96-108) (1-119) -*Homo sapiens* IGHG1*08p (100%), G1m3,1, G1v29 CH2 A84.4, G1v20 CH2 A105 (CH1 R120 (216) (120-217), bisagra 1-15 (218-232), CH2 N84.4>A (299), K105>A (324) (233-342), CH3 D12 (358), L14 (360) (343-447), CHS (448-449)) (120-449)], (222-211')-disulfuro con la cadena ligera kappa anti-GD2 fusionada con scFv anti-CD3E (1'-484') [cadena ligera kappa anti-GD2 (1'-211' [V-KAPPA anti-GD2 (*Mus musculus* IGKV6-32*02 (84.9%) -(IGHD) -IGKJ2*03 (90.0%) S120>Q (97)/*Homo sapiens* IGKV3-15*01 (78.9%) -IGKJ2*03 (100%)) CDR-IMGT [6.3.6] (27-32.50-52.89-94) (1'-104') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (150), V101 (188) (105'-211')]-17-mer treonil-seril-tris(tetraglicil-seril) linker (212'-228') -scFv pesado-kappa anti-CD3E (229'-484') [VH anti-CD3E G49>C (272), C114>S (333) (*Homo sapiens* IGHV3-30*10 (70.4%) -(IGHD) -IGHJ4*01 (85.7%) L123>P (342)) CDR-IMGT

[8.8.12] (254-261.279-286.325-336) (229'-347') -30-mer hexakis(tetraglicil-seril linker (348'-377') -V-KAPPA anti-CD3E (*Homo sapiens* IGKV1-33*01 (81.1%) - IGKJ2*02 (80.0%) Q120>C (476), E125>Q (481)) CDR-IMGT [5.3.9] (404-408.426-428.465-473) (378'-484')]]; dímero (228-228":231-231")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), no glicosilado

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVESGPG VVQPGRSLRI SCAVSGFSVT NYGVHWVRQP PGKGLEWLGV  50
IWAGGITNYN SAFMSRLTIS KDNSKNTVYL QMNSLRAEDT AMYYCASRGG 100
HYGYALDYWG QGTLVTVSSA STKGPSVFPL APSSKSTSGG TAALGCLVKD 150
YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY 200
ICNVNHKPSN TKVDKRVEPK SCDKTHTCPP CPAPELLGGP SVFLFPPKPK 250
DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VDGVEVHNAK TKPREEQYAS 300
TYRVVSVLTV LHQDWLNGKE YKCAVSNKAL PAPIEKTISK AKGQPREPQV 350
YTLPPSRDEL TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL 400
DSDGSFFLYS KLTVDKSRWQ QGNVFSCSVM HEALHNHYTQ KSLSLSPGK  449
```

Light chain / Chaîne légère / Cadena ligera

```
EIVMTQTPAT LSVSAGERVT ITCKASQSVS NDVTWYQQKP GQAPRLLIYS  50
ASNRYSGVPA RFSGSGYGTE FTFTISSVQS EDFAVYFCQQ DYSSFGQGTK 100
LEIKRTVAAP SVFIFPPSDE QLKSGTASVV CLLNNFYPRE AKVQWKVDNA 150
LQSGNSQESV TEQDSKDSTY SLSSTLTLSK ADYEKHKVYA CEVTHQGLSS 200
PVTKSFNRGE CTSGGGGSGG GGSGGGGSQV QLVQSGGGVV QPGRSLRLSC 250
KASGYTFTRY TMHWVRQAPG KCLEWIGYIN PSRGYTNYNQ KFKDRFTISR 300
DNSKNTAFLQ MDSLRPEDTG VYFCARYYDD HYSLDYWGQG TPVTVSSGGG 350
GSGGGGSGGG GSGGGGSGGG GSGGGGSDIQ MTQSPSSLSA SVGDRVTITC 400
SASSSVSYMN WYQQTPGKAP KRWIYDTSKL ASGVPSRFSG SGSGTDYTFT 450
ISSLQPEDIA TYYCQQWSSN PFTFGCGTKL QITR                  484
```

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' 131'-191' 250'-324' 400'-464'
23'"-88'" 131'"-191'" 250'"-324'" 400'"-464'"
Intra-L (scFv VH C49 -VL IGKJ C120) 272'-476'
272'"-476'"
Inter-H-L (h 5-CL 126) 222-211' 222"-211'"
Inter-H-H (h 11, h 14) 228-228" 231-231"

N-terminal glutaminyl cyclization to pyroglutamyl (pE, 5-oxoprolyl)
L VH Q1:
1, 1"

No N-glycosylation sites / pas de sites de N-glycosylation / ningún posición de N-glicosilación
CH2 N84.4>A:
299, 299"
Aglycosylated

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
449, 449"

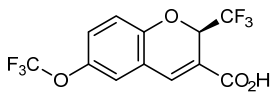
ocarocoxibum

ocarocoxib — *rac*-(2*R*)-6-(trifluoromethoxy)-2-(trifluoromethyl)-2*H*-1-benzopyran-3-carboxylic acid

ocarocoxib — acide *rac*-(2*R*)-6-(trifluorométhoxy)-2-(trifluorométhyl)-2*H*-1-benzopyrane-3-carboxylique

ocarocoxib — ácido *rac*-(2*R*)-2-(trifluorometil)-6-(trifluorometoxi)-2*H*-1-benzopirano-3-carboxílico

$C_{12}H_6F_6O_4$



and enantiomer
et énantiomère
y enantiómero

onilcamotidum

onilcamotide

RhoC (Rho-related GTP-binding protein RhoC, Ras homolog gene family member C protein) proprotein C-terminal (174-193)-peptide: L-alanyl-L-threonyl-L-arginyl-L-alanylglycyl-L-leucyl-L-glutaminyl-L-valyl-L-arginyl-L-lysyl-L-asparaginyl-L-lysyl-L-arginyl-L-arginyl-L-arginylglycyl-L-cysteinyl-L-prolyl-L-isoleucyl-L-leucine

onilcamotide

peptide 174-193 C-terminal de la proprotéine de RhoC (protéine RhoC de liaison au GTP RhoC apparentée à Rho, membre C des protéines de la famille de gènes homologues Ras): L-alanyl-L-thréonyl-L-arginyl-L-alanylglycyl-L-leucyl-L-glutaminyl-L-valyl-L-arginyl-L-lysyl-L-asparaginyl-L-lysyl-L-arginyl-L-arginyl-L-arginylglycyl-L-cystéinyl-L-prolyl-L-isoleucyl-L-leucine

onilcamotida

péptido 174-193 C-terminal de la proproteína del RhoC (proteína RhoC de unión a GTP relacionada con Rho, miembro C de proteínas en la familia de genes homólogos Ras): L-alanil-L-treonil-L-arginil-L-alanilglicil-L-leucil-L-glutaminil-L-valil-L-arginil-L-lisil-L-asparaginil-L-lisil-L-arginil-L-arginil-L-arginilglicil-L-cisteinil-L-prolil-L-isoleucil-L-leucina

$C_{96}H_{177}N_{39}O_{24}S$

H–Ala–Thr–Arg–Ala–Gly–Leu–Gln–Val–Arg–Lys–
10
Asn–Lys–Arg–Arg–Arg–Gly–Cys–Pro–Ile–Leu–OH
20

onzigolidum

onzigolide

S^2,*S*^{7}-cyclo[*N*^{2},*N*^{6}-bis({[(6-propylergolin-8β-yl)methyl]sulfanyl}acetyl)-D-lysyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-(2*S*)-2-aminobutanoyl-L-cysteinyl-L-threoninamide]

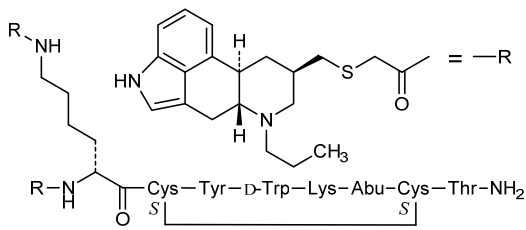
onzigolide

S^2,*S*^{7}-cyclo[*N*^{2},*N*^{6}-bis({[(6-propylergolin-8β-yl)méthyl]sulfanyl}acétyl)-D-lysyl-L-cystéinyl-L-tyrosyl-D-tryptophyl-L-lysyl-(2*S*)-2-aminobutanoyl-L-cystéinyl-L-thréoninamide]

onzigolida

S^2,*S*^{7}-ciclo[*N*^{2},*N*^{6}-bis({[(6-propilergolin-8β-il)metil]sulfanil}acetil)-D-lisil-L-cisteinil-L-tirosil-D-triptofil-L-lisil-(2*S*)-2-aminobutanoil-L-cisteinil-L-treoninamida]

$C_{86}H_{116}N_{16}O_{12}S_4$



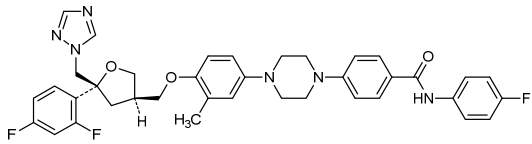
opelconazolum

opelconazole — (6^2R,6^4R)-6^2-(2,4-difluorophenyl)-*N*-(4-fluorophenyl)-3^3-methyl-4-oxa-2(1,4)-piperazina-8(1)-[1,2,4]triazola-6(4,2)-oxolana-1(1),3(1,4)-dibenzenaoctaphane-1^4-carboxamide

opelconazole — (6^2R,6^4R)-6^2-(2,4-difluorophényl)-*N*-(4-fluorophényl)-3^3-méthyl-4-oxa-2(1,4)-pipérazina-8(1)-[1,2,4]triazola-6(4,2)-oxolana-1(1),3(1,4)-dibenzénaoctaphane-1^4-carboxamide

opelconazol — (6^2R,6^4R)-6^2-(2,4-difluorofenil)-*N*-(4-fluorofenil)-3^3-metil-4-oxa-2(1,4)-piperazina-8(1)-[1,2,4]triazola-6(4,2)-oxolana-1(1),3(1,4)-dibencenaoctafano-1^4-carboxamida

$C_{38}H_{37}F_3N_6O_3$



ordesekimabum #

ordesekimab — immunoglobulin G1-kappa, anti-[*Homo sapiens* IL15 (interleukin 15, IL-15)], *Homo sapiens* monoclonal antibody;
gamma1 heavy chain *Homo sapiens* (1-448) [VH (*Homo sapiens* IGHV5-51*01 (95.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) -*Homo sapiens* IGHG1*08p (100%), G1m3,1 (CH1 R120 (215) (119-216), hinge 1-15 (217-231), CH2 (232-341), CH3 D12 (357), E14 (359) (342-446), CHS (447-448)) (119-448)], (221-214')-disulfide with kappa light chain *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (97.9%) -IGKJ2*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 (227-227":230-230")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

ordésékimab — immunoglobuline G1-kappa, anti-[*Homo sapiens* IL15 (interleukine 15, IL-15)], anticorps monoclonal *Homo sapiens*;
chaîne lourde gamma1 *Homo sapiens* (1-448) [VH (*Homo sapiens* IGHV5-51*01 (95.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) -*Homo* IGHG1*08p (100%), G1m3,1 (CH1 R120 (215) (119-216), charnière 1-15 (217-231), CH2 (232-341), CH3 D12 (357), E14 (359) (342-446), CHS (447-448)) (119-448)], (221-214')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (97.9%) -IGKJ2*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 (227-227":230-230")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

ordesekimab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* IL15 (interleukina 15, IL-15)], anticuerpo monoclonal *Homo sapiens*;cadena pesada gamma1 *Homo sapiens* (1-448) [VH (*Homo sapiens* IGHV5-51*01 (95.9%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118) -*Homo* IGHG1*08p (100%), G1m3,1 (CH1 R120 (215) (119-216), bisagra 1-15 (217-231), CH2 (232-341), CH3 D12 (357), E14 (359) (342-446), CHS (447-448)) (119-448)], (221-214')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (97.9%) -IGKJ2*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 (227-227'':230-230'')-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVQSGAE VKKPGESLKI SCKVSGYFFT TYWIGWVRQM PGKGLEYMGI  50
IYPGDSDTRY SPSFQGQVTI SADKSISTAY LQWSSLKASD TAMYYCARGG 100
NWNCFDYWGQ GTLVTVSSAS TKGPSVFPLA PSSKSTSGGT AALGCLVKDY 150
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTQTYI 200
CNVNHKPSNT KVDKRVEPKS CDKTHTCPPC PAPELLGGPS VFLFPPKPKD 250
TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY 350
TLPPSRDELT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD 400
SDGSFFLYSK LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPGK   448
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Light chain / Chaîne légère / Cadena ligera

```
EIVLTQSPGT LSLSPGERAT LSCRASQSVS SSYLAWYQQK PGQAPRLLIY  50
GASRRATGIP DRFSGSGSGT DFTLTISRLE PEDFAVYYCQ RYGSSHTFGQ 100
GTKLEISRTV 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'-89' 134'-194'
23'"-89"' 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"

oremeperminum alfa #

oremepermin alfa

human hepatocyte growth factor isoform 3 (HGF3, hepatopoietin A isoform 3, five amino acid-deleted variant of hepatocyte growth factor, dHGF), heterodimer (alpha and beta chains), glycosylated, produced in Chinese hamster ovary (CHO) cells;
hepatocyte growth factor isoform 3 (*Homo sapiens* HGF3, hepatopoietin A isoform 3, des[SFLPS (130-134)]-hepatocyte growth factor, dHGF), produced in Chinese hamster ovary (CHO) cells, glycoform alfa

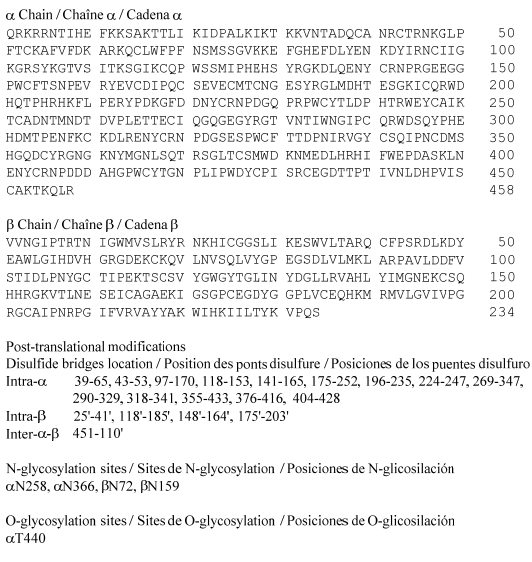
orémépermine alfa

isoforme 3 du factor de croissance des hépatocytes humains (HGF3, isoforme 3 de l'hépatopoïétine A, variant du facteur de croissance des hépatocytes avec cinq acides aminés supprimé, dHGF), hétérodimère (chaînes alpha et bêta), glycosylée, produite dans des cellules ovariennes de hamster (CHO);

isoforme 3 du facteur de croissance des hépatocytes (HGF3 *d'Homo sapiens*, isoforme 3 de l'hépatopoïétine A, dés[SFLPS (130-134)]-facteur de croissance des hépatocytes, dHGF), produite dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

oremepermina alfa

factor de crecimiento de hepatocitos humano isoforma 3 (HGF3, hepatopoyetina A isoforma 3, cinco aminoácidos eliminiados variante del factor de crecimiento de hepatocitos, dHGF), heterodímero (cadenas alfa y beta), glicosilado, producido en células ováricas de hámster chino (CHO);
factor de crecimiento de hepatocitos, isoforma 3 (HGF3 de *Homo sapiens*, isoforma 3 de hepatopoyetina A, des[SFLPS (130-134)]-factor de crecimiento de hepatocitos, dHGF), producido en células ováricas de hámster chino (CHO), glicoforma alfa



α Chain / Chaîne α / Cadena α

```
QRKRRNTIHE FKKSAKTTLI KIDPALKIKT KKVNTADQCA NRCTRNKGLP    50
FTCKAFVFDK ARKQCLWFPF NSMSSGVKKE FGHEFDLYEN KDYIRNCIIG   100
KGRSYKGTVS ITKSGIKCQP WSSMIPHEHS YRGKDLQENY CRNPRGEGG    150
PWCFTSNPEV RYEVCDIPQC SEVECMTCNG ESYRGLMDHT ESGKICQRWD   200
HQTPHRHKFL PERYPDKGFD DNYCRNPDGQ PRPWCYTLDP HTRWEYCAIK   250
TCADNTMNDT DVPLETTECI QGQGEGYRGT VNTIWNGIPC QRWDSQYPHE   300
HDMTPENFKC KDLRENYCRN PDGSESPWCF TTDPNIRVGY CSQIPNCDMS   350
HGQDCYRGNG KNYMGNLSQT RSGLTCSMWD KNMEDLHRHI FWEPDASKLN   400
ENYCRNPDDD AHGPWCYTGN PLIPWDYCPI SRCEGDTTPT IVNLDHPVIS   450
CAKTKQLR                                                 458
```

β Chain / Chaîne β / Cadena β

```
VVNGIPTRTN IGWMVSLRYR NKHICGGSLI KESWVLTARQ CFPSRDLKDY    50
EAWLGIHDVH GRGDEKCKQV LNVSQLVYGP EGSDLVLMKL ARPAVLDDFV   100
STIDLPNYGC TIPEKTSCSV YGWGYTGLIN YDGLLRVAHL YIMGNEKCSQ   150
HHRGKVTLNE SEICAGAEKI GSGPCEGDYG GPLVCEQHKM RMVLGVIVPG   200
RGCAIPNRPG IFVRVAYYAK WIHKIILTYK VPQS                    234
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-α 39-65, 43-53, 97-170, 118-153, 141-165, 175-252, 196-235, 224-247, 269-347, 290-329, 318-341, 355-433, 376-416, 404-428
Intra-β 25'-41', 118'-185', 148'-164', 175'-203'
Inter-α-β 451-110'

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
αN258, αN366, βN72, βN159

O-glycosylation sites / Sites de O-glycosylation / Posiciones de O-glicosilación
αT440

orludodstatum

orludodstat

N-(2-chloro-6-fluorophenyl)-4-[4-ethyl-3-(hydroxymethyl)-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-1-yl]-5-fluoro-2-{[(2*S*)-1,1,1-trifluoropropan-2-yl]oxy}benzamide

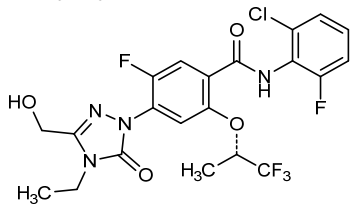
orludodstat

N-(2-chloro-6-fluorophényl)-4-[4-éthyl-3-(hydroxyméthyl)-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-1-yl]-5-fluoro-2-{[(2*S*)-1,1,1-trifluoropropan-2-yl]oxy}benzamide

orludodstat

N-(2-cloro-6-fluorofenil)-4-[4-etil-3-(hidroximetil)-5-oxo-4,5-dihidro-1*H*-1,2,4-triazol-1-il]-5-fluoro-2-{[(2*S*)-1,1,1-trifluoropropan-2-il]oxi}benzamida

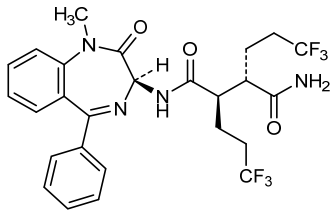
$C_{21}H_{18}ClF_5N_4O_4$



osugacestatum

osugacestat	(2*R*,3*S*)-*N*^{1}-[(3*S*)-1-methyl-2-oxo-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-3-yl]-2,3-bis(3,3,3-trifluoropropyl)butanediamide
osugacestat	(2*R*,3*S*)-*N*^{1}-[(3*S*)-1-méthyl-2-oxo-5-phényl-2,3-dihydro-1*H*-1,4-benzodiazépin-3-yl]-2,3-bis(3,3,3-trifluoropropyl)butanediamide
osugacestat	(2*R*,3*S*)-*N*^{1}-[(3*S*)-5-fenil-1-metil-2-oxo-2,3-dihidro-1*H*-1,4-benzodiazepin-3-il]-2,3-bis(3,3,3-trifluoropropil)butanodiamida

$C_{26}H_{26}F_6N_4O_3$



ozarlimogenum inteplasmidum

ozarlimogene inteplasmid	A DNA plasmid encoding *Streptococcus pyogenes* serotype M55 (emm55) cell surface protein (variant). A DNA plasmid encoding *Streptococcus pyogenes* serotype M55 (emm55) cell surface protein [variant, with 98% identity to the original source isolate A928171 (X72090.1)] under the control of a human cytomegalovirus (CMV) enhancer/promoter and an SV40 polyA signal sequence. Absence of the original stop codon results in the addition of 15 C-terminal plasmid-encoded amino acid residues. The plasmid also contains a bacterial origin (ori) of replication, F1 bacteriophage origin of replication, the SV40 virus origin of replication and a NeoR/KanR resistance coding sequence under the control of AmpR/SV40 promoters and a Herpes simplex virus (HSV) thymidine kinase (TK) poly(A) signal.
ozarlimogène intéplasmide	Un plasmide d'ADN codant pour une protéine de surface cellulaire (variant) du *Streptococcus pyogenes* de sérotype M55 (emm55). Un plasmide d'ADN codant pour une protéine de surface cellulaire du *Streptococcus pyogenes* de sérotype M55 (emm55) [variant, ayant une identité de 98% avec la source originelle de l'isolat A928171 (X72090.1)] sous le contrôle d'un activateur/promoteur du cytomégalovirus (CMV) humain et d'une séquence signal polyA SV40. L'absence du codon stop originel.

résulte de l'addition de 15 résidus d'acides aminés en C-terminal encodés par le plasmide. Le plasmide contient aussi une origine (ori) de réplication bactérienne, une origine de réplication du bactériophage F1, une origine de réplication du virus SV40 et une séquence codant une résistance NeoR/KanR sous le contrôle des promoteurs AmpR/SV40 et d'un signal poly(A) de la thymidine kinase (TK) du virus Herpès simplex (HSV).

ozarlimogén inteplásmido

Un plásmido de DNA que codifica para una variante de la proteína de superficie de *Streptococcus pyogenes* serotipo M55 (emm55).
Un plásmido de DNA que codifica para la proteína de superficie de *Streptococcus pyogenes* serotipo M55 (emm55) [variante, con un 98% de identidad con el aislado original A928171 (X72090.1)] bajo el control de un potenciador/promotor del citomegalovirus (CMV) humano y una secuencia señal polyA de SV40. La ausencia del codón de terminación original resulta en la adición a la región C-terminal de 15 residuos de aminoácidos codificados en el plásmido. El plásmido también contiene un origen de replicación (ori) bacteriano, un origen de replicación del bacteriófago F1, el origen de replicación del virus SV40 y una secuencia que codifica la resistencia NeoR/KanR, bajo el control de los promotores AmpR/SV40 y una señal poly(A) de la timidín quinasa (TK) del virus Herpes simplex (HSV).

pafolacianinum

pafolacianine

(2*E*,4^{3}*E*,8*S*)-14^{2}-amino-8-carboxy-4^{3}-{(2*E*)-2-[3,3-dimethyl-5-sulfo-1-(4-sulfobutyl)-1,3-dihydro-2*H*-indol-2-ylidene]ethylidene}-1^{3},1^{3}-dimethyl-10,14^{4}-dioxo-1^{1}-(4-sulfobutyl)-14^{3},14^{4}-dihydro-1^{3}*H*-5-oxa-9,12-diaza-14(6)-pteridina-1(2)-indola-6,11(1,4)-dibenzena-4(1,2)-cyclohexanatetradecaphane-2,4^{1}-dien-1^{1}-ium-1^{5}-sulfonate

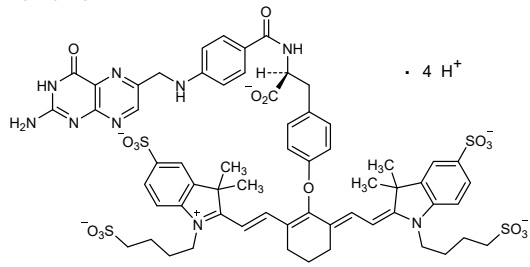
pafolacianine

(2*E*,4^{3}*E*,8*S*)-14^{2}-amino-8-carboxy-4^{3}-{(2*E*)-2-[3,3-diméthyl-5-sulfo-1-(4-sulfobutyl)-1,3-dihydro-2*H*-indol-2-ylidène]éthylidène}-1^{3},1^{3}-diméthyl-10,14^{4}-dioxo-1^{1}-(4-sulfobutyl)-14^{3},14^{4}-dihydro-1^{3}*H*-5-oxa-9,12-diaza-14(6)-ptéridina-1(2)-indola-6,11(1,4)-dibenzéna-4(1,2)-cyclohexanatétradécaphane-2,4^{1}-dién-1^{1}-ium-1^{5}-sulfonate

pafolacianina

(2*E*,4^{3}*E*,8*S*)-14^{2}-amino-8-carboxi-4^{3}-{(2*E*)-2-[3,3-dimetil-5-sulfo-1-(4-sulfobutil)-1,3-dihidro-2*H*-indol-2-ilideno]etilideno}-1^{3},1^{3}-dimetil-10,14^{4}-dioxo-1^{1}-(4-sulfobutil)-14^{3},14^{4}-dihidro-1^{3}*H*-5-oxa-9,12-diaza-14(6)-pteridina-1(2)-indola-6,11(1,4)-dibenceno-4(1,2)-ciclohexanatetradecafano-2,4^{1}-dien-1^{1}-ium-1^{5}-sulfonato

$C_{61}H_{67}N_9O_{17}S_4$



palopegteriparatidum

palopegteriparatide

human parathyroid hormone (PTH) synthetic peptide fragment (1-34), conjugated at the N-terminal amino group via a cleavable linker to *O*-methylpolyethylene glycol (2 x 20 kDa mPEG);
2-methylalanyl-(1-34)-peptide of parathyroid hormone (*Homo sapiens* parathyrin, parathormone, PTH) conjugated with *O*-methylpolyethylene glycol via a cleavable linker at the N-terminal amino group:
N-({2-[(6-{[(3*RS*)-1-{3-[(3-{(2Ξ)-2,3-bis[α-methylpoly(oxyethylene)-ω-oxy]propoxy}propyl)amino]-3-oxopropyl}-2,5-dioxopyrrolidin-3-yl]sulfanyl}hexyl)amino]ethyl}carbamoyl)-2-methylalanyl-L-seryl-L-valyl-L-seryl-L-α-glutamyl-L-isoleucyl-L-glutaminyl-L-leucyl-L-methionyl-L-histidyl-L-asparaginyl-L-leucylglycyl-L-lysyl-L-histidyl-L-leucyl-L-asparaginyl-L-seryl-L-methionyl-L-α-glutamyl-L-arginyl-L-valyl-L-α-glutamyl-L-tryptophyl-L-leucyl-L-arginyl-L-lysyl-L-lysyl-L-leucyl-L-glutaminyl-L-α-aspartyl-L-valyl-L-histidyl-L-asparaginyl-L-phenylalanine

palopegtériparatide

fragment peptidique synthétique (1-34) de l'hormone parathyroïdienne humaine (HPT) conjugué au groupe aminé en N-terminal via un linker clivable au *O*-méthylpolyéthylène glycol (2 x 20 kDa mPEG);
2-methylalanyl-(1-34)-peptide de l'hormone parathyroïdienne d'*Homo sapiens* (parathyrine, parathormone, PTH), conjugué à un *O*-méthylpoly-éthylène glycol via un linker clivable au groupe aminé en N-terminal:
N-({2-[(6-{[(3*RS*)-1-{3-[(3-{(2Ξ)-2,3-bis[α-méthylpoly(oxyéthylène)-ω-oxy]propoxy}propyl)amino]-3-oxopropyl}-2,5-dioxopyrrolidine-3-yl]sulfanyl}hexyl)amino]éthyl}carbamoyl)-2-méthylalanyl-L-séryl-L-valyl-L-séryl-L-α-glutamyl-L-isoleucyl-L-glutaminyl-L-leucyl-L-méthionyl-L-histidyl-L-asparaginyl-L-leucylglycyl-L-lysyl-L-histidyl-L-leucyl-L-asparaginyl-L-séryl-L-méthionyl-L-α-glutamyl-L-arginyl-L-valyl-L-α-glutamyl-L-tryptophyl-L-leucyl-L-arginyl-L-lysyl-L-lysyl-L-leucyl-L-glutaminyl-L-α-aspartyl-L-valyl-L-histidyl-L-asparaginyl-L-phénylalanine

palopegteriparatida

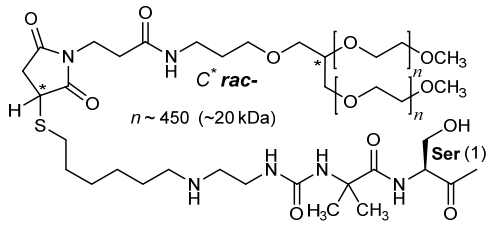
fragmento de péptido sintético (1-34) de la hormona paratiroidea humana (PTH) conjugado en el grupo amino N-terminal, a través de un enlace escindible, al glicol *O*-metilpolietileno (2 x 20 kDa mPEG);
2-metilalanil-péptido 1-34 de la hormona paratiroidiea del *Homo sapiens* (paratirina, parathormona, PTH), conjugado con O-metilpolietilenglicol a través de un grupo de unión separable escindible en el grupo amino N-terminal:
N-({2-[(6-{[(3*RS*)-1-{3-[(3-{(2Ξ)-2,3-bis[α-metilpoli(oxietileno)-ω-oxi]propoxi}propil)amino]-3-oxopropil}-2,5-dioxopirrolidin-3-il]sulfanil}hexil)amino]etil}carbamoil)-2-metilalanil-L-seril-L-valil-L-seril-L-α-glutamil-L-isoleucil-L-glutaminil-L-leucil-L-metionil-L-histidil-L-asparaginil-L-leucilglicil-L-lisil-L-histidil-L-leucil-L-asparaginil-L-seril-L-metionil-L-α-glutamil-L-arginil-L-valil-L-α-glutamil-L-triptofil-L-leucil-L-arginil-L-lisil-L-lisil-L-leucil-L-glutaminil-L-α-aspartil-L-valil-L-histidil-L-asparaginil-L-fenilalanina

$C_{209}H_{340}N_{60}O_{59}S_3(C_2H_4O)_{2n}$, n ≈ 450 (2 × ~20 kDa)

Sequence / Séquence / Secuencia

SVSEIQLMHN LGKHLNSMER VEWLRKKLQD VHNF 34

Modified residue / Résidu modifié / Resto modificado



peboctocogenum camaparvovecum #

peboctocogene camaparvovec

A non-replicating adeno-associated virus serotype hu37 (AAVhu37) vector encoding B-domain deleted human blood-coagulation factor VIII.
A recombinant, non-replicating, adeno-associated virus serotype hu37 (AAVhu37) vector, encoding a codon-optimised B-domain deleted SQ variant of human blood-coagulation factor VIII (hFVIII-SQ), under the control of a hybrid liver promoter (*Mus musculus* transthyretin enhancer-human transthyretin promoter) and a synthetic polyA signal sequence, flanked by AAV2 inverted terminal repeats; the A2 and A3 domains of hFVIII are linked by a DNA sequence encoding a 14-amino acid peptide (SQ) from the B domain.

péboctocogène camaparvovec

Un vecteur du virus adéno-associé de sérotype hu37 (AAVhu37) non-répliquant codant le facteur VIII de coagulation sanguine humaine avec délétion du domaine B.
Un vecteur du virus adéno-associé de sérotype hu37 (AAVhu37) non-répliquant, recombinant, codant un variant SQ aux codons optimisés avec délétion du domaine B du facteur VIII de coagulation sanguine humaine (hFVIII-SQ), sous le contrôle d'un promoteur hybride de foie (activateur de la transthyrétine de *Mus musculus* - promoteur de la transthyrétine humaine) et d'une séquence signal polyA synthétique, flanquée de répétitions terminales inversées du AAV2; les domaines A2 et A3 du hFVIII sont liés par une séquence d'ADN codant un peptide (SQ) de 14 acides aminés provenant du domaine B.

peboctocogén camaparvovec

Un vector de virus adeno-asociado de serotipo hu37 (AAVhu37) no replicativo que codifica para el factor de coagulación sanguínea VIII humano con el dominio B delecionado.
Un vector de virus adeno-asociado de serotipo hu37 (AAVhu37) recombinante, no replicativo, que codifica una variante SQ con el dominio B delecionado del factor de coagulación sanguínea VIII humano (hFVIII-SQ), con codones optimizados, bajo el control de un promotor híbrido de hígado (potenciador de transtiretina de *Mus musculus* - promotor de transtiretina humana) y una secuencia señal de polyA sintética, flanqueado por las repeticiones terminales invertidas de AAV2; los dominios A2 y A3 de hFVIII están ligados mediante una secuencia de DNA que codifica para un péptido de 14 aminoácidos (SQ) del dominio B.

pelgifatamabum corixetanum #

pelgifatamab corixetan

immunoglobulin G1-kappa, anti-[*Homo sapiens* FOLH1 (folate hydrolase, prostate specific membrane antigen, PSMA)], *Homo sapiens* monoclonal antibody conjugated to chelator *corixetan*;
gamma1 heavy chain *Homo sapiens* (1-453) [VH (*Homo sapiens* IGHV3-33*01 (96.9%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (220) (124-221), hinge 1-15 (222-236), CH2 (237-346), CH3 E12 (362), M14 (364) (347-451), CHS (452-453)) (124-453)], (226-214')-disulfide with kappa light chain *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-27*01 (94.7%) -IGKJ3*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 (232-232":235-235")-bisdisulfide, produced in a Chinese hamster ovary (CHO)-K1 cell line, glycoform alfa; conjugated to chelator *corixetan*, with an average of 0.8 chelator groups per antibody
For the *corixetan* part, please refer to the Proposed INN List 121, published in the *WHO Drug Information, Vol.33, No.2, 2019.*

pelgifatamab corixétan

immunoglobuline G1-kappa, anti-[*Homo sapiens* FOLH1 (folate hydrolase, antigène membranaire spécifique de la prostate, PSMA)], anticorps monoclonal *Homo sapiens* conjugué au chélateur *corixétan*;
chaîne lourde gamma1 *Homo sapiens* (1-453) [VH (*Homo sapiens* IGHV3-33*01 (96.9%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (220) (124-221), charnière 1-15 (222-236), CH2 (237-346), CH3 E12 (362), M14 (364) (347-451), CHS (452-453)) (124-453)], (226-214')-disulfure avec la chaîne légère kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-27*01 (94.7%) -IGKJ3*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 (232-232":235-235")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-K1, glycoforme alfa; conjugué au chélateur *corixétan*, avec une moyenne de 0.8 groupes chélateurs par anticorps
Pour la partie *corixétan*, veuillez-vous référer à la Liste 121 des DCI proposées, publiée dans le *WHO Drug Information, Vol.33, No.2, 2019.*

pelgifatamab corixetán

inmunoglobulina G1-kappa, anti-[*Homo sapiens* FOLH1 (folato hidrolasa, antígeno membranario específico de la próstata, PSMA)], anticuerpo monoclonal *Homo sapiens* conjugado con el quelante *corixetán*;

cadena pesada gamma1 *Homo sapiens* (1-453) [VH *(Homo sapiens* IGHV3-33*01 (96.9%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (220) (124-221), bisagra 1-15 (222-236), CH2 (237-346), CH3 E12 (362), M14 (364) (347-451), CHS (452-453)) (124-453)], (226-214')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-27*01 (94.7%) -IGKJ3*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 (232-232":235-235")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-K1, forma glicosilada alfa; conjugado con el quelante *corixetán*, con una media de 0.8 grupos quelantes por anticuerpo

Para la parte corixetán, por favor vaya a la Lista 121 de los DCI propuestas, publicada en el WHO Drug Information, Vol.33, No.2, 2019.

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVESGGG VVQPGRSLRL SCAASGFAFS RYGMHWVRQA PGKGLEWVAV  50
IWYDGSNKYY ADSVKGRFTI SRDNSKNTQY LQMNSLRAED TAVYYCARGG 100
DFLYYYYYGM DVWGQGTTVT VSSASTKGPS VFPLAPSSKS TSGGTAALGC 150
LVKDYFPEPV TVSWNSGALT SGVHTFPAVL QSSGLYSLSS VVTVPSSSLG 200
TQTYICNVNH KPSNTKVDKR VEPKSCDKTH TCPPCPAPEL LGGPSVFLFP 250
PKPKDTLMIS RTPEVTCVVV DVSHEDPEVK FNWYVDGVEV HNAKTKPREE 300
QYNSTYRVVS VLTVLHQDWL NGKEYKCKVS NKALPAPIEK TISKAKGQPR 350
EPQVYTLPPS REEMTKNQVS LTCLVKGFYP SDIAVEWESN GQPENNYKTT 400
PPVLDSDGSF FLYSKLTVDK SRWQQGNVFS CSVMHEALHN HYTQKSLSLS 450
PGK                                                     453
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS LSASVGDRVT ITCRASQGIS NYLAWYQQKT GKVPKFLIYE  50
ASTLQSGVPS RFSGGGSGTD FTLTISSLQP EDVATYYCQN YNSAPFTFGP 100
GTKVDIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
LSSPVTKSFN RGEC                                         214
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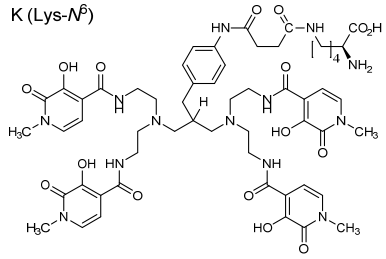
Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 150-206 267-327 373-431
22"-96" 150"-206" 267"-327" 373"-431"
Intra-L (C23-C104) 23'-88' 134'-194'
23'"-88'" 134'"-194'"
Inter-H-L (h 5-CL 126) 226-214' 226"-214'"
Inter-H-H (h 11, h 14) 232-232" 235-235"

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:
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"

Potential modified residues / résidus modifiés potentiels / restos modificados potenciales:



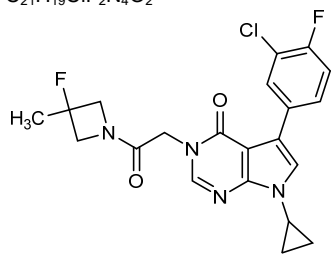
plazinemdorum

plazinemdor — 5-(3-chloro-4-fluorophenyl)-7-cyclopropyl-3-[2-(3-fluoro-3-methylazetidin-1-yl)-2-oxoethyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

plazinemdor — 5-(3-chloro-4-fluorophényl)-7-cyclopropyl-3-[2-(3-fluoro-3-méthylazétidin-1-yl)-2-oxoéthyl]-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

plazinemdor — 7-ciclopropil-5-(3-cloro-4-fluorofenil)-3-[2-(3-fluoro-3-metilazetidin-1-il)-2-oxoetil]-3,7-dihidro-4*H*-pirrolo[2,3-*d*]pirimidin-4-ona

$C_{21}H_{19}ClF_2N_4O_2$



plonmarlimabum #

plonmarlimab — immunoglobulin G1-kappa, anti-[*Homo sapiens* CSF2 (colony stimulating factor 2 (granulocyte-macrophage), GM-CSF, GMCSF)], humanized monoclonal antibody; gamma1 heavy chain humanized (1-450) [VH (*Homo sapiens* IGHV1-2*02 (85.7%) -(IGHD) -IGHJ3*01 (92.9%) M123>T (115)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 R120>K (217) (121-218), hinge 1-15 (219-233), CH2 (234-343), CH3 E12 (359), M14 (361) (344-448), CHS (449-450)) (121-450)], (223-214')-disulfide with kappa light chain humanized (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-9*01 (78.9%) -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 (229-229'':232-232'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

plonmarlimab — immunoglobuline G1-kappa, anti-[*Homo sapiens* CSF2 (facteur 2 stimulant les colonies (granulocyte-macrophage), GM-CSF, GMCSF)], anticorps monoclonal humanisé;
chaîne lourde gamma1 humanisée (1-450) [VH (*Homo sapiens* IGHV1-2*02 (85.7%) -(IGHD) -IGHJ3*01 (92.9%) M123>T (115)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 R120>K (217) (121-218), charnière 1-15 (219-233), CH2 (234-343), CH3 E12 (359), M14 (361) (344-448), CHS (449-450)) (121-450)], (223-214')-disulfure avec la chaîne légère kappa

humanisée (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-9*01 (78.9%) -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 (229-229'':232-232'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

plonmarlimab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* CSF2 (factor 2 estimulante de las colonias (granulocito-macrófago), GM-CSF, GMCSF)], anticuerpo monoclonal humanizado;
cadena pesada gamma1 humanizada (1-450) [VH (*Homo sapiens* IGHV1-2*02 (85.7%) -(IGHD) -IGHJ3*01 (92.9%) M123>T (115)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 R120>K (217) (121-218), bisagra 1-15 (219-233), CH2 (234-343), CH3 E12 (359), M14 (361) (344-448), CHS (449-450)) (121-450)], (223-214')-disulfuro con la cadena ligera kappa humanizada (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-9*01 (78.9%) -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 (229-229'':232-232'')-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVQSGAE VKKPGASVKV SCKASGYTFT SHYLHWVRQA PGQGLEWMGW  50
IFPGDDKTKY NEKFKGRVTM TSDTSISTAY MELSRLRSDD TAVYYCARGT 100
KYLNWNFDVW GQGTTVTVSS 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
VYTLPPSREE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPGK 450
```

Light chain / Chaîne légère / Cadena ligera

```
DIQLTQSPSF LSASVGDRVT ITCKANQNVG TTLAWYQQKP GKSPKALIYS  50
ASYRYSGVPD RFSGSGSGTD FTLTISSLQP EDFATYFCHQ YTTYPLTFGG 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 (h5-CL 126) 223-214' 223"-214'"
Inter-H-H (h11, 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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
450, 450"

ponsegromabum #
ponsegromab

immunoglobulin G1-kappa, anti-[*Homo sapiens* GDF15 (growth differentiation factor 15, PLAB, MIC-1, PDF, MIC1, NAG-1, PTGFB)], monoclonal antibody;

	gamma1 heavy chain (1-449) [VH (*Homo sapiens* IGHV1-69*01 (93.9%) -(IGHD) -IGHJ1*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) - *Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1, G1v14 CH2 A1.3, A1.2 (CH1 R120>K (217) (121-218), hinge 1-15 (219-233), CH2 L1.3>A (237), L1.2>A (238), G1>A (240) (234-343), CH3 E12 (359), M14 (361) (344-448), CHS K>del (449)) (121-449)], (223-214')-disulfide with kappa light chain (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-11*01 (91.6%) - 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 (229-229'':232-232'')-bisdisulfide, produced in Chinese hamster ovary (CHO)-K1SV cell line lacking the glutamine synthetase gene (GSKO), glycoform alfa
ponségromab	immunoglobuline G1-kappa, anti-[*Homo sapiens* GDF15 (facteur 15 de croissance et de différenciation, PLAB, MIC-1, PDF, MIC1, NAG-1, PTGFB)], anticorps monoclonal; chaîne lourde gamma1 (1-449) [VH (*Homo sapiens* IGHV1-69*01 (93.9%) -(IGHD) -IGHJ1*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) - *Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1, G1v14 CH2 A1.3, A1.2 (CH1 R120>K (217) (121-218), charnière 1-15 (219-233), CH2 L1.3>A (237), L1.2>A (238), G1>A (240) (234-343), CH3 E12 (359), M14 (361) (344-448), CHS K>del (449)) (121-449)], (223-214')-disulfure avec la chaîne légère kappa (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-11*01 (91.6%) - 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 (229-229'':232-232'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-K1SV ne présentant pas le gène de la glutamine synthétase (GSKO), glycoforme alfa
ponsegromab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* GDF15 (factor 15 de crecimiento y de diferenciación, PLAB, MIC-1, PDF, MIC1, NAG-1, PTGFB)], anticuerpo monoclonal; cadena pesada gamma1 (1-449) [VH (*Homo sapiens* IGHV1-69*01 (93.9%) -(IGHD) -IGHJ1*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) - *Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1, G1v14 CH2 A1.3, A1.2 (CH1 R120>K (217) (121-218), bisagra 1-15 (219-233), CH2 L1.3>A (237), L1.2>A (238), G1>A (240) (234-343), CH3 E12 (359), M14 (361) (344-448), CHS K>del (449)) (121-449)], (223-214')-disulfuro con la cadena ligera kappa (1'-214') [V-KAPPA (*Homo sapiens* IGKV3-11*01 (91.6%) - 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 (229-229'':232-232'')-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-K1SV en ausencia del gen glutamina sintetasa (GSKO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGSSVKV SCKASGYTFS SYNIDWVRQA PGQGLEWMGG  50
INPIFGTAFY NQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCAREA 100
ITTVGAMDHW GQGTLVTVSS ASTKGPSVFP LAPSSKSTSG GTAALGCLVK 150
DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT 200
YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPEAAGA PSVFLFPPKP 250
KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ 350
VYTLPPSREE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPG  449
```

Light chain / Chaîne légère / Cadena ligera

```
EIVLTQSPAT LSLSPGERAT LSCRTSQSVH NYLAWYQQKP GQAPRLLIYD  50
ASTRADGIPA RFSGSGSGTD FTLTISSLEP EDFAVYYCQQ FWSWPWTFGQ 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 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:
300, 300"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados.

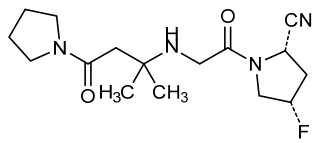
prusogliptinum

prusogliptin — (2*S*,4*S*)-4-fluoro-1-({[2-methyl-4-oxo-4-(pyrrolidin-1-yl)butan-2-yl]amino}acetyl)pyrrolidine-2-carbonitrile

prusogliptine — (2*S*,4*S*)-4-fluoro-1-({[2-méthyl-4-oxo-4-(pyrrolidin-1-yl)butan-2-yl]amino}acétyl)pyrrolidine-2-carbonitrile

prusogliptina — (2*S*,4*S*)-4-fluoro-1-({[2-metil-4-oxo-4-(pirrolidin-1-il)butan-2-il]amino}acetil)pirrolidina-2-carbonitrilo

$C_{16}H_{25}FN_4O_2$



pucotenlimabum #

pucotenlimab — immunoglobulin G4-kappa, anti-[*Homo sapiens* PDCD1 (programmed cell death 1, PD1, PD-1, CD279)], monoclonal antibody;
gamma4 heavy chain (1-445) [VH (*Mus musculus* IGHV5-9-2*01 (87.8%) -(IGHD) -IGHJ3*01 (93.3%)/*Homo sapiens* IGHV3-23*04 (86.7%) -(IGHD) -IGHJ6*01 (90.9%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118)-*Homo sapiens* IGHG4*01, G4v5 h P10, G4v22 CH2 T16, P91, CH3 A114 (CH1 (119-216), hinge 1-12 S10>P (226) (217-228), CH2 S16>T (252), V91>P (306) (229-338), CH3 N114>A (432) (339-443), CHS (444-445)) (119-445)], (132-218')-disulfide with kappa light chain (1'-218') [V-KAPPA (*Mus musculus* IGKV3-2*01 (92.9%) -IGKJ1*01 (100%)/*Homo sapiens* IGKV3D-11*02 (64.9%) -IGKJ4*01 (90.9%)) 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 (224-224":227-227")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

pucotenlimab

immunoglobuline G4-kappa, anti-[*Homo sapiens* PDCD1 (protéine 1 de mort cellulaire programmée, PD-1, PD1, CD279)], anticorps monoclonal;
chaîne lourde gamma4 (1-445) [VH (*Mus musculus* IGHV5-9-2*01 (87.8%) -(IGHD) -IGHJ3*01 (93.3%)/*Homo sapiens* IGHV3-23*04 (86.7%) -(IGHD) -IGHJ6*01 (90.9%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118)-*Homo sapiens* IGHG4*01, G4v5 h P10, G4v22 CH2 T16, P91, CH3 A114 (CH1 (119-216), charnière 1-12 S10>P (226) (217-228), CH2 S16>T (252), V91>P (306) (229-338), CH3 N114>A (432) (339-443), CHS (444-445)) (119-445)], (132-218')-disulfure avec la chaîne légère kappa (1'-218') [V-KAPPA (*Mus musculus* IGKV3-2*01 (92.9%) -IGKJ1*01 (100%)/*Homo sapiens* IGKV3D-11*02 (64.9%) -IGKJ4*01 (90.9%)) 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 (224-224'':227-227'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

pucotenlimab

inmunoglobulina G4-kappa, anti-[*Homo sapiens* PDCD1 (proteína 1 de muerte celular programada, PD-1, PD1, CD279)], anticuerpo monoclonal;
cadena pesada gamma4 (1-445) [VH (*Mus musculus* IGHV5-9-2*01 (87.8%) -(IGHD) -IGHJ3*01 (93.3%)/*Homo sapiens* IGHV3-23*04 (86.7%) -(IGHD) -IGHJ6*01 (90.9%)) CDR-IMGT [8.8.11] (26-33.51-58.97-107) (1-118)-*Homo sapiens* IGHG4*01, G4v5 h P10, G4v22 CH2 T16, P91, CH3 A114 (CH1 (119-216), bisagra 1-12 S10>P (226) (217-228), CH2 S16>T (252), V91>P (306) (229-338), CH3 N114>A (432) (339-443), CHS (444-445)) (119-445)], (132-218')-disulfuro con la cadena ligera kappa (1'-218') [V-KAPPA (*Mus musculus* IGKV3-2*01 (92.9%) -IGKJ1*01 (100%)/*Homo sapiens* IGKV3D-11*02 (64.9%) -IGKJ4*01 (90.9%)) 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 (224-224'':227-227'')-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVQSGGG LVQPGGSLKL SCAASGFTFS SYGMSWVRQA PGKGLDWVAT  50
ISGGGRDTYY PDSVKGRFTI SRDNSKNNLY LQMNSLRAED TALYYCARQK 100
GEAWFAYWGQ GTLVTVSSAS TKGPSVFPLA PCSRSTSEST AALGCLVKDY 150
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTKTYT 200
CNVDHKPSNT KVDKRVESKY GPPCPPCPAP EFLGGPSVFL FPPKPKDTLM 250
ITRTPEVTCV VVDVSQEDPE VQFNWYVDGV EVHNAKTKPR EEQFNSTYRV 300
VSVLTPLHQD WLNGKEYKCK VSNKGLPSSI EKTISKAKGQ PREPQVYTLP 350
PSQEEMTKNQ VSLTCLVKGF YPSDIAVEWE SNGQPENNYK TTPPVLDSDG 400
SFFLYSRLTV DKSRWQEGNV FSCSVMHEAL HAHYTQKSLS LSLGK      445
```

Light chain / Chaîne légère / Cadena ligera

```
DIVLTQSPAS LAVSPGQRAT ITCRASESVD NYGISFMNWF QQKPGQPPKL  50
LIYAASNKGT GVPARFSGSG SGTDFTLNIN PMEENDTAMY FCQQSKEVPW 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   145-201    259-319   365-423
                    22"-96" 145"-201"  259"-319" 365"-423"
Intra-L (C23-C104)  23'-92'   138'-198'
                    23'"-92'" 138'"-198'"
Inter-H-L (CH1 10-CL 126)  132-218' 132"-218'"
Inter-H-H (h 8, h 11)      224-224" 227-227"
```

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 / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
445, 445"

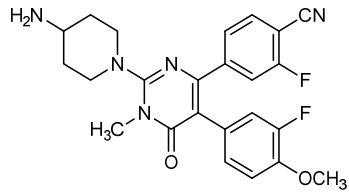
pulrodemstatum

pulrodemstat — 4-[2-(4-aminopiperidin-1-yl)-5-(3-fluoro-4-methoxyphenyl)-1-methyl-6-oxo-1,6-dihydropyrimidin-4-yl]-2-fluorobenzonitrile

pulrodemstat — 4-[2-(4-aminopipéridin-1-yl)-5-(3-fluoro-4-méthoxyphényl)-1-méthyl-6-oxo-1,6-dihydropyrimidin-4-yl]-2-fluorobenzonitrile

pulrodemstat — 4-[2-(4-aminopiperidin-1-il)-5-(3-fluoro-4-metoxifenil)-1-metil-6-oxo-1,6-dihidropirimidin-4-il]-2-fluorobenzonitrilo

$C_{24}H_{23}F_2N_5O_2$



quaratusugenum ozeplasmidum #

quaratusugene ozeplasmid — A DNA plasmid encoding tumour suppressor candidate 2 (TUSC2).
A DNA plasmid encoding tumour suppressor candidate 2 (TUSC2), also referred to as fusion 1 protein (FUS1), under the control of an adenovirus E1 enhancer, human cytomegalovirus (hCMV) immediate early enhancer/ promoter and a bovine growth hormone (bGH) polyadenylation signal (polyA). The plasmid also contains a pMB1origin of replication and a NeoR/KanR antibiotic resistance coding sequence.

quaratusugène ozéplasmide — Un plasmide d'ADN codant pour le candidat 2 suppresseur de tumeur (TUSC2).
Un plasmide d'ADN codant pour le candidat 2 suppresseur de tumeur (TUSC2), aussi appelé la protéine de fusion (FUS1), sous le contrôle d'un activateur de l'adénovirus E1, du promoteur/activateur précoce immédiat du cytomégalovirus humain (hCMV) et d'un signal de polyadénylation (polyA) de l'hormone de croissance bovine (bGH). Le plasmide contient aussi une origine de réplication pMB1 et une séquence codant une résistance aux antibiotiques NeoR/KanR.

quaratusugén ozeplásmido — Un plásmido de DNA que codifica para el candidato supresor de tumores 2 (TUSC2).
Un plásmido de DNA que codifica para el candidato supresor de tumores 2 (TUSC2), también referido como proteína de fusión 1 (FUS1), bajo el control de un potenciador E1 de adenovirus, un potenciador/promotor inmediato temprano de citomegalovirus humano (hCMV) y una señal de poliadenilación (polyA) de la hormona de crecimiento bovina (bGH). El plásmido también contiene un origen de replicación pMB1 y una secuencia NeoR/KanR que codifica para la resistencia a antibióticos.

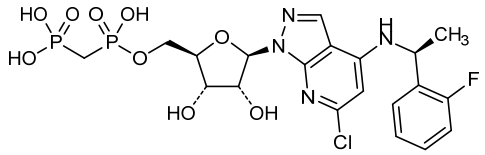
quemliclustatum

quemliclustat — 2-chloro-N^6-[(1*S*)-1-(2-fluorophenyl)ethyl]-8-aza-1,7-dicarbaadenosine 5'-(trihydrogen 2-carbadiphosphate)

quémliclustat — 2-chloro-N^6-[(1*S*)-1-(2-fluorophényl)éthyl]-8-aza-1,7-dicarbaadenosine 5'-(trihydrogéno-2-carbadiphosphate)

quemliclustat — 2-cloro-N^6-[(1*S*)-1-(2-fluorofenil)etil]-8-aza-1,7-dicarbaadenosina 5'-(trihidrógeno-2-carbadifosfato)

$C_{20}H_{24}ClFN_4O_9P_2$



retlirafuspum alfa #

retlirafusp alfa — human immunoglobulin G4-kappa anti-(human programmed cell death 1 ligand 1, PD-L1) variant (H^{52}>G, G^{57}>F, S^{227}>P, F^{233}>A, L^{234}>A, K^{446}>A in the heavy chain and N^{85}>E in the light chain), fused at the C-terminus of both heavy chains (1-446) via peptidyl linker ^{447}GGGGSGGGGSGGGGSGGGGSG^{467} to human transforming growth factor β type II (TGFR-2) extracellular fragment (20-136, 468-584 in the current sequence), dimer; glycosylated; produced in Chinese hamster ovary (CHO) cells;
immunoglobulin G4-kappa, anti-[*Homo sapiens* programmed cell death 1 ligand 1 (PD-L1, programmed death ligand 1, PDCD1 ligand 1, B7 homolog 1, B7-H1, CD274)], *Homo sapiens* monoclonal antibody, fused at the C-terminus of both heavy chains via a $(G_4S)_4G$ peptide linker (447-467) to fragment 20-136 of the extracellular domain of transforming growth factor β receptor type II (*Homo sapiens* TGF-β receptor 2, TGFR-2, TGFBR2) (468-584);
gamma4 heavy chain *Homo sapiens* (1-446) [*Homo sapiens* IGHV1-46*01; *Homo sapiens* IGHJ4*01; *Homo sapiens* IGHG4*01; VH: 1-119 (H52G G57F); CH1: 120-217; hinge 218-229 (S227P); CH2: 230-339 (F233A L234A); CH3: 340-444; CHS: 445-446 (K446A); CDRKabatH1: SYWMH (31-35); CDRKabatH2: RIGPNSGFTSYNEKFKN (50-66); CDRKabatH3: GGSSYDYFDY (99-108)], (133-218')-disulfide with kappa light chain *Homo sapiens* (1'-218') [*Homo sapiens* IGKV4-1*01; *Homo sapiens* IGKJ2*01; *Homo sapiens* IGKC*01; VL: 1-111 (N85E); CL: 112-218; CDRKabatL1: RASESVSIHGTHLMH (24-38); CDRKabatL2: AASNLES (54-60); CDRKabatL: QQSFEDPLT (93-101)]; dimer (225-225":228-228")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

rétlirafusp alfa	immunoglobuline G4-kappa humaine anti-(ligand 1 humain de mort cellulaire programmée 1, PD-L1) variant (H52>G, G57>F, S227>P, F233>A, L234>A, K446>A dans la chaîne lourde et N85>E dans la chaîne légère), fusionné à la partie C-terminale des deux chaînes lourdes (1-446) via le linker peptidique ^{447}GGGGSGGGGSGGGGSGGGGSG^{467} au fragment extracellulaire (20-136, 468-584 dans la séquence actuelle) du récepteur de type II du facteur β de croissance transformant humain (TGFR-2), dimère; glycosylé; produit dans des cellules ovariennes de hamster chinois (CHO); immunoglobuline G4-kappa, anti-[ligand 1 de mort cellulaire programmée 1 d'*Homo sapiens* (PD-L1, ligand 1 de PDCD1, homologue 1 de B7, B7-H1, CD274)], anticorps monoclonal d'*Homo sapiens*, fusionnée à la partie C-terminale des deux chaînes lourdes via un linker peptidique $(G_4S)_4G$ (447-467) au fragment 20-136 du domaine extracellulaire du récepteur de type II du facteur β de croissance transformant (récepteur 2 de TGF-β d'*Homo sapiens*, TGFR-2, TGFBR2) (468-584); chaîne lourde gamma4 d'*Homo sapiens* (1-446) [*Homo sapiens* IGHV1-46*01; *Homo sapiens* IGHJ4*01; *Homo sapiens* IGHG4*01; VH: 1-119 (H52G G57F); CH1: 120-217; charnière 218-229 (S227P); CH2: 230-339 (F233A L234A); CH3: 340-444; CHS: 445-446 (K446A); CDRKabatH1: SYWMH (31-35); CDRKabatH2: RIGPNSGFTSYNEKFKN (50-66); CDRKabatH3: GGSSYDYFDY (99-108)], (133-218')-disulfure avec la chaîne légère kappa d'*Homo sapiens* (1'-218') [*Homo sapiens* IGKV4-1*01; *Homo sapiens* IGKJ2*01; *Homo sapiens* IGKC*01; VL: 1-111 (N85E); CL: 112-218; CDRKabatL1: RASESVSIHGTHLMH (24-38); CDRKabatL2: AASNLES (54-60); CDRKabatL: QQSFEDPLT (93-101)]; dimère (225-225":228-228")-bisdisulfure, produite dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa
retlirafusp alfa	inmunoglobulina G4-kappa humana anti-(muerte celular programada 1 humana ligando 1, PD-L1) variante (H^{52}>G, G^{57}>F, S^{227}>P, F^{233}>A, L^{234}>A, K^{446}>A en la cadena pesada y N^{85}>E en la cadena ligera), fusionado al C-terminal de ambas cadenas pesadas (1-446) a través de un enlace peptidil ^{447}GGGGSGGGGSGGGGSGGGGSG^{467} al factor de crecimiento transformante β tipo II humano (TGFR-2) fragmento extracelular (20-136, 468-584 en la secuencia actual), dímero; glicosilado; producido en células ováricas de hámster chino (CHO); inmunoglobulina G4-kappa, anti-[*Homo sapiens* ligando 1 de muerte programada (PD-L1, ligando 1 de PDCD1, homólogo 1 de B7, B7-H1, CD274)], anticuerpo monoclonal *Homo sapiens*, fusionado en los residuos C-terminales de ambas cadenas pesadas a través de un péptido conector $(G_4S)_4G$ (447-467) con el fragmento 20-136 del dominio extracelular del receptor de tipo II del factor β de crecimiento transformante (receptor 2 de TGF-β de *Homo sapiens*, TGFR-2, TGFBR2) (468-584); cadena pesada gamma4 *Homo sapiens* (1-446) [*Homo sapiens* IGHV1-46*01; *Homo sapiens* IGHJ4*01; *Homo sapiens* IGHG4*01; VH: 1-119 (H52G G57F); CH1: 120-217; hinge 218-229 (S227P); CH2: 230-339 (F233A L234A); CH3: 340-444; CHS: 445-446 (K446A); CDRKabatH1: SYWMH (31-35); CDRKabatH2: RIGPNSGFTSYNEKFKN (50-66); CDRKabatH3: GGSSYDYFDY (99-108)], (133-218')-disulfuro con la cadena ligera kappa *Homo sapiens* (1'-214') [*Homo sapiens* IGKV4-1*01; *Homo sapiens* IGKJ2*01; *Homo sapiens* IGKC*01; VL: 1-111 (N85E); CL: 112-218; CDRKabatL1: RASESVSIHGTHLMH (24-38); CDRKabatL2: AASNLES (54-60); CDRKabatL: QQSFEDPLT (93-101)];dímero (225-225":228-228")-bisdisulfuro, producida en células ováricas de hámsters chinos (CHO), glicoforma alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGASVKV SCKASGYTFT SYWMHWVRQA PGQGLEWMGR   50
IGPNSGFTSY NEKFKNRVTM TRDTSTSTVY MELSSLRSED TAVYYCARGG  100
SSYDYFDYWG QGTTVTVSSA STKGPSVFPL APCSRSTSES TAALGCLVKD  150
YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTKTY  200
TCNVDHKPSN TKVDKRVESK YGPPCPPCPA PEAAGGPSVF LFPPKPKDTL  250
MISRTPEVTC VVVDVSQEDP EVQFNWYVDG VEVHNAKTKP REEQFNSTYR  300
VVSVLTVLHQ DWLNGKEYKC KVSNKGLPSS IEKTISKAKG QPREPQVYTL  350
PPSQEEMTKN QVSLTCLVKG FYPSDIAVEW ESNGQPENNY KTTPPVLDSD  400
GSFFLYSRLT VDKSRWQEGN VFSCSVMHEA LHNHYTQKSL SLSLGAGGGG  450
SGGGGSGGGG SGGGGSGGAV KFPQLCKFCD VRFSTCDNQK SCMSNCSITS  500
ICEKPQEVCV AVWRKNDENI TLETVCHDPK LPYHDFILED AASPKCIMKE  550
KKKPGETFFM CSCSSDECND NIIFSEEYNT SNPD                    584
```

Light chain / Chaîne légère / Cadena ligera

```
DIVLTQSPAS LAVSPGQRAT ITCRASESVS IHGTHLMHWY QQKPGQPPKL   50
LIYAASNLES GVPARFSGSG SGTDFTLTIN PVEAEDTANY YCQQSFEDPL  100
TFGQGTKLEI KRTVAAPSVF IFPPSDEQLK SGTASVVCLL NNFYPREAKV  150
QWKVDNALQS GNSQESVTEQ DSKDSTYSLS STLTLSKADY EKHKVYACEV  200
THQGLSSPVT KSFNRGEC                                     218
```

Mutation sites / Sites de mutation / Posiciones de mutación

H52>G, G57>F, S227>P, F233>A, L234>A, K446>A, N85'>E
H52">G, G57">F, S227">P, F233">A, L234">A, K446">A, N85'">E

Post-translational modifications / Modifications post-traductionnelles / Modificaciones postraduccionales

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

Intra-H	22-96	146-202	260-320	366-424	
	22"-96"	146"-202"	260"-320"	366"-424"	
Intra-PDL1	476-509	479-496	486-492	502-526	546-561	563-568
	476"-509"	479"-496"	486"-492"	502"-526"	546"-561"	563"-568"
Intra-L	23'-92'	138'-198'				
	23'"-92'"	138'"-198'"				
Inter-H-L	133-218'	133"-218'"				
Inter-H-H	225-225"	228-228"				

Glycosylation sites / Sites de glycosylation / Posiciones de glicosilación

N296, N495, N519, N579,
N296", N495", N519", N579"

N-terminal pyroglutamyl / Pyroglutamyl N-terminal / Piroglutamil N-terminal

Q1,Q1">pE (5-oxo-L-prolyl, pyroglutamyl)

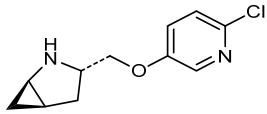
ropanicantum

ropanicant — (1*R*,3*S*,5*R*)-3-{[(6-chloropyridin-3-yl)oxy]methyl}-2-azabicyclo[3.1.0]hexane

ropanicant — (1*R*,3*S*,5*R*)-3-{[(6-chloropyridin-3-yl)oxy]méthyl}-2-azabicyclo[3.1.0]hexane

ropanicant — (1*R*,3*S*,5*R*)-3-{[(6-cloropiridin-3-il)oxi]metil}-2-azabiciclo[3.1.0]hexano

$C_{11}H_{13}ClN_2O$



runimotamabum

runimotamab — 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)] and anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], monoclonal antibody, bispecific;
gamma1 heavy chain anti-ERBB2 (1-450) [VH anti-ERBB2 (*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*03v, G1m3>G1m17, nG1m1, G1v30 CH2 G84.4, G1v32 CH3 W22 (CH1 R120>K (217) (121-218), hinge 1-15 (219-233), CH2 N84.4>G (300) (234-343), CH3 E12 (359), M14 (361), T22>W (369) (344-448), CHS (449-450)) (121-450)], (223-214')-disulfide with kappa light chain anti-ERBB2 (1'-214') [V-KAPPA anti-ERBB2 (*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')];

	gamma1 heavy chain anti-CD3E (1''-449'') [VH anti-CD3E (*Mus musculus* IGHV1-66*01 (82.7%) -(IGHD) -IGHJ2*01 (86.7%)/*Homo sapiens* anti-CD3E IGHV1-3*01(82.7%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1''-119'') -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1, G1v30 CH2 G84.4, G1v33 CH3 S22, A24, V86 (CH1 R120>K (216) (120''-217''), hinge 1-15 (218''-232''), CH2 N84.4>G (299) (233-342), CH3 E12 (358), M14 (360), T22>S (368), L24>A (370), Y86>V (409) (343''-447''), CHS (448''-449'')) (120''-449'')], (222''-219''')-disulfide with kappa light chain anti-CD3E (1'''-219''') [V-KAPPA anti-CD3E (*Homo sapiens* IGKV4-1*01 (91.8%) -IGKJ1*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 (229-228'':232-231'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, non-glycosylated
runimotamab	immunoglobuline G1-kappa, anti-[*Homo sapiens* ERBB2 (récepteur 2 du facteur de croissance épidermique, récepteur tyrosine-protéine kinase erbB2, EGFR2, HER2, HER-2, p185c-erbB2, NEU, CD340)] et anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)], anticorps monoclonal, bispécifique; chaîne lourde gamma1 anti-ERBB2 (1-450) [VH anti-ERBB2 (*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*03v, G1m3>G1m17, nG1m1, G1v30 CH2 G84.4, G1v32 CH3 W22 (CH1 R120>K (217) (121-218), charnière1-15 (219-233), CH2 N84.4>G (300) (234-343), CH3 E12 (359), M14 (361), T22>W (369), (344-448), CHS (449-450)) (121-450)], (223-214')-disulfure avec la chaîne légère kappa anti-ERBB2 (1'-214') [V-KAPPA anti-ERBB2 (*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')]; chaîne lourde gamma1 anti-CD3E (1''-449'') [VH anti-CD3E (*Mus musculus* IGHV1-66*01 (82.7%) -(IGHD) -IGHJ2*01 (86.7%)/*Homo sapiens* IGHV1-3*01 (82.7%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1''-119'') -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1, G1v30 CH2 G84.4, G1v33 CH3 S22, A24, V86 (CH1 R120>K (216) (120''-217''), charnière1-15 (218''-232''), CH2 N84.4>G (299) (233-342), CH3 E12 (358), M14 (360), T22>S (368), L24>A (370), Y86>V (409) (343''-447''), CHS (448''-449'')) (120''-449'')], (222''-219''')-disulfure avec la chaîne légère kappa anti-CD3E (1'''-219''') [V-KAPPA anti-CD3E (*Homo sapiens* IGKV4-1*01 (91.8%) -IGKJ1*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 (229-228'':232-231'')-bidisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), non-glycosylé
runimotamab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* ERBB2 (receptor 2 del factor de crecimiento epidérmico, receptor tirosina-proteína kinasa erbB2, EGFR2, HER2, HER-2, p185c-erbB2, NEU, CD340)] y anti-[*Homo sapiens* CD3E (CD3 épsilon, Leu-4)], anticuerpo monoclonal, biespecífico; cadena pesada gamma1 anti-ERBB2 (1-450) [VH anti-ERBB2 (*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*03v, G1m3>G1m17, nG1m1, G1v30 CH2 G84.4, G1v32 CH3 W22 (CH1 R120>K (217) (121-218), bisagra 1-15 (219-233), CH2 N84.4>G (300) (234-343), CH3 E12 (359), M14 (361), T22>W (369), (344-448), CHS (449-450)) (121-450)], (223-214')-disulfuro con la cadena ligera kappa anti-ERBB2 (1'-214') [V-KAPPA anti-ERBB2 (*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')];

cadena pesada gamma1 anti-CD3E (1"-449") [VH anti-CD3E (*Mus musculus* IGHV1-66*01 (82.7%) -(IGHD) -IGHJ2*01 (86.7%)/*Homo sapiens* IGHV1-3*01 (82.7%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1"-119") -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1, G1v30 CH2 G84.4, G1v33 CH3 S22, A24, V86 (CH1 R120>K (216) (120"-217"), bisagra 1-15 (218"-232"), CH2 N84.4>G (299) (233-342), CH3 E12 (358), M14 (360), T22>S (368), L24>A (370), Y86>V (409) (343"-447"), CHS (448"-449")) (120"-449")], (222"-219"')-disulfuro con la cadena ligera kappa anti-CD3E (1"'-219"') [V-KAPPA anti-CD3E (*Homo sapiens* IGKV4-1*01 (91.8%) -IGKJ1*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 (229-228":232-231")-bidisulfuro, producido en las células ováricas de hámster chino (CHO), no glicosilado

Heavy chain / Chaîne lourde / Cadena pesada (anti-ERBB2)

```
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 KTKPREEQYG 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ 350
VYTLPPSREE MTKNQVSLWC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPGK 450
```

Heavy chain / Chaîne lourde / Cadena pesada (anti-CD3E)

```
EVQLVQSGAE VKKPGASVKV SCKASGYTFT NYYIHWVRQA PGQGLEWIGW  50
IYPGDGNTKY NEKFKGRATL TADTSTSTAY LELSSLRSED TAVYYCARDS 100
YSNYYFDYWG QGTLVTVSSA STKGPSVFPL APSSKSTSGG TAALGCLVKD 150
YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY 200
ICNVNHKPSN TKVDKKVEPK SCDKTHTCPP CPAPELLGGP SVFLFPPKPK 250
DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VDGVEVHNAK TKPREEQYGS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKAL PAPIEKTISK AKGQPREPQV 350
YTLPPSREEM TKNQVSLSCA VKGFYPSDIA VEWESNGQPE NNYKTTPPVL 400
DSDGSFFLVS KLTVDKSRWQ QGNVFSCSVM HEALHNHYTQ KSLSLSPGK  449
```

Light chain / Chaîne légère / Cadena ligera (anti-ERBB2)

```
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
```

Light chain / Chaîne légère / Cadena ligera (anti-CD3E)

```
DIVMTQSPDS LAVSLGERAT INCKSSQSLL NSRTRKNYLA WYQQKPGQPP  50
KLLIYWASTR ESGVPDRFSG SGSGTDFTLT ISSLQAEDVA VYYCTQSFIL 100
RTFGQGTKVE 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) 22-96 147-203 264-324 370-428
22"-96" 146"-202" 263"-323" 369"-427"
Intra-L (C23-C104) 23'-88' 134'-194'
23"'-94"' 139"'-199"'
Inter-H-L (h 5-CL 126) 223-214' 222"-219"'
Inter-H-H (h 11, h 14) 229-228" 232-231"

No N-glycosylation sites / pas de sites de N-glycosylation / ningún posición de N-glicosilación
CH2 N84.4>G:
300, 299"
Aglycosylated

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
450, 449"

sapablursenum

sapablursen

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*-thiocytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyluridylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyluridylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyluridylyl-(3'→5')-2'-*O*-(2-methoxyethyl)adenylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-deoxy-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-deoxy-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-deoxy-*P*-thioadenylyl-(3'→5')-2'-deoxy-*P*-thioadenylyl-(3'→5')-2'-deoxy-*P*-thioadenylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methylcytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)adenylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-*P*-thioguanylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyluridine

sapablursen

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*-thiocytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyluridylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyluridylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyluridylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)adénylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-*P*-thiothymidylyl-(3'→5')-2'-désoxy-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-désoxy-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-désoxy-*P*-thioadénylyl-(3'→5')-2'-désoxy-*P*-thioadénylyl-(3'→5')-2'-désoxy-*P*-thioadénylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthylcytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)adénylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-*P*-thioguanylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyluridine

sapablursén

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)-5-metil-2'-*O*-(2-metoxietil)-*P*-tiocitidilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)uridilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)uridilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)uridilil-(3'→5')-2'-*O*-(2-metoxietil)adenilil-(3'→5')-*P*-tiotimidilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-desoxi-5-metil-*P*-tiocitidilil-(3'→5')-2'-desoxi-5-metil-*P*-tiocitidilil-(3'→5')-2'-desoxi-*P*-tioadenilil-(3'→5')-2'-desoxi-*P*-tioadenilil-(3'→5')-2'-desoxi-*P*-tioadenilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)citidilil-(3'→5')-2'-*O*-(2-metoxietil)adenilil-(3'→5')-2'-*O*-(2-metoxietil)-*P*-tioguanilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)-*P*-tiocitidilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)uridina

$C_{296}H_{436}N_{80}O_{155}P_{20}S_{13}$

(3'-5') R1-C=U-U-U-A-d(T=T=C=C=A=A=A=G=G=G=)C-A-G=C=U

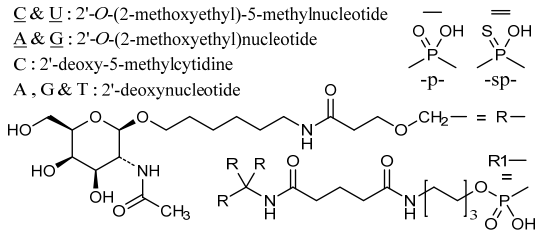
Legend:

C & U : 2'-*O*-(2-methoxyethyl)-5-methylnucleotide

A & G : 2'-*O*-(2-methoxyethyl)nucleotide

C : 2'-deoxy-5-methylcytidine

A , G & T : 2'-deoxynucleotide



sesiclenegenum cosaparvovecum #

sesiclenegene cosaparvovec	A non-replicating self-complementary adeno-associated virus (scAAV) vector encoding human ceroid-lipofuscinosis neuronal protein 6. A recombinant non-replicating self-complementary adeno-associated virus serotype 9 (scAAV9) vector, encoding human ceroid-lipofuscinosis neuronal protein 6 (CLN6), under the control of a hybrid CMV enhancer/chicken-beta-actin promoter and a bovine growth hormone (bGH) polyA sequence, with an SV40 intron 5' to the transgene, and flanked by AAV2 inverted terminal repeats (ITRs). The vector genome is a head-to-head, self-complementary dimer, with the vector genome cassette located 5′ of the mutated internal inverted terminal repeat (Δ-ITR) in a reverse complementary orientation and 3′ of the Δ-ITR in a forward orientation.
sésiclénégène cosaparvovec	Un vecteur viral adéno-associé auto-complémentaire (scAAV) non-répliquant codant la protéine neuronale céroïde-lipofuscinose 6 humaine. Un vecteur viral adéno-associé de sérotype 9 auto-complémentaire (scAAV9), recombinant, non-répliquant, codant la protéine neuronale céroïde-lipofuscinose 6 (CLN6) humaine, sous le contrôle de l'activateur hybride CMV/promoteur de la bêta-actine de poulet et d'une séquence polyA de l'hormone de croissance bovine (bGH), avec un intron SV40 dans la partie 5' du transgène, et flanquée de répétitions terminales inversées (ITRs) AAV2. Le génome du vecteur est un dimère en tête à tête, auto-complémentaire, avec la cassette génomique du vecteur localisée en 5' des répétitions terminales internes inversées mutées (Δ-ITR) en une orientation complémentaire inverse et en 3' de la Δ-ITR en une orientation en avant.
sesiclenegén cosaparvovec	Un vector de virus adeno-asociado auto complementario (scAAV), no replicativo, que codifica para la proteína 6 de la lipofuscinosis neuronal ceroidea humana.

	Un vector de virus adeno-asociado serotipo 9 auto complementario (scAAV9), recombinante, no replicativo, que codifica para la proteína 6 de la lipofuscinosis neuronal ceroidea (CLN6) humana, bajo el control de un híbrido del potenciador de CMV/promotor de la beta actina de pollo y una secuencia polyA de la hormona de crecimiento bovina (bGH), con un intrón de SV40 en 5' del transgén, y flanqueado por las repeticiones terminales invertidas (ITRs) del AAV2. El genoma del vector es un dímero cabeza con cabeza auto complementario, con el casete del genoma del vector localizado 5' de la repetición terminal invertida mutada (Δ-ITR) en una orientación complementaria reversa y 3' de (Δ-ITR) en orientación hacia delante.
sibeprenlimabum #	
sibeprenlimab	immunoglobulin G2-kappa, anti-[*Homo sapiens* TNFSF13 (tumor necrosis factor (TNF) superfamily member 13, APRIL, CD256)], humanized monoclonal antibody; gamma2 heavy chain humanized (1-446) [VH (*Homo sapiens* IGHV1-46*01 (85.7%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG2*01 (100%), G2m.. CH2 V45.1 (CH1 (121-218), hinge 1-12 (219-230), CH2 V45.1 (281) (231-339), CH3 (340-444), CHS (445-446)) (121-446)], (134-218')-disulfide with kappa light chain humanized (1'-218') [V-KAPPA (*Homo sapiens* IGKV3-15*01 (85.9%) -IGKJ4*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 (222-222":223-223":226-226":229-229")-tetrakisdisulfide, produced in a Chinese hamster ovary (CHO)-K1 derived cell line, glycoform alfa
sibéprenlimab	immunoglobuline G2-kappa, anti-[*Homo sapiens* TNFSF13 (membre 13 de la superfamille du facteur de nécrose tumorale, APRIL, CD256)], anticorps monoclonal humanisé; chaîne lourde gamma2 humanisée (1-446) [VH (*Homo sapiens* IGHV1-46*01 (85.7%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG2*01 (100%), G2m.. CH2 V45.1 (CH1 (121-218), charnière 1-12 (219-230), CH2 V45.1 (281) (231-339), CH3 (340-444), CHS (445-446)) (121-446)], (134-218')-disulfure avec la chaîne légère kappa humanisée (1'-218') [V-KAPPA (*Homo sapiens* IGKV3-15*01 (85.9%) -IGKJ4*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 (222-222":223-223":226-226":229-229")-tétrakisdisulfure, produite dans une lignée cellulaire dérivée des cellules ovariennes de hamster chinois (CHO)-K1, glycoforme alfa

sibeprenlimab

inmunoglobulina G2-kappa, anti-[*Homo sapiens* TNFSF13 (miembro 13 de la superfamilia del factor de necosis tumoral, APRIL, CD256)], anticuerpo monoclonal humanizado;
cadena pesada gamma2 humanizada (1-446) [VH (*Homo sapiens* IGHV1-46*01 (85.7%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.8.13] (26-33.51-58.97-109) (1-120) -*Homo sapiens* IGHG2*01 (100%), G2m.. CH2 V45.1 (CH1 (121-218), bisagra 1-12 (219-230), CH2 V45.1 (281) (231-339), CH3 (340-444), CHS (445-446)) (121-446)], (134-218')-disulfuro con la cadena ligera kappa humanizada (1'-218') [V-KAPPA (*Homo sapiens* IGKV3-15*01 (85.9%) -IGKJ4*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 (222-222":223-223":226-226":229-229")-tetrakisdisulfuro, producido en una línea celular derivada de las células ováricas de hámster chino (CHO)-K1, forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGASVKV SCKASGYTFT DYTIHWVRQA TGQGLEWMGW  50
IYPLRGSINY AQKFQGRVTM TADKSISTVY MELSSLRSED TAVYFCARHG 100
AYYSNAFDYW 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 SLSPGK     446
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Light chain / Chaîne légère / Cadena ligera

```
EIVMTQSPAT LSVSPGERAT LSCRASESVD NDGIRFLHWY QQKPGQAPRL  50
LIYRASTRAT GIPARFSGSG SRTEFTLTIS SLQSEDFAVY YCQQSNKDPY 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 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'-92' 138'-198'
23'"-92'" 138'"-198'"
Inter-H-L (CH1 10-CL 126) 134-218' 134"-218'"
Inter-H-H (h 4, h 5, h 8, h 11) 222-222" 223-223" 226-226" 229-229"

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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
446, 446"

simpiniclinum

simpinicline

5-{(1*E*)-2-[(3*R*)-pyrrolidin-3-yl]ethen-1-yl}pyrimidine

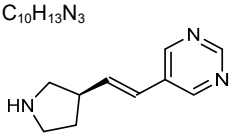
simpinicline

5-{(1*E*)-2-[(3*R*)-pyrrolidin-3-yl]éthén-1-yl}pyrimidine

simpiniclina

5-{(1*E*)-2-[(3*R*)-pirrolidin-3-il]eten-1-il}pirimidina

$C_{10}H_{13}N_3$



sirelretigenum suboparvovecum #

sirelretigene suboparvovec	A non-replicating self-complementary adeno-associated virus serotype 8 (scAAV8) vector, encoding human cellular retinaldehyde-binding protein (CRALBP). A recombinant non-replicating self-complementary adeno-associated virus serotype 8 (scAAV8) vector, encoding human cellular retinaldehyde-binding protein (CRALBP) under the control of the retinaldehyde-binding protein 1 promoter (pRLBP1) and terminated with SV40 poly adenylation (polyA) sequence. The vector genome is a head-to-head, self-complementary dimer, with the vector genome cassette located 5' of the mutated internal inverted terminal repeat (Δ-ITR) in a reverse complementary orientation and 3' of the Δ-ITR in a forward orientation.
sirelrétigène suboparvovec	Un vecteur du virus adéno-associé de sérotype 8 auto-complémentaire (scAAV8), non-répliquant, codant la protéinecellulaire humaine liée au rétinaldéhyde (CRALBP). Un vecteur du virus adéno-associé de sérotype 8 auto-complémentaire (scAAV8) recombinant, non-répliquant codant la protéine cellulaire humaine liée au rétinaldéhyde (CRALBP) sous le contrôle du promoteur de la protéine 1 liée au rétinaldéhyde (pRLBP1) et terminé par la séquence polyadénylée (polyA) SV40. Le génome du vecteur est un dimère en tête à tête, auto-complémentaire, avec la cassette génomique du vecteur localisée en 5' des répétitions terminales internes inversées mutées (Δ-ITR) en une orientation complémentaire inverse et en 3' de la Δ-ITR en une orientation en avant.
sirelretigén suboparvovec	Un vector de virus adeno-asociado serotipo 8 auto complementario (scAAV8), no replicativo, que codifica para la proteína de unión a retinaldehído celular (CRALBP) humana. Un vector de virus adeno-asociado serotipo 8 auto complementario (scAAV8) recombinante, no replicativo, que codifica para la proteína de unión a retinaldehído celular (CRALBP) humana bajo el control del promotor de la proteína de unión a retinaldehído 1 (pRLBP1) y terminado por la secuencia de poliadenilación (polyA) de SV40. El genoma del vector es un dímero cabeza con cabeza auto complementario, con el casete del genoma del vector localizado 5' de la repetición terminal invertida mutada (Δ-ITR) en una orientación complementaria reversa y 3' de (Δ-ITR) en orientación hacia delante.

sudubrilimabum #

sudubrilimab	immunoglobulin G1-kappa, anti-[*Homo sapiens* CD274 (programmed death ligand 1, PDL1, PD-L1, B7 homolog 1, B7H1)], monoclonal antibody;

	gamma1 heavy chain (1-447) [VH (*Homo sapiens* IGHV3-23*04 (85.7%) -(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 R120>K (215) (119-216), hinge 1-15 (217-231), CH2 N84.4>A (298) (232-341), CH3 E12 (357), M14 (359) (342-446), CHS K>del (447)) (119-447)], (221-214')-disulfide with kappa light chain (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (90.0%) -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 (227-227'':230-230'')-bisdisulfide, produced in a Chinese hamster ovary (CHO)-K1 cell line, non-glycosylated
sudubrilimab	immunoglobuline G1-kappa, anti-[*Homo sapiens* CD274 (ligand 1 de mort programmée, PDL1, PD-L1, homologue 1 de B7, B7H1)], anticorps monoclonal; chaîne lourde gamma1 (1-447) [VH (*Homo sapiens* IGHV3-23*04 (85.7%) -(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 R120>K (215) (119-216), charnière 1-15 (217-231), CH2 N84.4>A (298) (232-341), CH3 E12 (357), M14 (359) (342-446), CHS K>del (447)) (119-447)], (221-214')-disulfure avec la chaîne légère kappa (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (90.0%) -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 (227-227'':230-230'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-K1, non-glycosylé
sudubrilimab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* CD274 (ligando 1 de muerte programada, PDL1, PD-L1, homólogo 1 de B7, B7H1)], anticuerpo monoclonal; cadena pesada gamma1 (1-447) [VH (*Homo sapiens* IGHV3-23*04 (85.7%) -(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 R120>K (215) (119-216), bisagra 1-15 (217-231), CH2 N84.4>A (298) (232-341), CH3 E12 (357), M14 (359) (342-446), CHS K>del (447)) (119-447)], (221-214')-disulfuro con la cadena ligera kappa (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (90.0%) -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 (227-227'':230-230'')-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-K1, no glicosilado

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGGSLRL SCAASGFTFS ETWLHWVRQA PGKGLEWVAW  50
VSPFGGSTYY ADSVKGRFTI SADTSKNTAY LQMNSLRAED TAVYYCARRH 100
WPGGFDYWGQ GTLVTVSSAS TKGPSVFPLA PSSKSTSGGT AALGCLVKDY 150
FPEPVTVSWN SGALTSGVHT FPAVLQSSGL YSLSSVVTVP SSSLGTQTYI 200
CNVNHKPSNT KVDKKVEPKS CDKTHTCPPC PAPELLGGPS VFLFPPKPKD 250
TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYAST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY 350
TLPPSREEMT KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD 400
SDGSFFLYSK LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPG    447
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Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS LSASVGDRVT ITCRASQDVS TAVAWYQQKP GKAPKLLIYS  50
ASFLYSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ FLYHPATFGQ 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) 22-96 145-201 262-322 368-426
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 (h11, h 14) 227-227" 230-230"

No N-glycosylation sites / Pas de sites de N-glycosylation / ningún posición de N-glicosilación
CH2 N84.4>A:
298, 298"
Aglycosylated

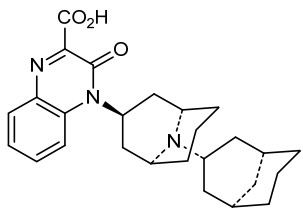
sunobinopum

sunobinop — 4-[(1*R*,1'*R*,3*r*,3'*r*,5*S*,5'*S*)-9'-aza[3,9'-bi(bicyclo[3.3.1]nonan)]-3'-yl]-3-oxo-3,4-dihydroquinoxaline-2-carboxylic acid

sunobinop — acide 4-[(1*R*,1'*R*,3*r*,3'*r*,5*S*,5'*S*)-9'-aza[3,9'-bi(bicyclo[3.3.1]nonan)]-3'-yl]-3-oxo-3,4-dihydroquinoxaline-2-carboxylique

sunobinop — ácido 4-[(1*R*,1'*R*,3*r*,3'*r*,5*S*,5'*S*)-9'-aza[3,9'-bi(biciclo[3.3.1]nonan)]-3'-il]-3-oxo-3,4-dihidroquinoxalina-2-carboxílico

$C_{26}H_{33}N_3O_3$



surzebiclimabum #

surzebiclimab — immunoglobulin G1-kappa, anti-[*Homo sapiens* HAVCR2 (hepatitis A virus cellular receptor 2, T-cell immunoglobulin mucin family member 3, Tim-3, TIM3, TIMD3, CD366)], monoclonal antibody; gamma1 heavy chain (1-448) [VH (*Homo sapiens* IGHV3-23*04 (93.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.7.13] (26-33.51-57.96-108) (1-119) -*Homo sapiens* IGHG1*01, G1m17,1, G1v4 CH2 A114 (CH1 K120 (217) (120-217), hinge 1-15 (218-232), linker (233-237), CH2 P114>A (330) (238-341), CH3 D12 (357), L14 (359) (342-446), CHS (447-448)) (120-448)], (222-218')-disulfide with kappa light chain (1'-218') [V-KAPPA (*Homo sapiens* IGKV3-15*01 (84%) -IGKJ4*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 (228-228":231-231")-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

surzébiclimab

immunoglobuline G1-kappa, anti-[*Homo sapiens* HAVCR2 (récepteur cellulaire 2 du virus de l'hépatite A, CD366, membre 3 de la famille mucine immunoglobuline des cellules T, Tim-3, TIM3, TIMD3, CD366)], anticorps monoclonal;
chaîne lourde gamma1 (1-448) [VH (*Homo sapiens* IGHV3-23*04 (93.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.7.13] (26-33.51-57.96-108) (1-119) -*Homo sapiens* IGHG1*01, G1m17,1, G1v4 CH2 A114 (CH1 K120 (217) (120-217), charnière 1-15 (218-232), linker (233-237), CH2 P114>A (330) (238-341), CH3 D12 (357), L14 (359) (342-446), CHS (447-448)) (120-448)], (222-218')-disulfure avec la chaîne légère kappa (1'-218') [V-KAPPA (*Homo sapiens* IGKV3-15*01 (84.0%) -IGKJ4*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 (228-228":231-231")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

surzebiclimab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* HAVCR2 (receptor celular 2 del virus de la hepatitis A, CD366, miembro 3 de la familia mucina inmunoglobulina de las células T, Tim-3, TIM3, TIMD3, CD366)], anticuerpo monoclonal;
cadena pesada gamma1 (1-448) [VH (*Homo sapiens* IGHV3-23*04 (93.8%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.7.13] (26-33.51-57.96-108) (1-119) -*Homo sapiens* IGHG1*01, G1m17,1, G1v4 CH2 A114 (CH1 K120 (217) (120-217), bisagra 1-15 (218-232), linker (233-237), CH2 P114>A (330) (238-341), CH3 D12 (357), L14 (359) (342-446), CHS (447-448)) (120-448)], (222-218')-disulfuro con la cadena ligera kappa (1'-218') [V-KAPPA (*Homo sapiens* IGKV3-15*01 (84.0%) -IGKJ4*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 (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 RYAMSWVRQA PGKGLEWVAA  50
ISSGGSLYYP DSVKGRFTIS RDNAKNTLYL QMNSLRAEDT AVYYCARGRE 100
ADGGYFDYWG QGTLVTVSSA STKGPSVFPL APSSKSTSGG TAALGCLVKD 150
YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY 200
ICNVNHKPSN TKVDKKVEPK SCDKTHTCPP CPAPPAAGPS VFLFPPKPKD 250
TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKALA 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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EIVLTQSPAT LSVSPGERAT LSCRASESVE YYGTSLMQWY QQKPGQAPRL  50
LIYAASNVES GIPARFSGSG SGTEFTLTIS SLQSEDFAVY YCQQSLKVPL 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 disulfuro
Intra-H (C23-C104) 22-95 146-202 262-322 368-426
22"-95" 146"-202" 262"-322" 368"-426"
Intra-L (C23-C104) 23'-92' 138'-198'
23'"-92'" 138'"-198'"
Inter-H-L (h 5-CL 126) 222-218' 222"-218'"
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:
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"

tacatresgenum autoleucelum #

tacatresgene autoleucel	Autologous T cells obtained from the peripheral blood of patients, collected by leukapheresis, modified by CRISPR/Cas9 (clustered regularly interspaced short palindromic repeats/CRISPR-associated protein 9) mediated gene editing consisting of two guide RNAs (gRNAs) introduced transiently as ribonucleoprotein (RNP) complex, and a neoepitope T cell receptor (neo-TCR) gene cassette encoded by plasmid DNA to replace the endogenous T cell receptor (TCR) with a single patient-derived tumour-specific neo-TCR per T cell, with a maximum of three different neo-TCRs in the final drug substance. The constant elements of the neo-TCR are identical for each patient and the neo-TCR gene expression is regulated by the native endogenous TCR promoter. The T cells are cultured in the presence of growth media containing IL-7 and IL-15 and a combination of membrane bound anti-CD3 and anti-CD28 for activation. The T cells are predominantly CD4 and CD8 T cells (generally >80%), including Tmsc (memory stem cells) and Tcm (central memory) phenotypes.
tacatresgène autoleucel	Lymphocytes T autologues obtenus du sang périphérique de patients, recueillis par leucophérèse, modifiés par CRISPR/Cas9 (courtes répétitions palindromiques groupées et régulièrement espacées / protéine 9 associée à CRISPR) induisant une édition génétique consistant en deux ARN guides (gRNAs) introduisant transitoirement un complexe ribonucléoprotéique, et la cassette du gène du récepteur néo-épitope du lymphocyte T (néo-TCR) encodés par un plasmide d'ADN pour remplacer le récepteur endogène du lymphocyte T (TCR) avec un seul néo-TCR tumeur-spécifique dérivé de patients pour chaque lymphocyte T, avec un maximum de trois néo-TCRs différents dans la substance médicamenteuse finale. Les éléments constants des néo-TCR sont identiques pour chaque patient et l'expression du gène néo-TCR est régulée par le promoteur natif endogène du TCR. Les lymphocytes T sont cultivés en présence de milieu de croissance contenant IL-7 et IL-15 et une combinaison d'anti-CD3 et anti-CD28 liés à la membrane pour l'activation. Les lymphocytes T sont majoritairement des lymphocytes T CD4 et CD8 (généralement >80%), incluant les phénotypes Tmsc (cellules souches à mémoire) et Tcm (à mémoire centrale).
tacatresgén autoleucel	Linfocitos T autólogos obtenidos de sangre periférica de pacientes, recogidos por leucoaféresis, modificados por CRISPR/Cas9 (repeticiones palindrómicas cortas agrupadas y regularmente espaciadas/proteína asociada a CRISPR 9) mediante edición genética consistente en dos RNAs guía (gRNAs) introducidos transitoriamente como un complejo de ribonucleoproteína (RNP), y un casete genético de un receptor de linfocitos T para un neoepítopo (neo-TCR) codificado en un plásmido de DNA, para reemplazar el receptor de linfocitos T (TCR) endógeno con un solo neo-TCR específico de tumor y derivado del paciente por linfocito T, con un máximo de tres neo-TCRs diferentes en el principio activo final. Los

elementos constantes de los neo-TCR son idénticos para cada paciente y la expresión del gen del neo-TCR está rgulada por el promotor nativo del TCR endógeno. Los linfocitos T se cultivan en presencia de medio de crecimiento que contiene IL-7 e IL-15 y una combinación de anti-CD3 y anti-CD28 de membrana para la activación. Los linfocitos T son predominantemente CD4 y CD8 (generalmente >80%), incluyendo fenotipos de Tmsc (células madre de memoria) y Tcm (memoria central).

tadnersenum

tadnersen	*all-P-ambo*-2'-*O*-(2-methoxyethyl)-*P*-thioguanylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methylcytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methylcytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-deoxy-5-methyl-*P*-thiocytidylyl-(3'→5')-*P*-thiothymidylyl-(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-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-deoxy-*P*-thioguanylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methylcytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)guanylyl-(3'→5')-2'-*O*-(2-methoxyethyl)adenylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-methoxyethyl)-5-methylcytidine
tadnersen	*tout-P-ambo*-2'-*O*-(2-méthoxyéthyl)-*P*-thioguanylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthylcytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthylcytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-désoxy-5-méthyl-*P*-thiocytidylyl-(3'→5')-*P*-thiothymidylyl-(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-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-désoxy-*P*-thioguanylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthylcytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)guanylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)adénylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthyl-*P*-thiouridylyl-(3'→5')-2'-*O*-(2-méthoxyéthyl)-5-méthylcytidine
tadnersén	*todo-P-ambo*-2'-*O*-(2-metoxietil)-*P*-tioguanilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)citidilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)citidilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)-*P*-tiocitidilil-(3'→5')-2'-deoxi-5-metil-*P*-tiocitidilil-(3'→5')-*P*-tiotimidilil-(3'→5')-2'-deoxi-*P*-tioadenilil-(3'→5')-2'-deoxi-*P*-tioguanilil-(3'→5')-2'-deoxi-5-metil-*P*-tiocitidilil-(3'→5')-2'-deoxi-*P*-tioguanilil-(3'→5')-2'-deoxi-5-metil-*P*-tiocitidilil-(3'→5')-2'-deoxi-*P*-tioguanilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)citidilil-(3'→5')-2'-*O*-(2-metoxietil)guanilil-(3'→5')-2'-*O*-(2-metoxietil)adenilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)-*P*-tiocitidilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)-*P*-tiouridilil-(3'→5')-5-metil-2'-*O*-(2-metoxietil)citidina

$C_{210}H_{297}N_{66}O_{114}P_{17}S_{12}$

(3'-5') G=C=C−C−d(C=T=A=G=C=G=C=G=)C=G−A−C=U=C

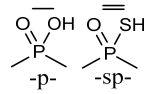
Legend:

A , G & T : 2'-deoxynucleotide

C : 2'-deoxy-5-methylnucleotide

A & G : 2'-*O*-(2-methoxyethyl)nucleotide

C & U : 2'-*O*-(2-methoxyethyl)-5-methylnucleotide



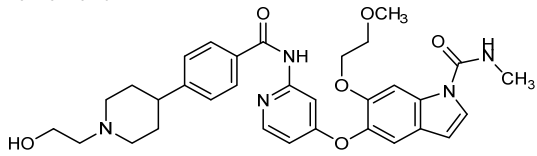
tasurgratinibum

tasurgratinib — 1^1-(2-hydroxyethyl)-7^6-(2-methoxyethoxy)-*N*-methyl-3-oxo-7^1*H*-6-oxa-4-aza-7(5)-indola-5(2,4)-pyridina-1(4)-piperidina-2(1,4)-benzenahepta-phane-7^1-carboxamide

tasurgratinib — 1^1-(2-hydroxyéthyl)-7^6-(2-méthoxyéthoxy)-*N*-méthyl-3-oxo-7^1*H*-6-oxa-4-aza-7(5)-indola-5(2,4)-pyridina-1(4)-pipéridina-2(1,4)-benzénahepta-phane-7^1-carboxamide

tasurgratinib — 1^1-(2-hidroxietil)-*N*-metil-7^6-(2-metoxietoxi)-3-oxo-7^1*H*-6-oxa-4-aza-7(5)-indola-5(2,4)-piridina-1(4)-piperidina-2(1,4)-bencenaheptafano-7^1-carboxamida

$C_{32}H_{37}N_5O_6$



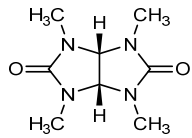
temgicolurilum

temgicoluril — *cis*-1,3,4,6-tetramethyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione

temgicoluril — *cis*-1,3,4,6-tétraméthyltétrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione

temgicoluril — *cis*-1,3,4,6-tetrametiltetrahidroimidazo[4,5-*d*]imidazola-2,5(1*H*,3*H*)-diona

$C_8H_{14}N_4O_2$



tenofovirum amibufenamidum

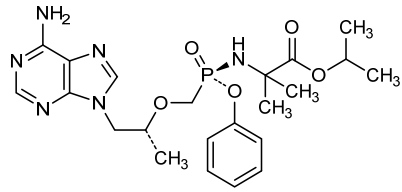
tenofovir amibufenamide — propan-2-yl 2-{[(*S*)-({[(2*R*)-1-(6-amino-9*H*-purin-9-yl)propan-2-yl]oxy}methyl)(phenoxy)phosphinoyl]amino}-2-methylpropanoate

ténofovir amibufénamide — 2-{[(*S*)-({[(2*R*)-1-(6-amino-9*H*-purin-9-yl)propan-2-yl]oxy}méthyl)(phénoxy)phosphinoyl]amino}-2-méthylpropanoate de propan-2-yle

tenofovir amibufenamida

2-{[(*S*)-({[(2*R*)-1-(6-amino-9*H*-purin-9-il)propan-2-il]oxi}metil)(fenoxi)fosfinoil]amino}-2-metilpropanoato de propan-2-ilo

$C_{22}H_{31}N_6O_5P$



tifcemalimabum #

tifcemalimab

immunoglobulin G4-kappa, anti-[*Homo sapiens* BTLA (B and T lymphocyte associated, BTLA1, CD272)], chimeric monoclonal antibody;
gamma4 heavy chain chimeric (1-446) [VH (*Mus musculus* IGHV14-3*02 (82.3%) -IGHJ3*01 (91.7%)/*Homo sapiens* IGHV1-3*01 (77.1%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -*Homo sapiens* IGHG4*01, G4v5 h P10 (CH1 (120-217), hinge 1-12 S10>P (227) (218-229), CH2 (230-339), CH3 (340-444), CHS (445-446)) (120-446)], (133-219')-disulfide with kappa light chain chimeric (1'-219') [V-KAPPA (*Mus musculus* IGKV1-135*01 (92%) -IGKJ2*03 (91.7%)/*Homo sapiens* IGKV2-30*01 (87.0%) -IGKJ2*01 (100%)) CDR-IMGT [11.3.9] (27-47.55-57.94-102) (1'-112') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (158), V101 (196) (113'-219')];
dimer (225-225'':228-228'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

tifcémalimab

immunoglobuline G4-kappa, anti-[*Homo sapiens* BTLA (atténuateur des lymphocytes B et T, BTLA1, CD272)], anticorps monoclonal chimérique;
chaîne lourde gamma4 chimérique (1-446) [VH (*Mus musculus* IGHV14-3*02 (82.3%) -IGHJ3*01 (91.7%)/*Homo sapiens* IGHV1-3*01 (77.1%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -*Homo sapiens* IGHG4*01, G4v5 h P10 (CH1 (120-217), charnière 1-12 S10>P (227) (218-229), CH2 (230-339), CH3 (340-444), CHS (445-446)) (120-446)], (133-219')-disulfure avec la chaîne légère kappa chimérique (1'-219') [V-KAPPA (*Mus musculus* IGKV1-135*01 (92%) -IGKJ2*03 (91.7%)/*Homo sapiens* IGKV2-30*01 (87.0%) -IGKJ2*01 (100%)) CDR-IMGT [11.3.9] (27-47.55-57.94-102) (1'-112') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (158), V101 (196) (113'-219')];
dimère (225-225'':228-228'')-bisdisulfure, produite dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

tifcemalimab

inmunoglobulina G4-kappa, anti-[*Homo sapiens* BTLA (atenuador de linfocitos B y T, BTLA1, CD272)], anticuerpo monoclonal quimérico;
cadena pesada gamma4 quimérica (1-446) [VH (*Mus musculus* IGHV14-3*02 (82.3%) -IGHJ3*01 (91.7%)/*Homo sapiens* IGHV1-3*01 (77.1%) -(IGHD) -IGHJ4*01 (92.9%)) CDR-IMGT [8.8.12] (26-33.51-58.97-108) (1-119) -*Homo sapiens* IGHG4*01, G4v5 h P10 (CH1 (120-217), bisagra 1-12 S10>P (227) (218-229), CH2 (230-339), CH3 (340-444), CHS (445-446)) (120-446)], (133-219')-disulfuro con la cadena ligera kappa quimérica (1'-219') [V-KAPPA (*Mus musculus* IGKV1-135*01 (92%) -IGKJ2*03 (91.7%)/*Homo sapiens* IGKV2-30*01 (87.0%) -IGKJ2*01 (100%)) CDR-IMGT [11.3.9] (27-47.55-57.94-102) (1'-112') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (158), V101 (196) (113'-219')];
dímero (225-225'':228-228'')-bisdisulfuro, producida por células ováricas de hamster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLVQSGAE VKKPGASVKL SCKASGYNFK HTYAHWVRQA PGQGLEWIGR  50
IDPANGNTKY DPKFQGRATM TADTASNTAY LELSSLRSED TAVYYCVADH 100
YGSSLLDYWG QGTLVTVSSA 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
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Light chain / Chaîne légère / Cadena ligera

```
DVVMTQTPLS LSVTPGQPAS ISCKSSQSLL DSDGKTYLNW FQQRPGQSPR  50
RLIYLVSKLD SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCWQGTYFP 100
YTFGQGTKLE IKRTVAAPSV FIFPPSDEQL KSGTASVVCL LNNFYPREAK 150
VQWKVDNALQ SGNSQESVTE QDSKDSTYSL SSTLTLSKAD YEKHKVYACE 200
VTHQGLSSPV TKSFNRGEC                                   219
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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	146-202	260-320	366-424
	22''-96''	146''-202''	260''-320''	366''-424''
Intra-L (C23-C104)	23'-93'	139'-199'		
	23'''-93'''	139'''-199'''		
Inter-H-L (CH1 10-CL 126)	133-219'	133''-219'''		
Inter-H-H (h 8, h 11)	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-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

tigulixostatum

tigulixostat

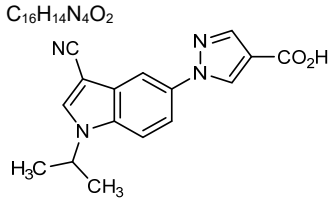
1-[3-cyano-1-(propan-2-yl)-1*H*-indol-5-yl]-1*H*-pyrazole-4-carboxylic acid

tigulixostat

acide 1-[3-cyano-1-(propan-2-yl)-1*H*-indol-5-yl]-1*H*-pyrazole-4-carboxylique

tigulixostat

ácido 1-[3-ciano-1-(propan-2-il)-1*H*-indol-5-il]-1*H*-pirazola-4-carboxílico



tirnovetmabum #

tirnovetmab	immunoglobulin G2-kappa, anti-[*Canis lupus familiaris* IL31 (interleukin 31)], caninized monoclonal antibody; gamma2 heavy chain caninized (1-453) [VH caninized (*Canis lupus familiaris* IGHV4-1*01 (61.2%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.7.12] (26-33.51-57.96-107) (1-118) -*Canis lupus familiaris* IGHG2*02 (100%) (CH1 (119-215), hinge 1-19 (216-234), CH2 (235-344), CH3 (345-451), CHS (452-453)) (119-453)], (133-217')-disulfide with kappa light chain caninized (1'-221') [V-KAPPA caninized (*Canis lupus familiaris* IGKV3-18*01 (63.8%) -IGKJ3*01 (83.3%) Q120>G (104)) CDR-IMGT [10.3.9](27-36.54-56.93-101) (1'-111') -*Canis lupus familiaris* IGKC*01 (100%) (112'-221')]; dimer (230-230'':233-233'')-bisdisulfide, produced in a Chinese hamster ovary (CHO)-K1 cell line, glycoform alfa
tirnovetmab	immunoglobuline G2-kappa, anti-[*Canis lupus familiaris* IL31 (interleukine 31)], anticorps monoclonal caninisé; chaîne lourde gamma2 caninisée (1-453) [VH caninisé (*Canis lupus familiaris* IGHV4-1*01 (61.2%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.7.12] (26-33.51-57.96-107) (1-118) CDR-IMGT [8.7.12] (26-33.51-57.96-107) (1-118) -*Canis lupus familiaris* IGHG2*02 (100%) (CH1 (119-215), charnière 1-19 (216-234), CH2 (235-344), CH3 (345-451), CHS (452-453)) (119-453)], (133-217')-disulfure avec la chaîne légère kappa caninisé (1'-221') [V-KAPPA caninisé (*Canis lupus familiaris* IGKV3-18*01 (63.8%) -IGKJ3*01 (83.3%) Q120>G (104)) CDR-IMGT [10.3.9](27-36.54-56.93-101) (1'-111') -*Canis lupus familiaris* IGKC*01 (100%) (112'-221')]; dimère (230-230'':233-233'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-K1, glycoforme alfa
tirnovetmab	inmunoglobulina G2-kappa, anti-[*Canis lupus familiaris* IL31 (interleukina 31)], anticuerpo monoclonal caninizado; cadena pesada gamma2 caninizada (1-453) [VH caninizado (*Canis lupus familiaris* IGHV4-1*01 (61.2%) -(IGHD) -IGHJ4*01 (100%)) CDR-IMGT [8.7.12] (26-33.51-57.96-107) (1-118) CDR-IMGT [8.7.12] (26-33.51-57.96-107) (1-118) -*Canis lupus familiaris* IGHG2*02 (100%) (CH1 (119-215), bisagra 1-19 (216-234), CH2 (235-344), CH3 (345-451), CHS (452-453)) (119-453)], (133-217')-disulfuro con la cadena ligera

kappa caninizada (1'-221') [V-KAPPA caninizado (*Canis lupus familiaris* IGKV3-18*01 (63.8%) -IGKJ3*01 (83.3%) Q120>G (104)) CDR-IMGT [10.3.9] (27-36.54-56.93-101) (1'-111') -*Canis lupus familiaris* IGKC*01 (100%) (112'-221')]; 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

```
EVQLVESGPS LVKPGGSLRL TCSVTGDSIT SGYWNWIRKF PGNKLEYMGY  50
ISYSGITDYN PSLKSRITIS RDTSKNQYYL QLNSVTTEDT ATYYCARYGN 100
YGYAMDYWGQ GTSVTVSSAS TTAPSVFPLA PSCGSTSGST VALACLVSGY 150
FPEPVTVSWN SGSLTSGVHT FPSVLQSSGL YSLSSMVTVP SSRWPSETFT 200
CNVAHPASKT KVDKPVPKRE NGRVPRPPDC PKCPAPEMLG GPSVFIFPPK 250
PKDTLLIART PEVTCVVVDL DPEDPEVQIS WFVDGKQMQT AKTQPREEQF 300
NGTYRVVSVL PIGHQDWLKG KQFTCKVNNK ALPSPIERTI SKARGQAHQP 350
SVYVLPPSRE ELSKNTVSLT CLIKDFFPPD IDVEWQSNGQ QEPESKYRTT 400
PPQLDEDGSY FLYSKLSVDK SRWQRGDTFI CAVMHEALHN HYTQESLSHS 450
PGK                                                     453
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Light chain / Chaîne légère / Cadena ligera

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DIVMTQSPAS LSVSLGQRAT ISCRASESVD TYGNSFMHWY QQKPGQSPKL  50
LIYRASNLES GIPARFGGSG SGTDFTLTID PVQADDVATY YCQQSYEDPW 100
TFGGGTKLEI KRNDAQPAVY LFQPSPDQLH TGSASVVCLL NSFYPKDINV 150
KWKVDGVIQD TGIQESVTEQ DKDSTYSLSS TLTMSSTEYL SHELYSCEIT 200
HKSLPSTLIK SFQRSECQRV D                                 221
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-95 145-201 265-325 371-431
22"-95" 145"-201" 265"-325" 371"-431"
Intra-L (C23-C104) 23'-92' 138'-197'
23'"-92'" 138'"-197'"
Inter-H-L (CH1 11-CL 126) 133-217' 133"-217'"
Inter-H-H (h 15, h 18) 230-230" 233-233"

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

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
453, 453"

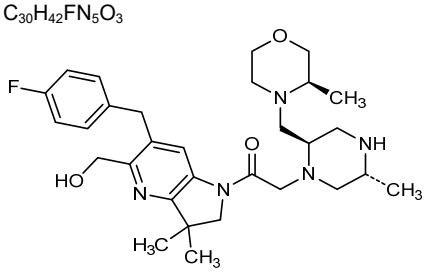
tolinapantum

tolinapant — (6^{2}*R*,6^{5}*R*,8^{3}*R*)-1^{4}-fluoro-3^{5}-(hydroxymethyl)-3^{3},3^{3},6^{5},8^{3}-tetramethyl-3^{2,3}-dihydro-3(6,1)-pyrrolo[3,2-*b*]pyridina-8(4)-morpholina-6(1,2)-piperazina-1(1)-benzenaoctaphan-4-one

tolinapant — (6^{2}*R*,6^{5}*R*,8^{3}*R*)-1^{4}-fluoro-3^{5}-(hydroxymethyl)-3^{3},3^{3},6^{5},8^{3}-tetramethyl-3^{2,3}-dihydro-3(6,1)-pyrrolo[3,2-*b*]pyridina-8(4)-morpholina-6(1,2)-piperazina-1(1)-benzenaoctaphan-4-one

tolinapant — (6^{2}*R*,6^{5}*R*,8^{3}*R*)-1^{4}-fluoro-3^{5}-(hidroximetil)-3^{3},3^{3},6^{5},8^{3}-tetrametil-3^{2,3}-dihidro-3(6,1)-pirrolo[3,2-*b*]piridina-8(4)-morfolina-6(1,2)-piperazina-1(1)-bencenaoctafan-4-ona

$C_{30}H_{42}FN_5O_3$



tomligisiranum

tomligisiran

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-(acetylamino)-2-deoxy-β-D-galactopyranosyl]oxy}-3,8-bis{[2-(2-{[2-(acetylamino)-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*-methylcytidylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-deoxy-2'-fluoroguanylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-deoxy-2'-fluoroadenylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methyl-*P*-thio-3'-adenylate,
duplex with *all-P-ambo*-2'-*O*-methyl-*P*-thiouridylyl-(3'→5')-2'-deoxy-2'-fluoro-*P*-thioadenylyl-(3'→5')-2'-*O*-methyl-*P*-thiocytidylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(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*-methyluridylyl-(3'→5')-2'-deoxy-2'-fluoroadenylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-deoxy-2'-fluoroguanylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-deoxy-2'-fluoroadenylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-deoxy-2'-fluoroadenylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-methylguanosine

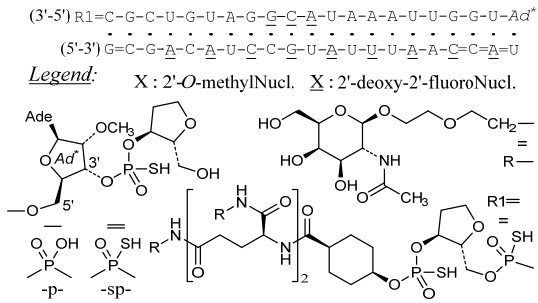
tomligisiran

tout-P-ambo-5'-*O*-({[(2*R*,3*S*)-3-{[({*cis*-4-[(3*S*,8*S*)-17-{[2-(acétylamino)-2-désoxy-β-D-galactopyranosyl]oxy}-3,8-bis{[2-(2-{[2-(acétylamino)-2-désoxy-β-D-galactopyranosyl]oxy}éthoxy)éthyl]carbamoyl}-6,11-dioxo-15-oxa-2,7,12-triazaheptadecan-1-oyl]cyclohexyl}oxy)hydroxyphos-phorothioyl]oxy}oxolan-2-yl]méthoxy}hydroxyphosphorothioyl)-2'-*O*-méthylcytidylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthylcytidylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-désoxy-2'-fluoroguanylyl-(3'→5')-2'-désoxy-2'-fluorocytidylyl-(3'→5')-2'-désoxy-2'-fluoroadénylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-hydrogéno-2'-*O*-méthyl-*P*-thio-3'-adénylate de *O*-[(2*R*,3*S*)-2-(hydroxyméthyl)oxolan-3-yle],
duplex avec *tout-P-ambo*-2'-*O*-méthyl-*P*-thiouridylyl-(3'→5')-2'-désoxy-2'-fluoro-*P*-thioadénylyl-(3'→5')-2'-*O*-méthyl-*P*-thiocytidylyl-(3'→5')-2'-désoxy-2'-fluorocytidylyl-(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*-méthyluridylyl-(3'→5')-2'-désoxy-2'-fluoroadénylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-désoxy-2'-fluoroguanylyl-(3'→5')-2'-*O*-méthylcytidylyl-(3'→5')-2'-désoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-désoxy-2'-fluoroadénylyl-(3'→5')-2'-*O*-méthylcytidylyl-(3'→5')-2'-désoxy-2'-fluoroadénylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthyl-*P*-thiocytidylyl-(3'→5')-2'-*O*-méthylguanosine

tomligisirán

all-P-ambo-5'-*O*-({[(2*R*,3*S*)-3-{[({*cis*-4-[(3*S*,8*S*)-17-{[2-(acetilamino)-2-desoxi-β-D-galactopiranosil]oxi}-3,8-bis{[2-(2-{[2-(acetilamino)-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*-metilcitidilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metilcitidilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-desoxi-2'-fluoroguanilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-desoxi-2'-fluoroadenilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-hidrógeno-2'-*O*-metil-*P*-tio-3'-adenilato de *O*-[(2*R*,3*S*)-2-(hidroximetil)oxolan-3-ilo], dúplex con *todo-P-ambo*-2'-*O*-metil-*P*-tiouridilil-(3'→5')-2'-desoxi-2'-fluoro-*P*-tioadenilil-(3'→5')-2'-*O*-metil-*P*-tiocitidilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(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*-metiluridilil-(3'→5')-2'-desoxi-2'-fluoroadenilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-desoxi-2'-fluoroguanilil-(3'→5')-2'-*O*-metilcitidilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-desoxi-2'-fluoroadenilil-(3'→5')-2'-*O*-metilcitidilil-(3'→5')-2'-desoxi-2'-fluoroadenilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metil-*P*-tiocitidilil-(3'→5')-2'-*O*-metilguanosina

$C_{492}H_{651}F_{12}N_{164}O_{310}P_{43}S_7$



torudokimabum #

torudokimab

immunoglobulin G4-kappa, anti-[*Homo sapiens* IL33 (interleukin 33, interleukin-1 family member 11, IL1F11, nuclear factor for high endothelial venules, NF-HEV)], monoclonal antibody; gamma4 heavy chain (1-449) [VH (*Homo sapiens* IGHV3-23*04 (95.9%) -(IGHD) -IGHJ3*02 (87.5%) M123>L (118)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123)-*Homo sapiens* IGHG4*01 G4v5 h P10, G4v4 CH2 A1.3, A1.2 (CH1 (124-221), hinge 1-12 S10>P (231) (222-233), CH2 F1.3>A (237), L1.2>A (238) (234-343), CH3 (344-448), CHS K>del (449)) (124-449)], (137-215')-disulfide with kappa light chain (1'-215') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (88.5%) -IGKJ4*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 (229-229'':232-232'')-bisdisulfide, produced in a Chinese hamster ovary (CHO)-K1 cell line, glycoform alfa

torudokimab

immunoglobuline G4-kappa, anti-[*Homo sapiens* IL33 (interleukine 33, membre 11 de la famille 1 d'interleukines, IL1F11, facteur nucléaire des veinules à haut endothélium, NF-HEV)], anticorps monoclonal;
chaîne lourde gamma4 (1-449) [VH (*Homo sapiens* IGHV3-23*04 (95.9%) -(IGHD) - IGHJ3*02 (87.5%) M123>L (118)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123)-*Homo sapiens* IGHG4*01 G4v5 h P10, G4v4 CH2 A1.3, A1.2 (CH1 (124-221), charnière 1-12 S10>P (231) (222-233), CH2 F1.3>A (237), L1.2>A (238) (234-343), CH3 (344-448), CHS K>del (449)) (124-449)], (137-215')-disulfure avec la chaîne légère kappa (1'-215') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (88.5%) -IGKJ4*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 (229-229'':232-232'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-K1, glycoforme alfa

torudokimab

inmunoglobulina G4-kappa, anti-[*Homo sapiens* IL33 (interleukina 33, miembro 11 de la familia 1 de interleukinas, IL1F11, factor nuclear de las vénulas del alto endotelio, NF-HEV)], anticuerpo monoclonal;
cadena pesada gamma4 *Homo sapiens* (1-449) [VH (*Homo sapiens* IGHV3-23*04 (95.9%) -(IGHD) - IGHJ3*02 (87.5%) M123>L (118)) CDR-IMGT [8.8.16] (26-33.51-58.97-112) (1-123)-*Homo sapiens* IGHG4*01 G4v5 h P10, G4v4 CH2 A1.3, A1.2 (CH1 (124-221), bisagra 1-12 S10>P (231) (222-233), CH2 F1.3>A (237), L1.2>A (238) (234-343), CH3 (344-448), CHS K>del (449)) (124-449)], (137-215')-disulfuro con la cadena ligera kappa (1'-215') [V-KAPPA (*Homo sapiens* IGKV3-20*01 (88.5%) -IGKJ4*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 (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

```
EVQLVETGGG LIQPGGSLRL SCAASGFTFS FYAMSWVRQA PGKGLEWVSA  50
ISGSGGSTYY ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARTI 100
HGIRAAYDAF IIWGQGTLVT VSSASTKGPS VFPLAPCSRS TSESTAALGC 150
LVKDYFPEPV TVSWNSGALT SGVHTFPAVL QSSGLYSLSS VVTVPSSSLG 200
TKTYTCNVDH KPSNTKVDKR VESKYGPPCP PCPAPEAAGG PSVFLFPPKP 250
KDTLMISRTP EVTCVVVDVS QEDPEVQFNW YVDGVEVHNA KTKPREEQFN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKG LPSSIEKTIS KAKGQPREPQ 350
VYTLPPSQEE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFFLY SRLTVDKSRW QEGNVFSCSV MHEALHNHYT QKSLSLSLG  449
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Light chain / Chaîne légère / Cadena ligera

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EIVLTQSPGT LSLSPGERAT LSCRASQSVG INLSWYQQKP GQAPRLLIYG  50
ASHRLTGIPD RFSGSGSGTD FTLTISRLEP EDFAVYYCHQ YSQPPPFTFG 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	150-206	264-324	370-428
	22"-96"	150"-206"	264"-324"	370"-428"
Intra-L (C23-C104)	23'-88'	135'-195'		
	23'"-88'"	135'"-195'"		
Inter-H-L (CH1 10-CL 126)	137-215'	137"-215'"		
Inter-H-H (h 8, h 11)	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.

tozorakimabum #

tozorakimab	immunoglobulin G1-lambda2, anti-[*Homo sapiens* IL33 (interleukin 33, DVS27, NF-HEV, IL1F11)], monoclonal antibody; gamma1 heavy chain (1-456) [VH (*Homo sapiens* IGHV3-23*01 (93.9%) -(IGHD) -IGHJ4*01 (85.7%) L123>M (121)) CDR-IMGT [8.8.19] (26-33.51-58.97-115) (1-126) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (223) (127-224), hinge 1-15 (225-239), CH2 (240-349), CH3 E12 (365), M14 (367) (350-454), CHS (455-456)) (127-456)], (229-211')-disulfide with lambda2 light chain (1'-212') [V-LAMBDA (*Homo sapiens* IGLV3-1*01 (86.2%) -IGLJ2*01 (100%)) CDR-IMGT [6.3.9] (26-31.49-51.88-96) (1'-106') -*Homo sapiens* IGLC2*01 (100%) (107'-212')]; dimer (235-235'':238-238'')-bisdisulfide, produced in a Chinese hamster ovary (CHO) cell line derived from CHO-K1, glycoform alfa
tozorakimab	immunoglobuline G1-lambda2, anti-[*Homo sapiens* IL33 (interleukine 33, DVS27, NF-HEV, IL1F11)], anticorps monoclonal; chaîne lourde gamma1 (1-456) [VH (*Homo sapiens* IGHV3-23*01 (93.9%) -(IGHD) -IGHJ4*01 (85.7%) L123>M (121)) CDR-IMGT [8.8.19] (26-33.51-58.97-115) (1-126) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (223) (127-224), charnière 1-15 (225-239), CH2 (240-349), CH3 E12 (365), M14 (367) (350-454), CHS (455-456)) (127-456)], (229-211')-disulfure avec la chaîne légère lambda2 (1'-212') [V-LAMBDA (*Homo sapiens* IGLV3-1*01 (86.2%) -IGLJ2*01 (100%)) CDR-IMGT [6.3.9] (26-31.49-51.88-96) (1'-106') -*Homo sapiens* IGLC2*01 (100%) (107'-212')]; dimère (235-235'':238-238'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) dérivant de la lignée cellulaire CHO-K1, glycoforme alfa
tozorakimab	inmunoglobulina G1-lambda2, anti-[*Homo sapiens* IL33 (interleukina 33, DVS27, NF-HEV, IL1F11)], anticuerpo monoclonal; cadena pesada gamma1 (1-456) [VH (*Homo sapiens* IGHV3-23*01 (93.9%) -(IGHD) -IGHJ4*01 (85.7%) L123>M (121)) CDR-IMGT [8.8.19] (26-33.51-58.97-115) (1-126) -*Homo sapiens* IGHG1*03 (100%) G1m3, nG1m1 (CH1 R120 (223) (127-224), bisagra 1-15 (225-239), CH2 (240-349), CH3 E12 (365), M14 (367) (350-454), CHS (455-456)) (127-456)], (229-211')-disulfuro con la cadena ligera lambda2 (1'-212') [V-LAMBDA (*Homo sapiens* IGLV3-1*01 (86.2%) -IGLJ2*01 (100%)) CDR-IMGT [6.3.9] (26-31.49-51.88-96) (1'-106') -*Homo sapiens* IGLC2*01 (100%) (107'-212')]; dímero (235-235'':238-238'')-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

```
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSG  50
ISAIDQSTYY ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARQK 100
FMQLWGGGLR YPFGYWGQGT MVTVSSASTK GPSVFPLAPS SKSTSGGTAA 150
LGCLVKDYFP EPVTVSWNSG ALTSGVHTFP AVLQSSGLYS LSSVVTVPSS 200
SLGTQTYICN VNHKPSNTKV DKRVEPKSCD KTHTCPPCPA PELLGGPSVF 250
LFPPKPKDTL MISRTPEVTC VVVDVSHEDP EVKFNWYVDG VEVHNAKTKP 300
REEQYNSTYR VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP IEKTISKAKG 350
QPREPQVYTL PPSREEMTKN QVSLTCLVKG FYPSDIAVEW ESNGQPENNY 400
KTTPPVLDSD GSFFLYSKLT VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL 450
SLSPGK                                                 456
```

Light chain / Chaîne légère / Cadena ligera

```
SYVLTQPPSV SVSPGQTASI TCSGEGMGDK YAAWYQQKPG QSPVLVIYRD  50
TKRPSGIPER FSGSNSGNTA TLTISGTQAM DEADYYCGVI QDNTGVFGGG 100
TKLTVLGQPK AAPSVTLFPP SSEELQANKA TLVCLISDFY PGAVTVAWKA 150
DSSPVKAGVE TTTPSKQSNN KYAASSYLSL TPEQWKSHRS YSCQVTHEGS 200
TVEKTVAPTE CS                                          212
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 153-209 270-330 376-434
22"-96" 153"-209" 270"-330" 376"-434"
Intra-L (C23-C104) 22'-87' 134'-193'
22'"-87'" 134'"-193'"
Inter-H-L (h 5-CL 126) 229-211' 229"-211'"
Inter-H-H (h 11, h 14) 235-235" 238-238"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
306, 306"
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:
456, 456"

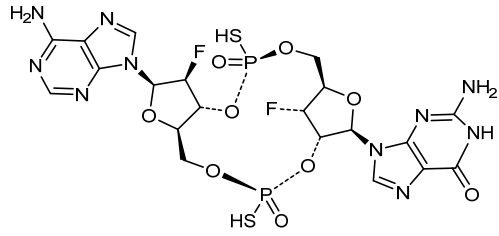
ulevostinagum

ulevostinag — cyclo[(*P*$^{3'}$*R*,2'*S*)-2'-deoxy-2'-fluoro-*P*-thioadenylyl-(3'→5')-(*P*$^{2'}$*R*)-3'-deoxy-3'-fluoro-*P*-thioguanylyl-(2'→5')]

ulévostinag — cyclo[(*P*$^{3'}$*R*,2'*S*)-2'-désoxy-2'-fluoro-*P*-thioadénylyl-(3'→5')-(*P*$^{2'}$*R*)-3'-désoxy-3'-fluoro-*P*-thioguanylyl-(2'→5')]

ulevostinag — cyclo[(*P*$^{3'}$*R*,2'*S*)-2'-désoxy-2'-fluoro-*P*-thioadénylyl-(3'→5')-(*P*$^{2'}$*R*)-3'-désoxy-3'-fluoro-*P*-thioguanylyl-(2'→5')]

$C_{20}H_{22}F_2N_{10}O_9P_2S_2$



uliledlimabum #

uliledlimab — immunoglobulin G1-kappa, anti-[*Homo sapiens* NT5E (5'-nucleotidase ecto, 5' nucleotidase, NT5, eN, eNT NTE, CALJA, CD73)], monoclonal antibody;

	gamma1 heavy chain (1-450) [VH (*Homo sapiens* IGHV4-38-2*01 (87.6%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [9.7.13] (26-34.52-58.97-109) (1-120) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 R>K 120 (217) (121-218), hinge 1-15 (219-233), CH2 N84.4>A (300) (234-343), CH3 E12 (359), M14 (361) (344-448), CHS(449-450)) (121-450)], (223-213')-disulfide with kappa light chain (1'-215') [V-KAPPA (*Mus musculus* IGKV4-72*01 (81.1%) -IGKJ1*01 (90.9%) L124>V (103)/*Homo sapiens* IGKV3-11*01 (77.9%) -IGKJ4*01 (100%)) CDR-IMGT [5.3.9] (26-31.59-51.88-96) (1'-106') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (152), V101 (190) (107'-213')]; dimer (229-229'':232-232'')-bisdisulfide, produced in a Chinese hamster ovary (CHO)-K1 cell line, non-glycosylated
ulilédlimab	immunoglobuline G1-kappa, anti-[*Homo sapiens* NT5E (5' ecto nucléotidase, 5' nucléotidase, NT5, eN, eNT NTE, CALJA, CD73)], anticorps monoclonal; chaîne lourde gamma1 (1-450) [VH (*Homo sapiens* IGHV4-38-2*01 (87.6%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [9.7.13] (26-34.52-58.97-109) (1-120) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 R>K 120 (217) (121-218), charnière 1-15 (219-233), CH2 N84.4>A (300) (234-343), CH3 E12 (359), M14 (361) (344-448), CHS(449-450)) (121-450)], (223-213')-disulfure avec la chaîne légère kappa (1'-215') [V-KAPPA (*Mus musculus* IGKV4-72*01 (81.1%) -IGKJ1*01 (90.9%) L124>V (103)/*Homo sapiens* IGKV3-11*01 (77.9%) -IGKJ4*01 (100%)) CDR-IMGT [5.3.9] (26-31.59-51.88-96) (1'-106') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (152), V101 (190) (107'-213')]; dimère (229-229'':232-232'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO) lignée cellulaire CHO-K1, non-glycosylé
ulileđlimab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* NT5E (5' ecto nucleotidasa, 5' nucleotidasa, NT5, eN, eNT NTE, CALJA, CD73)], anticuerpo monoclonal; cadena pesada gamma1 (1-450) [VH (*Homo sapiens* IGHV4-38-2*01 (87.6%) -(IGHD) -IGHJ6*01 (100%)) CDR-IMGT [9.7.13] (26-34.52-58.97-109) (1-120) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 R>K 120 (217) (121-218), bisagra 1-15 (219-233), CH2 N84.4>A (300) (234-343), CH3 E12 (359), M14 (361) (344-448), CHS(449-450)) (121-450)], (223-213')-disulfuro con la cadena ligera kappa (1'-215') [V-KAPPA (*Mus musculus* IGKV4-72*01 (81.1%) -IGKJ1*01 (90.9%) L124>V (103)/*Homo sapiens* IGKV3-11*01 (77.9%) -IGKJ4*01 (100%)) CDR-IMGT [5.3.9] (26-31.59-51.88-96) (1'-106') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (152), V101 (190) (107'-213')]; dímero (229-229'':232-232'')-bisdisulfuro, producido en las células ováricas de hámster chino (CHO) línea celular CHO-K1, no glicosilado

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLQESGPG LVKPSETLSL TCAVSGYSIT SGYYWNWIRQ PPGKKLEWMG  50
YINYGGSNGY NPSLKSRITI SRDTSKNQFS LKLSSVTAAD TAVYYCARDY 100
DAYYEALDDW GQGTTVTVSS ASTKGPSVFP LAPSSKSTSG GTAALGCLVK 150
DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT 200
YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG PSVFLFPPKP 250
KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYA 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ 350
VYTLPPSREE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPGK 450
```

Light chain / Chaîne légère / Cadena ligera

```
EIVLSQSPAT LSLSPGERAT LSCRASSRVN YMHWYQQKPG QSPRPWISAT  50
SNLASGVPAR FSGSGSGTSY TLTISSLEPE DFAVYYCQQW SSNPPTFGGG 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) 22-96 147-203 264-324 370-428
22"-96" 147"-203" 264"-324" 370"-428"
Intra-L (C23-C104) 23'-87' 133'-193'
23'"-87'" 133'"-193'"
Inter-H-L (h 5-CL 126) 223-213' 223"-213'"
Inter-H-H (h 11, h 14) 229-229" 232-232"

No N-glycosylation sites / pas de sites de N-glycosylation / ningún posición de N-glicosilación
CH2 N84.4>A:
300, 300"
Aglycosylated

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
450, 450"

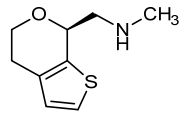
ulotarontum

ulotaront — 1-[(7*S*)-4,7-dihydro-5*H*-thieno[2,3-c]pyran-7-yl]-*N*-methylmethanamine

ulotaront — 1-[(7*S*)-4,7-dihydro-5*H*-thiéno[2,3-c]pyran-7-yl]-*N*-méthylméthanamine

ulotaront — 1-[(7*S*)-4,7-dihidro-5*H*-tieno[2,3-c]piran-7-il]-*N*-metilmetanamina

$C_9H_{13}NOS$



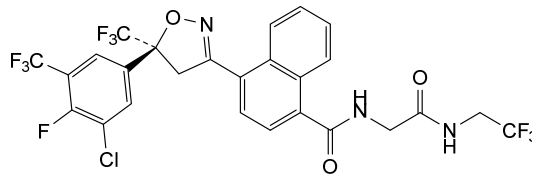
umifoxolanerum

umifoxolaner — 4-[(5*S*)-5-[3-chloro-4-fluoro-5-(trifluoromethyl)phenyl]-5-(trifluoromethyl)-4,5-dihydro-1,2-oxazol-3-yl]-*N*-{2-oxo-2-[(2,2,2-trifluoroethyl)amino]ethyl}naphthalene-1-carboxamide

umifoxolaner — 4-[(5*S*)-5-[3-chloro-4-fluoro-5-(trifluorométhyl)phényl]-5-(trifluorométhyl)-4,5-dihydro-1,2-oxazol-3-yl]-*N*-{2-oxo-2-[(2,2,2-trifluoroéthyl)amino]-éthyl}naphtalène-1-carboxamide

umifoxolaner — 4-[(5*S*)-5-[3-cloro-4-fluoro-5-(trifluorometil)fenil]-5-(trifluorometil)-4,5-dihidro-1,2-oxazol-3-il]-*N*-{2-oxo-2-[(2,2,2-trifluoroetil)amino]etil}-naftaleno-1-carboxamida

$C_{26}H_{16}ClF_{10}N_3O_3$



unasnemabum #

unasnemab	immunoglobulin G1-kappa, anti-[*Homo sapiens* RGMA (repulsive guidance molecule BMP co-receptor a, RGM)], monoclonal antibody; gamma1 heavy chain (1-446) [VH (*Mus musculus* IGHV6-6*01 (87%) -(IGHD) -IGHJ1*01 (90.9%)/*Homo sapiens* IGHV3-49*04 (85%) -(IGHD) -IGHJ6*04 (100%)) CDR-IMGT [8.10.7] (26-33.51-60.99-105) (1-116) -*Homo sapiens* IGHG1*01 (100%), G1m17,1 (CH1 K120 (213) (117-214), hinge 1-15 (215-229), CH2 (230-339), CH3 D12 (355), L14 (357) (340-444), CHS (445-446)) (117-446)], (219-214')-disulfide with kappa light chain (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (87.4%) -IGKJ4*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 (225-225'':228-228'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa
unasnémab	immunoglobuline G1-kappa, anti-[*Homo sapiens* RGMA (co-recepteur BMP de la molécule d'orientation répulsive a, RGM)], anticorps monoclonal; chaîne lourde gamma1 (1-446) [VH (*Mus musculus* IGHV6-6*01 (87%) -(IGHD) -IGHJ1*01 (90.9%)/*Homo sapiens* IGHV3-49*04 (85%) -(IGHD) -IGHJ6*04 (100%)) CDR-IMGT [8.10.7] (26-33.51-60.99-105) (1-116) -*Homo sapiens* IGHG1*01 (100%), G1m17,1 (CH1 K120 (213) (117-214), charnière 1-15 (215-229), CH2 (230-339), CH3 D12 (355), L14 (357) (340-444), CHS (445-446)) (117-446)], (219-214')-disulfure avec la chaîne légère kappa (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (87.4%) -IGKJ4*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 (225-225'':228-228'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa
unasnemab	inmunoglobulina G1-kappa, anti-[*Homo sapiens* RGMA (co-réceptor BMP de la molécula de orientación repulsiva a, RGM)], anticuerpo monoclonal;

cadena pesada gamma1 (1-446) [VH (*Mus musculus* IGHV6-6*01 (87%) -(IGHD) -IGHJ1*01 (90.9%)/*Homo sapiens* IGHV3-49*04 (85%) -(IGHD) -IGHJ6*04 (100%)) CDR-IMGT [8.10.7] (26-33.51-60.99-105) (1-116) -*Homo sapiens* IGHG1*01 (100%), G1m17,1 (CH1 K120 (213) (117-214), bisagra 1-15 (215-229), CH2 (230-339), CH3 D12 (355), L14 (357) (340-444), CHS (445-446)) (117-446)], (219-214')-disulfuro con la cadena ligera kappa (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*01 (87.4%) -IGKJ4*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 (225-225":228-228")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVESGGG LVQPGRSLRL SCTASGFTFS DAWMDWVRQA PGKGLEWVAE  50
IRSKANNHAT YYAESVKGRF TISRDDSKSI VYLQMNSLRT EDTALYYCTR 100
RDGAYWGKGT TVTVSSASTK GPSVFPLAPS SKSTSGGTAA LGCLVKDYFP 150
EPVTVSWNSG ALTSGVHTFP AVLQSSGLYS LSSVVTVPSS SLGTQTYICN 200
VNHKPSNTKV DKKVEPKSCD KTHTCPPCPA PELLGGPSVF LFPPKPKDTL 250
MISRTPEVTC VVVDVSHEDP EVKFNWYVDG VEVHNAKTKP REEQYNSTYR 300
VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP IEKTISKAKG QPREPQVYTL 350
PPSRDELTKN QVSLTCLVKG FYPSDIAVEW ESNGQPENNY KTTPPVLDSD 400
GSFFLYSKLT VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL SLSPGK     446
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS VSASVGDRVT ITCRASQDIS SYLNWYQQKP GKAPKLLIYY  50
TSRLHSGVPS RFSGSGSGTD FTLTISSLQP EDFASYFCQQ LNTLPWTFGG 100
GTKVEMERTV 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) 22-98 143-199 260-320 366-424
22"-98" 143"-199" 260"-320" 366"-424"
Intra-L (C23-C104) 23'-88' 134'-194'
23'"-88'" 134'"-194"
Inter-H-L (h 5-CL 126) 219-214' 219"-214"
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-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"

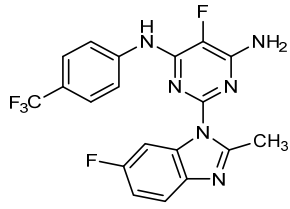
unesbulinum

unesbulin — 5-fluoro-2-(6-fluoro-2-methyl-1*H*-benzimidazol-1-yl)-N^4-[4-(trifluoromethyl)phenyl]pyrimidine-4,6-diamine

unesbuline — 5-fluoro-2-(6-fluoro-2-méthyl-1*H*-benzimidazol-1-yl)-N^4-[4-(trifluorométhyl)phényl]pyrimidine-4,6-diamine

unesbulina — 5-fluoro-2-(6-fluoro-2-metil-1*H*-benzimidazol-1-il)-N^4-[4-(trifluorometil)fenil]pirimidina-4,6-diamina

$C_{19}H_{13}F_5N_6$



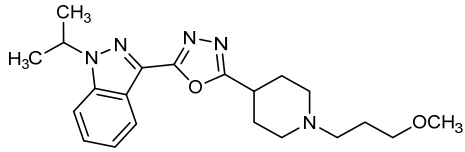
usmarapridum

usmarapride — 3-{5-[1-(3-methoxypropyl)piperidin-4-yl]-1,3,4-oxadiazol-2-yl}-1-(propan-2-yl)-1*H*-indazole

usmarapride — 3-{5-[1-(3-méthoxypropyl)pipéridin-4-yl]-1,3,4-oxadiazol-2-yl}-1-(propan-2-yl)-1*H*-indazole

usmaraprida — 3-{5-[1-(3-metoxipropil)piperidin-4-il]-1,3,4-oxadiazol-2-il}-1-(propan-2-il)-1*H*-indazol

$C_{21}H_{29}N_5O_2$



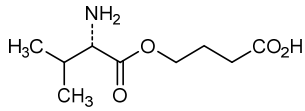
valiloxybatum

valiloxybate — 4-{[(2*S*)-2-amino-3-methylbutanoyl]oxy}butanoic acid, 4-(L-valyloxy)butanoic acid

valiloxybate — acide 4-{[(2*S*)-2-amino-3-méthylbutanoyl]oxy}butanoïque, acide 4-(L-valyloxy)butanoïque

valiloxibato — ácido 4-{[(2*S*)-2-amino-3-metilbutanoil]oxi}butanoico, ácido 4-(L-valiloxi)butanoico

$C_9H_{17}NO_4$



vanglusagenum ensiparvovecum #

vanglusagene ensiparvovec — A recombinant liver-directed adeno-associated virus vector expressing human acid alpha-glucosidase (GAA).
A recombinant liver-directed adeno-associated virus serotype rh74 (AAVrh74) vector that contains a bio-engineered capsid derived from AAVrh74 by four amino-acid substitutions and a codon-optimized transgene expression cassette to drive hepatic synthesis and secretion of the lysosomal enzyme human acid alpha-glucosidase (GAA, α-1,4-glucosidase, acid maltase) via an apolipoprotein E hepatic control region 1 (ApoE HCR1) enhancer/human alpha 1-antitrypsin (hAAT) promoter, a modified human beta-globin intron 2 (HBB2) and a bovine growth hormone (bGH) polyA signal sequence, flanked by adeno-associated virus 2 (AAV2) inverted terminal repeats (ITRs).

vanglusagène ensiparvovec — Un vecteur viral adéno-associé recombinant ciblant le foie exprimant l'alpha-glucosidase acide (GAA) humaine.

Un vecteur viral adéno-associé de sérotype rh74 recombinant (AAVrh74) ciblant le foie qui contient une capside issue de la bio-ingénierie dérivée du AAVrh74 par quatre substitutions d'acides aminés et une cassette d'expression d'un transgène aux codons optimisés pour induire la synthèse hépatique et la sécrétion de l'alpha-glucosidase acide (GAA, α-1,4-glucosidase, maltase acide) enzyme humaine des lysosomes via un activateur de la région 1 de contrôle hépatique de l'apolipoprotéine E (ApoE HCR1)/promoteur de l'alpha 1-antitrypsine humaine (hAAT), un intron 2 modifié de la bêta-globine humaine (HBB2) et une séquence signal polyA de l'hormone de croissance bovine (bGH), flanquée de répétitions terminales inversées (ITRs) du virus adéno-associé 2 (AAV2).

vanglusagén ensiparvovec

Un vector de virus adeno-asociado recombinante dirigido al hígado que expresa la alfa-glucosidasa ácida (GAA) humana.
Un vector de virus adeno-asociado serotipo rh74 (AAVrh74) recombinante dirigido al hígado que contiene una cápside bioingenierizada derivada de AAVrh74 mediante substituciones de cuatro aminoácidos y un casete de expresión con codones optimizados para dirigir la síntesis hepática y la secreción de la enzima lisosomal alfa-glucosidasa ácida humana (GAA, α-1,4-glucosidasa, maltasa ácida) mediante un potenciador de la región de control hepática 1 de la apolipoproteína E (ApoE HCR1)/promotor de alfa 1-antitripsina humana (hAAT), un intrón 2 modificado de la beta-globina humana (HBB2) y una secuencia señal polyA de la hormona de crecimiento bovina (bGH), flanqueado por las repeticiones terminales invertidas (ITRs) del virus adeno-asociado 2 (AAV2).

varoglutamstatum

varoglutamstat

(5*S*)-1-(1*H*-benzimidazol-5-yl)-5-(4-propoxyphenyl)imidazolidin-2-one

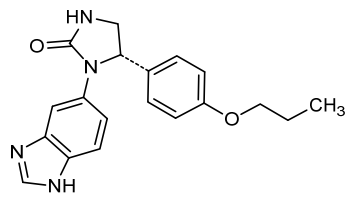
varoglutamstat

(5*S*)-1-(1*H*-benzimidazol-5-yl)-5-(4-propoxyphényl)imidazolidin-2-one

varoglutamstat

(5*S*)-1-(1*H*-benzimidazol-5-il)-5-(4-propoxifenil)imidazolidin-2-ona

$C_{19}H_{20}N_4O_2$



vemircopanum

vemircopan

(1*R*,3*S*,5*R*)-2-{[3-acetyl-5-(2-methylpyrimidin-5-yl)-1*H*-indazol-1-yl]acetyl}-*N*-(6-bromo-3-methylpyridin-2-yl)-5-methyl-2-azabicyclo[3.1.0]hexane-3-carboxamide

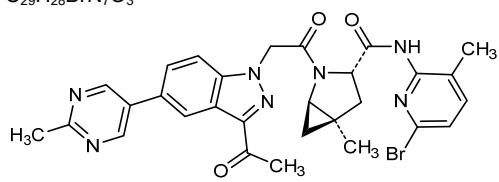
vémircopan

(1*R*,3*S*,5*R*)-2-{[3-acétyl-5-(2-méthylpyrimidin-5-yl)-1*H*-indazol-1-yl]acétyl}-*N*-(6-bromo-3-méthylpyridin-2-yl)-5-méthyl-2-azabicyclo[3.1.0]hexane-3-carboxamide

vemircopán

(1*R*,3*S*,5*R*)-2-{[3-acetil-5-(2-metilpirimidin-5-il)-1*H*-indazol-1-il]acetil}-*N*-(6-bromo-3-metilpiridin-2-il)-5-metil-2-azabiciclo[3.1.0]hexano-3-carboxamida

$C_{29}H_{28}BrN_7O_3$



vixtimotamabum #

vixtimotamab

immunoglobulin V-kappa-VH-V-lambda-VH' chain homodimer, anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)] and anti-[*Homo sapiens* CD33 (sialic acid binding Ig-like lectin 3, SIGLEC3, SIGLEC-3, gp67, p67)], monoclonal antibody V-kappa-VH-V-lambda-VH' chain noncovalent homodimer, bispecific, tetravalent; IG V-kappa-VH-V-lambda-VH' chain anti-CD3E and anti-CD33 (1-483) [anti-CD3E V-KAPPA (*Homo sapiens* IGKV1-17*01 (72.5%) -IGKJ1*01 (91.7%)) CDR-IMGT [9.3.9] (27-35.53-55.92-100) (1-110)] -6-mer bis(diglycyl-seryl) linker (111-116) -anti-CD33 VH (*Homo sapiens* IGHV1-8*01 (94.9%) -(IGHD) -IGHJ1*01 (100%)) CDR-IMGT [8.8.15] (142-149.167-174.213-227) (117-238) -4-mer diglycyl-seryl-glycyl linker (239-242) -anti-CD33 V-LAMBDA (*Homo sapiens* IGLV1-44*01 (95.9%) -IGLJ3*01 (86.7%)) CDR-IMGT [8.3.11] (268-275.293-295.332-342) (243-352)] -6-mer bis(diglycyl-seryl) linker (353-358) -anti-CD3E VH (*Mus musculus* IGHV10-1*02 (89.8%) -(IGHD) -IGHJ3*01 (86.7%))/*Homo sapiens* IGHV3-72*01 (88.0%) -(IGHD) -IGHJ4*01 (93.3%)) CDR-IMGT [8.10.16] (384-391.409-418.457-472) (359-483)]; noncovalent homodimer, produced in a Chinese hamster ovary (CHO)-derived cell line transfected with the glutamine synthetase (GS) gene, non-glycosylated

vixtimotamab

immunoglobuline chaîne V-kappa-VH-V-lambda-VH' homodimère, anti-[*Homo sapiens* CD3E (CD3 epsilon, Leu-4)] et anti-[*Homo sapiens* CD33 (lectine 3 de type Ig-like liant l'acide sialique, SIGLEC3, SIGLEC-3, gp67, p67)], anticorps monoclonal chaîne V-kappa-VH-V-lambda-VH' homodimère non-covalent, bispécifique, tétravalent;

IG chaîne V-kappa-VH-V-lambda-VH' anti-CD3E et anti-CD33 (1-483) [anti-CD3E V-KAPPA (*Homo sapiens* IGKV1-17*01 (72.5%) -IGKJ1*01 (91.7%)) CDR-IMGT [9.3.9] (27-35.53-55.92-100) (1-110)] -6-mer bis(diglycyl-séryl) linker (111-116) - anti-CD33 VH (*Homo sapiens* IGHV1-8*01 (94.9%) -(IGHD) - IGHJ1*01 (100%)) CDR-IMGT [8.8.15] (142-149.167-174.213-227) (117-238) -4-mer diglycyl-séryl-glycyl linker (239-242) - anti-CD33 V-LAMBDA (*Homo sapiens* IGLV1-44*01 (95.9%) - IGLJ3*01 (86.7%)) CDR-IMGT [8.3.11] (268-275.293-295.332-342) (243-352)] -6-mer bis(diglycyl-séryl) linker (353-358) - anti-CD3E VH (*Mus musculus* IGHV10-1*02 (89.8%) -(IGHD) - IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-72*01 (88.0%) - (IGHD) -IGHJ4*01 (93.3%)) CDR-IMGT [8.10.16] (384-391.409-418.457-472) (359-483)]; homodimère non-covalent, produite dans une lignée cellulaire dérivée des cellules ovariennes de hamster chinois (CHO) transfectée avec le gène de la glutamine synthétase (GS), non-glycosylé

vixtimotamab

inmunoglobulina cadena V-kappa-VH-V-lambda-VH' homodímero, anti-[*Homo sapiens* CD3E (CD3 épsilon, Leu-4)] y anti-[*Homo sapiens* CD33 (lectina 3 de tipo Ig-like de unión al ácido siálico, SIGLEC3, SIGLEC-3, gp67, p67)], anticuerpo monoclonal cadena V-kappa-VH-V-lambda-VH' homodímero no covalente, biespecífica, tetravalente;
IG cadena V-kappa-VH-V-lambda-VH' anti-CD3E y anti-CD33 (1-483) [anti-CD3E V-KAPPA (*Homo sapiens* IGKV1-17*01 (72.5%) -IGKJ1*01 (91.7%)) CDR-IMGT [9.3.9] (27-35.53-55.92-100) (1-110)] -6-mer bis(diglicil-seril) linker (111-116) - anti-CD33 VH (*Homo sapiens* IGHV1-8*01 (94.9%) -(IGHD) - IGHJ1*01 (100%)) CDR-IMGT [8.8.15] (142-149.167-174.213-227) (117-238) -4-mer diglicil-seril-glicil linker (239-242) -anti-CD33 V-LAMBDA (*Homo sapiens* IGLV1-44*01 (95.9%) - IGLJ3*01 (86.7%)) CDR-IMGT [8.3.11] (268-275.293-295.332-342) (243-352)] -6-mer bis(diglicil-seril) linker (353-358) -anti-CD3E VH (*Mus musculus* IGHV10-1*02 (89.8%) -(IGHD) - IGHJ3*01 (86.7%)/*Homo sapiens* IGHV3-72*01 (88.0%) - (IGHD) -IGHJ4*01 (93.3%)) CDR-IMGT [8.10.16] (384-391.409-418.457-472) (359-483)]; homodímero no covalente, producido en una línea celular derivada de las células ováricas de hámster chino (CHO) transfectada con el gen de la glutamina sintetasa (GS), no glicosilado

Chain / Chaîne / Cadena

```
DIQMTQSPSS LSASVGDRVT ITCRSSTGAV TTSNYANWVQ QKPGKAPKAL  50
IGGTNKRAPG VPSRFSGSLI GDKATLTISS LQPEDFATYY CALWYSNLWV 100
FGQGTKVEIK GGSGGSQVQL VQSGAEVKKP GASVKVSCKA SGYTFTSYDI 150
NWVRQAPGQG LEWMGWMNPN SGNTGFAQKF QGRVTMTRDT STSTVYMELS 200
SLRSEDTAVY YCARDRANTD YSLGMDVWGQ GTLVTVSSGG SGQSVLTQPP 250
SASGTPGQRV TISCSGSRSN IGSNTVNWYQ QLPGTAPKLL IYGNNQRPSG 300
VPDRFSGSKS GTSASLAISG LQSEDEADYY CATWDDSLIG WVFGGGTKLT 350
VLGGSGGSEV QLVESGGGLV QPGGSLRLSC AASGFTFSTY AMNWVRQAPG 400
KGLEWVGRIR SKYNNYATYY ADSVKDRFTI SRDDSKNSLY LQMNSLKTED 450
TAVYYCARHG NFGNSYVSYF AYWGQGTLVT VSS                   483
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-chain (C23-C104) 23-91 138-212 264-331 380-456

No N-glycosylation sites / pas de sites de N-glycosylation / ningún posición de N-glicosilación

voxeralgagenum autotemcelum #

voxeralgagene autotemcel	Autologous CD34+ hematopoietic stem cells (HSCs) transduced *ex vivo* with a self-inactivating lentiviral vector encoding human alpha-galactosidase A (GLA). Autologous CD34+ hematopoietic stem cells (HSCs) obtained by apheresis, transduced with a non-replicating, self-inactivating lentiviral vector encoding codon-optimized human alpha-galactosidase A (GLA) under the control of the human elongation factor 1 alpha short (EFS-1 alpha) promoter and a modified woodchuck hepatitis virus posttranscriptional regulatory element (WPRE). The vector genome also contains a packaging signal, a partial *gag* sequence, a Rev response element (RRE), a central polypurine tract (cPPT) and a Kozak sequence.
voxéralgagène autotemcel	Cellules souches hématopoïétiques autologues CD34+ (HSCs) transduites *ex vivo* avec un vecteur lentiviral auto-inactivant codant pour la galactosidase-alpha A (GLA). Les cellules souches hématopoïétiques autologues CD34+ (HSCs) obtenues par aphérèse, transduites avec un vecteur lentiviral non-répliquant, auto-inactivant codant pour une galactosidase-alpha A humaine aux codons optimisés (GLA) sous le contrôle du promoteur humain du facteur d'élongation 1 alpha court (EFS-1 alpha) et un élément de régulation post-transcriptionnelle du virus de l'hépatite de la marmotte (WPRE). Le génome du vecteur contient aussi un signal de compaction, une séquence partielle *gag*, un élément de réponse Rev (RRE), un tractus central de polypurine (cPPT) et une séquence Kozak.
voxeralgagén autotemcel	Células madre hematopoyéticas (HSC) CD34+ autólogas transducidas *ex vivo* con un vector lentiviral auto inactivante que codifica para la galactosidasa alfa A (GLA) humana. Células madre hematopoyéticas (HSC) CD34+ autólogas obtenidas por aféresis, transducidas con un vector lentiviral no replicativo y auto inactivante que codifica para la galactosidasa alfa A (GLA) humana, con codones optimizados, bajo el control del promotor del factor de elongación corto 1 alfa (EFS-1 alfa) humano y un elemento regulador post-transcripcional del virus de la hepatitis de la marmota (WPRE) modificado. El genoma del vector también contiene una señal empaquetadora, una secuencia *gag* parcial, un elemento de respuesta Rev (RRE), un segmento central de polipurinas (cPPT) y una secuencia Kozak.

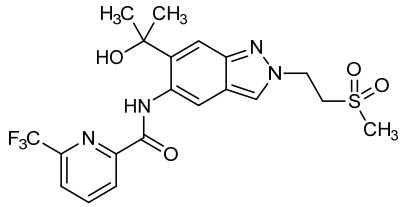
zabedosertibum

zabedosertib	*N*-{6-(2-hydroxypropan-2-yl)-2-[2-(methanesulfonyl)ethyl]-2*H*-indazol-5-yl}-6-(trifluoromethyl)pyridine-2-carboxamide
zabédosertib	*N*-{6-(2-hydroxypropan-2-yl)-2-[2-(méthanesulfonyl)éthyl]-2*H*-indazol-5-yl}-6-(trifluorométhyl)pyridine-2-carboxamide

zabedosertib

N-{6-(2-hidroxipropan-2-il)-2-[2-(metanosulfonil)etil]-2*H*-indazol-5-il}-6-(trifluorometil)piridina-2-carboxamida

$C_{20}H_{21}F_3N_4O_4S$



zaloglanstatum

zaloglanstat

N-[(4-chloro-3-{5-oxo-1-[4-(trifluoromethyl)phenyl]-2,5-dihydro-1*H*-1,2,4-triazol-3-yl}phenyl)methyl]-2,2-dimethylpropanamide

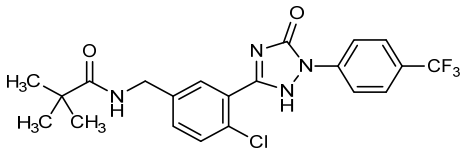
zaloglanstat

N-[(4-chloro-3-{5-oxo-1-[4-(trifluorométhyl)phényl]-2,5-dihydro-1*H*-1,2,4-triazol-3-yl}phényl)méthyl]-2,2-diméthylpropanamide

zaloglanstat

N-[(4-cloro-3-{5-oxo-1-[4-(trifluorometil)fenil]-2,5-dihidro-1*H*-1,2,4-triazol-3-il}fenil)metil]-2,2-dimetilpropanamida

$C_{21}H_{20}ClF_3N_4O_2$



zamtocabtagenum autoleucelum

zamtocabtagene autoleucel

Autologous T cells obtained from peripheral blood collected by leukapheresis, transduced with a non-replicating lentiviral vector, pseudotyped with vesicular stomatitis virus (VSV) glycoprotein (G), encoding a codon-optimized chimeric antigen receptor (CAR) targeting the human B-lymphocyte antigens CD19 and CD20. Cells are activated in the presence of a colloidal polymeric nanomatrix covalently attached to anti-CD3 and anti-CD28, transduced, and then cultured in the presence of IL-7 and IL-15. The T cells are predominantly central memory (>80%; CD4+/CD8+, CD62L+, CD45RO+) and effector memory T cells (CD4+/CD8+, CD62L-, CD45RO+). The target binding moieties of the CAR are two single-chain variable fragments (scFv), derived from a murine anti-human CD20 and a murine anti-human CD19 hybridoma clone linked with a $(GGGGS)_5$ sequence, fused to intracellular signalling domains from 4-1BB and CD3 zeta, under the control of the elongation factor 1 alpha (EF1α) promoter. The genome also contains a 5' splice donor site and a 3' splice acceptor site, a *gag* truncated open reading

	frame, an *env* truncated open reading frame, a Rev response element (RRE) 5' to the transgene, a non-coding artificial sequence for viral titre determination and a *nef* truncated open reading frame 3' to the transgene.
zamtocabtagène autoleucel	Lymphocytes T autologues du sang périphérique recueillis par leucophérèse, transduits avec un vecteur lentiviral non-répliquant, pseudotypés avec une glycoprotéine (G) du virus de la stomatite vésiculaire (VSV), codant un récepteur antigénique chimérique (CAR) aux codons optimisés ciblant les antigènes CD19 et CD20 du lymphocyte B humain. Les cellules sont activées en présence d'une nanomatrice polymérique colloïdale attachée de manière covalente à l'anti-CD3 et l'anti-CD28, transduites, et ensuite cultivées en présence d'IL-7 and IL-15. Les cellules sont majoritairement des lymphocytes T à mémoire centrale (>80%; CD4+/CD8+, CD62L+, CD45RO+) et à mémoire effectrice (CD4+/CD8+, CD62L-, CD45RO+). Les moitiés liées aux cibles du CAR sont deux fragments variables à chaîne simple (scFv), dérivées des clones murins antihumains d'hybridome CD19 et CD20 liés à la séquence $(GGGGS)_5$, fusionnées aux domaines de signalisation intracellulaire des zêta 4-1BB et CD3, sous le contrôle du promoteur du facteur 1 alpha d'élongation (EF1α). Le génome contient aussi un site d'épissage donneur en 5' et un site d'épissage accepteur en 3', un cadre de lecture ouvert *gag* tronqué, un cadre de lecture ouvert *env* tronqué, un élément de réponse Rev (RRE) dans la partie 5' du transgène, une séquence artificielle non-codante pour la détermination de la titration virale et un cadre de lecture *nef* tronqué dans la partie 3' du transgène.
zamtocabtagén autoleucel	Linfocitos T autólogos obtenidos de sangre periférica recogidos por leucoaféresis, transducidos con un vector lentiviral no replicativo, seudotipado con la glicoproteína (G) del virus de la estomatitis vesicular (VSV), que codifica, con codones optimizados, para un receptor de antígenos quimérico (CAR) dirigido a los antígenos CD19 y CD20 de los linfocitos B humanos. Las células se activan en presencia de una nanomatriz coloidal polimérica anclada covalentemente a anti-CD3 y anti-CD28, transducidas, y luego se cultivan en presencia de IL-7 e IL-15. Los linfocitos T son predominantemente de memoria central (>80%; CD4+/CD8+, CD62L+, CD45RO+) y memoria efectora (CD4+/CD8+, CD62L-, CD45RO+). Las fracciones de unión a la diana del CAR son dos fragmentos de cadena variable sencilla (scFv), derivados de un clon de hibridoma murino anti-CD20 humano y anti-CD19 humano ligados con una secuencia $(GGGGS)_5$, fusionada a los dominios de señalización intracelulares de 4-1BB y CD3 zeta, bajo el control del promotor del factor de elongación 1 alfa (EF1α). El genoma también contiene un sitio 5' donante del procesamiento y un sitio 3' aceptor del procesamiento, un marco de lectura abierto truncado *gag*, un marco de lectura abierto truncado *env*, un elemento de respuesta Rev (RRE) en 5' con respecto al transgén, una secuencia no codificante artificial para la determinación del título viral y un marco de lectura abierto truncado *nef* en 3' con respecto al transgén.

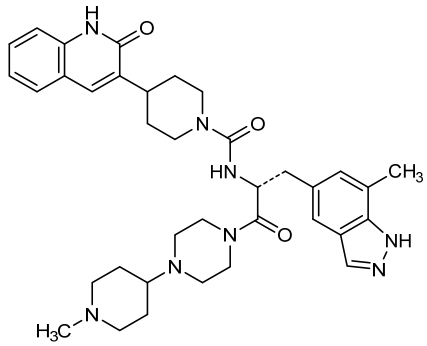
zavegepantum

zavegepant — *N*-{(2*R*)-3-(7-methyl-1*H*-indazol-5-yl)-1-[4-(1-methylpiperidin-4-yl)piperazin-1-yl]-1-oxopropan-2-yl}-4-(2-oxo-1,2-dihydroquinolin-3-yl)piperidine-1-carboxamide

zavégépant — *N*-{(2*R*)-3-(7-méthyl-1*H*-indazol-5-yl)-1-[4-(1-méthylpipéridin-4-yl)pipérazin-1-yl]-1-oxopropan-2-yl}-4-(2-oxo-1,2-dihydroquinoléin-3-yl)pipéridine-1-carboxamide

zavegepant — *N*-{(2*R*)-3-(7-metil-1*H*-indazol-5-il)-1-[4-(1-metilpiperidin-4-il)piperazin-1-il]-1-oxopropan-2-il}-4-(2-oxo-1,2-dihidroquinolein-3-il)piperidina-1-carboxamida

$C_{36}H_{46}N_8O_3$



zeluvalimabum #

zeluvalimab — immunoglobulin G1-kappa, anti-[*Homo sapiens* PDCD1 (programmed cell death 1, PD-1, PD1, CD279)], monoclonal antibody;
gamma1 heavy chain (1-450) [VH (*Homo sapiens* IGHV3-23*03 (92.8%) -(IGHD) -IGHJ3*01 (92.3%)) CDR-IMGT [8.8.13] (26-33.50-58.97-109) (1-120) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 R120>K (217) (121-218), hinge 1-15 (219-233), CH2 R83>C (295), N84.4>G (300), V85>C (305) (234-343), CH3 E12 (359), M14 (361) (344-448), CHS (449-450)) (121-450)], (223-214')-disulfide with kappa light chain (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*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, non-glycosylated

zéluvalimab — immunoglobuline G1-kappa, anti-[*Homo sapiens* PDCD1 (protéine 1 de mort cellulaire programmée, PD-1, PD1, CD279)], anticorps monoclonal;

chaîne lourde gamma1 (1-450) [VH (*Homo sapiens* IGHV3-23*03 (92.8%) -(IGHD) -IGHJ3*01 (92.3%)) CDR-IMGT [8.8.13] (26-33.50-58.97-109) (1-120) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 R120>K (217) (121-218), charnière 1-15 (219-233), CH2 R83>C (295), N84.4>G (300), V85>C (305) (234-343), CH3 E12 (359), M14 (361) (344-448), CHS (449-450)) (121-450)], (223-214')-disulfure avec la chaîne légère kappa (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*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), non-glycosylé

zeluvalimab

inmunoglobulina G1-kappa, anti-[*Homo sapiens* PDCD1 (proteína 1 de muerte celular programada, PD-1, PD1, CD279)], anticuerpo monoclonal; cadena pesada gamma1 (1-450) [VH (*Homo sapiens* IGHV3-23*03 (92.8%) -(IGHD) -IGHJ3*01 (92.3%)) CDR-IMGT [8.8.13] (26-33.50-58.97-109) (1-120) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 R120>K (217) (121-218), bisagra 1-15 (219-233), CH2 R83>C (295), N84.4>G (300), V85>C (305) (234-343), CH3 E12 (359), M14 (361) (344-448), CHS (449-450)) (121-450)], (223-214')-disulfuro con la cadena ligera kappa (1'-214') [V-KAPPA (*Homo sapiens* IGKV1-12*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), no glicosilado

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYDMSWVRQA PGKGLEWVSL  50
ISGGGSQTYY AESVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYFCASPS 100
GHYFYAMDVW GQGTTVTVSS ASTKGPSVFP LAPSSKSTSG GTAALGCLVK 150
DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT 200
YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG PSVFLFPPKP 250
KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPCEEQYG 300
STYRCVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ 350
VYTLPPSREE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV 400
LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPGK 450
```

Light chain / Chaîne légère / Cadena ligera

```
DIQMTQSPSS VSASVGDRVT ITCRASQGIS NWLAWYQQKP GKAPKLLIFA  50
ASSLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ AESFPHTFGG 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	295-305	370-428
	22"-96"	147"-203"	264"-324"	295"-305"	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"			

No N-glycosylation sites / pas de sites de N-glycosylation / ningún posición de N-glicosilación
CH2 N84.4>G:
300, 300"
Aglycosylated

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
450, 450"

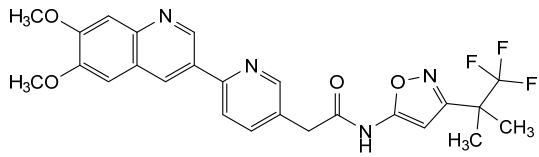
zeteletinibum

zeteletinib — 2-[6-(6,7-dimethoxyquinolin-3-yl)pyridin-3-yl]-*N*-[3-(1,1,1-trifluoro-2-methylpropan-2-yl)-1,2-oxazol-5-yl]acetamide

zételétinib — 2-[6-(6,7-diméthoxyquinoléin-3-yl)pyridin-3-yl]-*N*-[3-(1,1,1-trifluoro-2-méthylpropan-2-yl)-1,2-oxazol-5-yl]acétamide

zeteletinib — 2-[6-(6,7-dimetoxiquinolein-3-il)piridin-3-il]-*N*-[3-(1,1,1-trifluoro-2-metilpropan-2-il)-1,2-oxazol-5-il]acetamida

$C_{25}H_{23}F_3N_4O_4$



zilebesiranum

zilebesiran — [(2*S*,4*R*)-1-{1-[(2-acetamido-2-deoxy-β-D-galactopyranosyl)oxy]-16,16-bis({3-[(3-{5-[(2-acetamido-2-deoxy-β-D-galactopyranosyl)oxy]pentanamido}propyl)amino]-3-oxopropoxy}methyl)-5,11,18-trioxo-14-oxa-6,10,17-triazanonacosan-29-oyl}-4-hydroxypyrrolidin-2-yl]methyl *all-P-ambo*-2'-*O*-methyl-*P*-thioguanylyl-(3'→5')-2'-*O*-methyl-*P*-thiouridylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-deoxy-2'-fluorocytidylyl-(3'→5')-2'-deoxy-2'-fluoroadenylyl-(3'→5')-2'-deoxy-2'-fluoroadenylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-methyl-3'-adenylate, duplex with *all-P-ambo*-2'-*O*-methyl-*P*-thioadenylyl-(5'→3')-2'-*O*-methyl-*P*-thioguanylyl-(5'→3')-2'-*O*-methylcytidylyl-(5'→3')-2'-*O*-methyladenylyl-(5'→3')-2'-*O*-methylguanylyl-(5'→3')-2'-*O*-methyluridylyl-(5'→3')-2'-*O*-methyladenylyl-(5'→3')-2'-deoxy-2'-fluoroguanylyl-(5'→3')-2'-*O*-methylguanylyl-(5'→3')-2'-deoxy-2'-fluorouridylyl-(5'→3')-2'-*O*-methylguanylyl-(5'→3')-2'-*O*-methyluridylyl-(5'→3')-2'-*O*-methyluridylyl-(5'→3')-2'-*O*-methyladenylyl-(5'→3')-2'-*O*-methylcytidylyl-(5'→3')-2'-*O*-methyluridylyl-(5'→3')-2'-*O*-methylcytidylyl-(5'→2')-1-de-β-D-ribofuranosyl-1-[(2*S*)-2,3-dihydroxypropyl]-5-methyluridylyl-(3'→3')-2'-*O*-methylcytidylyl-(5'→3')-2'-*O*-methyladenylyl-(5'→3')-2'-*O*-methyl-*P*-thiouridylyl-(5'→3')-2'-deoxy-2'-fluoro-*P*-thioguanylyl-(5'→3')-2'-*O*-methyluridine

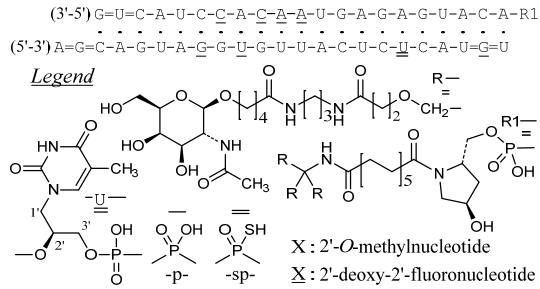
zilébésiran

tout-P-ambo-2'-*O*-méthyl-*P*-thioguanylyl-(3'→5')-2'-*O*-méthyl-*P*-thiouridylyl-(3'→5')-2'-*O*-méthylcytidylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthylcytidylyl-(3'→5')-2'-désoxy-2'-fluorocytidylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-désoxy-2'-fluorocytidylyl-(3'→5')-2'-désoxy-2'-fluoroadénylyl-(3'→5')-2'-désoxy-2'-fluoroadénylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthylguanylyl-(3'→5')-2'-*O*-méthyluridylyl-(3'→5')-2'-*O*-méthyladénylyl-(3'→5')-2'-*O*-méthylcytidylyl-(3'→5')-2'-*O*-méthyl-3'-adénylate de [(2*S*,4*R*)-1-{1-[(2-acétamido-2-désoxy-β-D-galactopyranosyl)oxy]-16,16-bis({3-[(3-{5-[(2-acétamido-2-désoxy-β-D-galactopyranosyl)oxy]pentanamido}propyl)amino]-3-oxopropoxy}méthyl)-5,11,18-trioxo-14-oxa-6,10,17-triazanonacosan-29-oyl}-4-hydroxypyrrolidin-2-yl]méthyle, duplex avec *tout-P-ambo*-2'-*O*-méthyl-*P*-thioadénylyl-(5'→3')-2'-*O*-méthyl-*P*-thioguanylyl-(5'→3')-2'-*O*-méthylcytidylyl-(5'→3')-2'-*O*-méthyladénylyl-(5'→3')-2'-*O*-méthylguanylyl-(5'→3')-2'-*O*-méthyluridylyl-(5'→3')-2'-*O*-méthyladénylyl-(5'→3')-2'-désoxy-2'-fluoroguanylyl-(5'→3')-2'-*O*-méthylguanylyl-(5'→3')-2'-désoxy-2'-fluorouridylyl-(5'→3')-2'-*O*-méthylguanylyl-(5'→3')-2'-*O*-méthyluridylyl-(5'→3')-2'-*O*-méthyluridylyl-(5'→3')-2'-*O*-méthyladénylyl-(5'→3')-2'-*O*-méthylcytidylyl-(5'→3')-2'-*O*-méthyluridylyl-(5'→3')-2'-*O*-méthylcytidylyl-(5'→2')-1-des-β-D-ribofuranosyl-1-[(2*S*)-2,3-dihydroxypropyl]-5-methyluridylyl-(3'→3')-2'-*O*-méthylcytidylyl-(5'→3')-2'-*O*-méthyladénylyl-(5'→3')-2'-*O*-méthyl-*P*-thiouridylyl-(5'→3')-2'-désoxy-2'-fluoro-*P*-thioguanylyl-(5'→3')-2'-*O*-méthyluridine

zilebesirán

todo-P-ambo-2'-*O*-metil-*P*-tioguanilil-(3'→5')-2'-*O*-metil-*P*-tiouridilil-(3'→5')-2'-*O*-metilcitidilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metilcitidilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-desoxi-2'-fluorocitidilil-(3'→5')-2'-desoxi-2'-fluoroadenilil-(3'→5')-2'-desoxi-2'-fluoroadenilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metilguanilil-(3'→5')-2'-*O*-metiluridilil-(3'→5')-2'-*O*-metiladenilil-(3'→5')-2'-*O*-metilcitidilil-(3'→5')-2'-*O*-metil-3'-adenilato de [(2*S*,4*R*)-1-{1-[(2-acetamido-2-desoxi-β-D-galactopiranosil)oxi]-16,16-bis({3-[(3-{5-[(2-acetamido-2-desoxi-β-D-galactopiranosil)oxi]pentanamido}propil)amino]-3-oxopropoxi}metil)-5,11,18-trioxo-14-oxa-6,10,17-triazanonacosan-29-oil}-4-hidroxipirrolidin-2-il]metilo, dúplex con *todo-P-ambo*-2'-*O*-metil-*P*-tioadenilil-(5'→3')-2'-*O*-metil-*P*-tioguanilil-(5'→3')-2'-*O*-metilcitidilil-(5'→3')-2'-*O*-metiladenilil-(5'→3')-2'-*O*-metilguanilil-(5'→3')-2'-*O*-metiluridilil-(5'→3')-2'-*O*-metiladenilil-(5'→3')-2'-desoxi-2'-fluoroguanilil-(5'→3')-2'-*O*-metilguanilil-(5'→3')-2'-desoxi-2'-fluorouridilil-(5'→3')-2'-*O*-metilguanilil-(5'→3')-2'-*O*-metiluridilil-(5'→3')-2'-*O*-metiluridilil-(5'→3')-2'-*O*-metiladenilil-(5'→3')-2'-*O*-metilcitidilil-(5'→3')-2'-*O*-metiluridilil-(5'→3')-2'-*O*-metilcitidilil-(5'→2')-1-des-β-D-ribofuranosil-1-[(2*S*)-2,3-dihidroxipropil]-5-metiluridilil-(3'→3')-2'-*O*-metilcitidilil-(5'→3')-2'-*O*-metiladenilil-(5'→3')-2'-*O*-metil-*P*-tiouridilil-(5'→3')-2'-desoxi-2'-fluoro-*P*-tioguanilil-(5'→3')-2'-*O*-metiluridina

$C_{532}H_{721}F_7N_{177}O_{321}P_{43}S_6$



zilovertamabum #

zilovertamab — immunoglobulin G1-kappa, anti-[*Homo sapiens* ROR1 (receptor tyrosine kinase like orphan receptor 1, NTRKR1)], humanized monoclonal antibody; gamma1 heavy chain humanized (1-446) [VH (*Homo sapiens* IGHV2-70*19 (65.0%) -(IGHD) -IGHJ4*01 (93.3%) Q120>H (108)) CDR-IMGT [8.7.10] (26-33.51-57.96-105) (1-116) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (213) (117-214), hinge 1-15 (215-229), CH2 (230-339), CH3 D12 (355), L14 (357) (340-444), CHS (445-446)) (117-446)], (219-214')-disulfide with kappa light chain humanized (1'-214') [V-KAPPA (*Homo sapiens* IGKV3D-11*02 (67.8%) -IGKJ4*01 (90.9%) G120>E (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'':228-228'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

zilovertamab — immunoglobuline G1-kappa, anti-[*Homo sapiens* ROR1 (récepteurs orphelins de type récepteur 1 à tyrosine kinase, NTRKR1)], anticorps monoclonal humanisé; chaîne lourde gamma1 humanisée (1-446) [VH (*Homo sapiens* IGHV2-70*19 (65%) -(IGHD) -IGHJ4*01 (93.3%) Q120>H (108)) CDR-IMGT [8.7.10] (26-33.51-57.96-105) (1-116) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (213) (117-214), charnière 1-15 (215-229), CH2 (230-339), CH3 D12 (355), L14 (357) (340-444), CHS (445-446)) (117-446)], (219-214')-disulfure avec la chaîne légère kappa humanisée (1'-214') [V-KAPPA (*Homo sapiens* IGKV3D-11*02 (67.8%) -IGKJ4*01 (90.9%) G120>E (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'':228-228'')-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa

zilovertamab — inmunoglobulina G1-kappa, anti-[*Homo sapiens* ROR1 (receptores huérfanos de tipo receptor 1 con tirosina kinasa, NTRKR1)], anticuerpo monoclonal humanizado;

cadena pesada gamma1 humanizada (1-446) [VH (*Homo sapiens* IGHV2-70*19 (65%) -(IGHD) -IGHJ4*01 (93.3%) Q120>H (108)) CDR-IMGT [8.7.10] (26-33.51-57.96-105) (1-116) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (213) (117-214), bisagra 1-15 (215-229), CH2 (230-339), CH3 D12 (355), L14 (357) (340-444), CHS (445-446)) (117-446)], (219-214')-disulfuro con la cadena ligera kappa humanizada (1'-214') [V-KAPPA (*Homo sapiens* IGKV3D-11*02 (67.8%) -IGKJ4*01 (90.9%) G120>E (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":228-228")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLQESGPG LVKPSQTLSL TCTVSGYAFT AYNIHWVRQA PGQGLEWMGS  50
FDPYDGGSSY NQKFKDRLTI SKDTSKNQVV LTMTNMDPVD TATYYCARGW 100
YYFDYWGHGT LVTVSSASTK GPSVFPLAPS SKSTSGGTAA LGCLVKDYFP 150
EPVTVSWNSG ALTSGVHTFP AVLQSSGLYS LSSVVTVPSS SLGTQTYICN 200
VNHKPSNTKV DKKVEPKSCD KTHTCPPCPA PELLGGPSVF LFPPKPKDTL 250
MISRTPEVTC VVVDVSHEDP EVKFNWYVDG VEVHNAKTKP REEQYNSTYR 300
VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP 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

```
DIVMTQTPLS LPVTPGEPAS ISCRASKSIS KYLAWYQQKP GQAPRLLIYS  50
GSTLQSGIPP RFSGSGYGTD FTLTINNIES EDAAYYFCQQ HDESPYTFGE 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) 22-96 143-199 260-320 366-424
22"-96" 143"-199" 260"-320" 366"-424"
Intra-L (C23-C104) 23'-88' 134'-194'
23'"-88'" 134'"-194'"
Inter-H-L (h 5-CL 126) 219-214' 219"-214'"
Inter-H-H (h 11, h 14) 225-225" 228-228"

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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
446, 446"

zilovertamabum vedotinum #
zilovertamab vedotin

immunoglobulin G1-kappa, anti-[*Homo sapiens* ROR1 (receptor tyrosine kinase like orphan receptor 1, NTRKR1)], humanized monoclonal antibody conjugated to auristatin E; gamma1 heavy chain humanized (1-446) [VH (*Homo sapiens* IGHV2-70*19 (65.0%) -(IGHD) -IGHJ4*01 (93.3%) Q120>H (108)) CDR-IMGT [8.7.10] (26-33.51-57.96-105) (1-116) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (213) (117-214), hinge 1-15 (215-229), CH2 (230-339), CH3 D12 (355), L14 (357) (340-444), CHS (445-446)) (117-446)], (219-214')-disulfide with kappa light chain humanized (1'-214') [V-KAPPA (*Homo sapiens* IGKV3D-11*02 (67.8%) -IGKJ4*01 (90.9%) G120>E (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":228-228")-bisdisulfide, produced in *

	Chinese hamster ovary (CHO) cells, glycoform alfa; conjugated on an average of 4.0 ± 0.5 cysteinyl to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker *For the vedotin* part, please refer to the document *"INN for pharmaceutical substances: Names for radicals, groups and others"*
zilovertamab védotine	immunoglobuline G1-kappa, anti-[*Homo sapiens* ROR1 (récepteurs orphelins de type récepteur 1 à tyrosine kinase, NTRKR1)], anticorps monoclonal humanisé conjugué à l'auristatine E; chaîne lourde gamma1 humanisée (1-446) [VH (*Homo sapiens* IGHV2-70*19 (65%) -(IGHD) -IGHJ4*01 (93.3%) Q120>H (108)) CDR-IMGT [8.7.10] (26-33.51-57.96-105) (1-116) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (213) (117-214), charnière 1-15 (215-229), CH2 (230-339), CH3 D12 (355), L14 (357) (340-444), CHS (445-446)) (117-446)], (219-214')-disulfure avec la chaîne légère kappa humanisée (1'-214') [V-KAPPA (*Homo sapiens* IGKV3D-11*02 (67.8%) -IGKJ4*01 (90.9%) G120>E (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":228-228")-bisdisulfure, produit dans des cellules ovariennes de hamster chinois (CHO), glycoforme alfa; conjugué sur 4.0 ± 0.5 cystéinyl en moyenne, au monométhylauristatine E (MMAE), via un linker clivable de type maléimidocaproyl-valyl-citrullinyl-*p*-aminobenzyloxycarbonyl (mc-val-cit-PABC) Pour la partie *védotine*, veuillez-vous référer au document *"INN for pharmaceutical substances: Names for radicals, groups and others"**
zilovertamab vedotina	inmunoglobulina G1-kappa, anti-[*Homo sapiens* ROR1 (receptores huérfanos de tipo receptor 1 con tirosina kinasa, NTRKR1)], anticuerpo monoclonal humanizado conjugado con la auristatina E; cadena pesada gamma1 humanizada (1-446) [VH (*Homo sapiens* IGHV2-70*19 (65%) -(IGHD) -IGHJ4*01 (93.3%) Q120>H (108)) CDR-IMGT [8.7.10] (26-33.51-57.96-105) (1-116) -*Homo sapiens* IGHG1*01 (100%) G1m17,1 (CH1 K120 (213) (117-214), bisagra 1-15 (215-229), CH2 (230-339), CH3 D12 (355), L14 (357) (340-444), CHS (445-446)) (117-446)], (219-214')-disulfuro con la cadena ligera kappa humanizada 1'-214') [V-KAPPA (*Homo sapiens* IGKV3D-11*02 (67.8%) -IGKJ4*01 (90.9%) G120>E (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":228-228")-bisdisulfuro, producido en las células ováricas de hámster chino (CHO), forma glicosilada alfa; conjugado en 4.0 ± 0.5 restos cisteinil por término medio, con monometilauristatina E (MMAE), mediante un conector escindible de tipo maleimidocaproil-valil-citrulinil-*p*-aminobenziloxicarbonil (mc-val-cit-PABC) *Para la parte vedotina, por favor vaya al documento "INN for pharmaceutical substances: Names for radicals, groups and others"**

Heavy chain / Chaîne lourde / Cadena pesada

```
QVQLQESGPG LVKPSQTLSL TCTVSGYAFT AYNIHWVRQA PGQGLEWMGS  50
FDPYDGGSSY NQKFKDRLTI SKDTSKNQVV LTMTNMDPVD TATYYCARGW 100
YYFDYWGHGT LVTVSSASTK GPSVFPLAPS SKSTSGGTAA LGCLVKDYFP 150
EPVTVSWNSG ALTSGVHTFP AVLQSSGLYS LSSVVTVPSS SLGTQTYICN 200
VNHKPSNTKV DKKVEPKSCD KTHTCPPCPA PELLGGPSVF LFPPKPKDTL 250
MISRTPEVTC VVVDVSHEDP EVKFNWYVDG VEVHNAKTKP REEQYNSTYR 300
VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP IEKTISKAKG QPREPQVYTL 350
PPSRDELTKN QVSLTCLVKG FYPSDIAVEW ESNGQPENNY KTTPPVLDSD 400
GSFFLYSKLT VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL SLSPGK     446
```

Light chain / Chaîne légère / Cadena ligera

```
DIVMTQTPLS LPVTPGEPAS ISCRASKSIS KYLAWYQQKP GQAPRLLIYS  50
GSTLQSGIPP RFSGSGYGTD FTLTINNIES EDAAYYFCQQ HDESPYTFGE 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) 22-96 143-199 260-320 366-424
22"-96" 143"-199" 260"-320" 366"-424"

Intra-L (C23-C104) 23'-88' 134'-194'
23'"-88'" 134'"-194'"

Inter-H-L (h 5-CL 126)* 219-214' 219"-214'"

Inter-H-H (h 11, h 14)* 225-225" 228-228"

*At least two of the four inter-chain disulfide bridges are not present, an average of 4 cysteinyl being conjugated each via a thioether bond to a drug linker. *Au moins deux des quatre ponts disulfures inter-chaînes ne sont pas présents, 4 cystéinyl en moyenne étant chacun conjugué via une liaison thioéther à un linker-principe actif. *Al menos dos de los cuatro puentes disulfuro inter-catenarios no estan presentes, una media de 4 cisteinil está conjugada a conectores de principio activo.

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.

C-terminal lysine clipping / Coupure de la lysine C-terminale / Recorte de lisina C-terminal
H CHS K2:
446, 446"

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 5
(WHO Chronicle, Vol. 19, No. 4-5-6, 1965)

p.14 **oxymetholonum**
oxymetholone — *replace the chemical name by the following one*
17β-hydroxy-2-(hydroxymethylene)-17α-methyl-5α-androstan-3-one

Dénominations communes internationales recommandées (DCI Rec.): Liste 5
(Chronique OMS, Vol. 19, No 4-5-6, 1965)

p.14 **oxymetholonum**
oxyméthol one — *remplacer le nom chimique par le suivant*
17β-hydroxy-2-(hydroxyméthylène)-17α-méthyl-5α-androstan-3-one

Denominaciones Comunes Internacionales Recommendadas (DCI Rec.): Lista 5
(Crónica de la OMS, Vol. 20, No 6, 1966)

p.263 **oxymetholonum**
oximetolona — *sustitúyase el nombre químico por el siguiente*
17β-hidroxi-2-(hidroximetileno)-17α-metil-5α-androstan-3-ona

Recommended International Nonproprietary Names (Rec. INN): List 9
(WHO Chronicle, Vol. 23, No. 10, 1969)

p.491 **androstanolonum**
androstanolone — *replace the chemical name by the following one*
17β-hydroxy-5α-androstan-3-one

Dénominations communes internationales recommandées (DCI Rec.): Liste 9
(Chronique OMS, Vol. 23, No 10, 1969)

p.513 **androstanolonum**
androstanolone — *remplacer le nom chimique par le suivant*
17β-hydroxy-5α-androstan-3-one

Denominaciones Comunes Internacionales Recommendadas (DCI Rec.): Lista 9
(Crónica de la OMS, Vol. 23, No 10, 1969)

p.531 **androstanolonum**
androstanolona — *sustitúyase el nombre químico por el siguiente*
17β-hidroxi-5α-androstan-3-ona

Recommended International Nonproprietary Names (Rec. INN): List 63
Dénominations communes internationales recommandées (DCI Rec.): Liste 63
Denominaciones Comunes Internacionales Recomendadas (DCI Rec.): Lista 63
(WHO Drug Information, Vol. 24, No. 1, 2010)

p.62	*suprimáse*	*insertese*
	iodine (^{124}I) girentuximab	iodo (^{124}I) girentuximab

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. 33, No. 1, 2019)

p.123 **tirzepatidum**

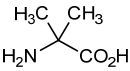
tirzepatide	*replace the structure by the following one*
tirzépatide	*remplacer la structure par la suivante*
tirzepatida	*sustitúyase la estructura por la siguiente*

Sequence / Séquence / Secuencia

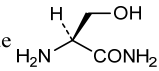
YXEGTFTSDY SIXLDKIAQK AFVQWLIAGG PSSGAPPPS 39

Modified residues / Résidus modifiés / Restos modificados

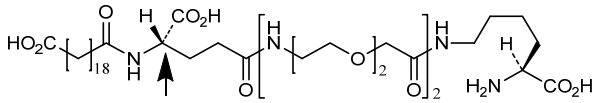
X (2, 13) 2-methylalanine (Aib)



S (39) L-serinamide



K (20): N^6-{*N*-(hydrogen icosanedioyl)-γ-Glu-bis[iminobis(ethylenoxy)acetyl]}-Lysine



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.34 **betibeglogenum autotemcelum #**

betibeglogene autotemcel	*replace the description by the following one*
bétibéglogène autotemcel	*remplacer la description par la suivante*
betibeglogén autotemcel	*sustitúyase la descripción por la siguiente*

autologous CD34+ hematopoietic stem cells **obtained from mobilised peripheral blood of patients with beta-thalassemia**, transduced *ex vivo* with *betibeglogene darolentivec (116)(78),* a self-inactivating human immunodeficiency virus-1 (HIV-1)-derived lentiviral vector encoding a T87Q-mutated form of the human hemoglobin subunit beta (HBB, beta-globin) gene under the control of a human β-globin promoter and a 3' β-globin enhancer.

cellules souches hématopoïétiques CD34+ autologues **obtenues à partir de sang périphérique mobilisé de patients atteints de bêta-thalassémie,** transduites *ex vivo*

avec le *bétibéglogène darolentivec (116)(78),* vecteur lentiviral auto-inactivant dérivé du virus de l'immunodéficience humaine-1 (HIV-1) codant pour une forme mutée (T87Q) du gène de la sous-unité bêta de l'hémoglobine humaine (HBB, bêta-globine) sous le contrôle d'un promoteur de la β-globine humaine et un activateur de la bêta-globine en position 3'.

células madre hematopoyéticas CD34+ autólogas **obtenidas a partir de sangre periférica mobilisada de pacientes con beta-talasemia,** transducidas *ex vivo* con *betibeglogén darolentivec (116)(78)*, un vector lentiviral, auto-inactivante, derivado del virus de la inmunodeficiencia humana-1 (VIH-1) que codifica para una forma mutada T87Q del gen de la subunidad beta de la hemoglobina humana (HBB, beta-globina) bajo el control del promotor de la beta-globina humana y un potenciador de la beta-globina localizado en posición 3'.

p. 124 **veverimerum**

veverimer

vévérimère

veverímero

replace the chemical name and the structure by the following ones

remplacer le nom chimique et la structure par les suivants

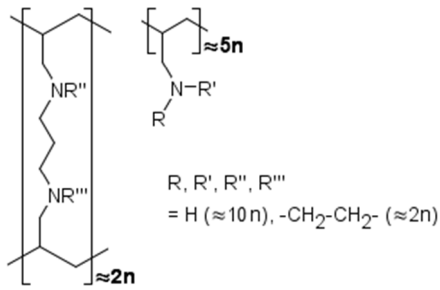
sustitúyase el nombre químico y la estructura por los siguientes

poly[*N*^{1},*N*^{3}-di(prop-2-en-1-yl)propane-1,3-diamine)-co-prop-2-en-1-amine], crosslinked with *N,N'*-ethane-1,2-diyl bridges (molar ratio ≈ 2:5:2)

poly[*N*^{1},*N*^{3}-di(prop-2-én-1-yl)propane-1,3-diamine)-co-prop-2-én-1-amine], réticulé avec des ponts *N,N'*-éthane-1,2-diyle (rapport molaire ≈ 2:5:2)

poli[*N*^{1},*N*^{3}-di(prop-2-en-1-il)propano-1,3-diamina)-co-prop-2-en-1-amina], reticulada con puentes *N,N'*-etano-1,2-diilo (cociente molar ≈ 2:5:2)

$[(C_9H_{18}N_2)_{\approx 2}\ (C_3H_7N)_{\approx 5}\ (C_2H_2)_{\approx 2}]_n$



p.127 **zagotenemabum #**
-128 zagotenemab *replace the structure by the following one*
zagoténémab *remplacer la structure par la suivante*
zagotenemab *sustitúyase la estructura por la siguiente*

Heavy chain / Chaîne lourde / Cadena pesada

```
EVQLVQSGAE VKKPGESLKI SCKGSGYTFS NYWIEWVRQM PGKGLEWMGE  50
ILPGSDSIKY EKNFKGQVTI SADKSISTAY LQWSSLKASD TAMYYCARRG 100
NYVDDWGQGT LVTVSSASTK GPSVFPLAPC SRSTSESTAA LGCLVKDYFP 150
EPVTVSWNSG ALTSGVHTFP AVLQSSGLYS LSSVVTVPSS SLGTKTYTCN 200
VDHKPSNTKV DKRVESKYGP PCPPCPAPEA AGGPSVFLFP PKPKDTLMIS 250
RTPEVTCVVV DVSQEDPEVQ FNWYVDGVEV HNAKTKPREE QFNSTYRVVS 300
VLTVLHQDWL NGKEYKCKVS NKGLPSSIEK TISKAKGQPR EPQVYTLPPS 350
QEEMTKNQVS LTCLVKGFYP SDIAVEWESN GQPENNYKTT PPVLDSDGSF 400
FLYSRLTVDK SRWQEGNVFS CSVMHEALHN HYTQKSLSLS LG         442
```

Light chain / Chaîne légère / Cadena ligera

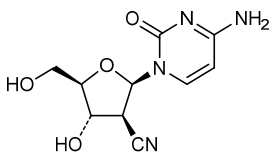
```
EIVLTQSPGT LSLSPGERAT LSCRSSQSLV HSNQNTYLHW YQQKPGQAPR  50
LLIYKVDNRF SGIPDRFSGS GSGTDFTLTI SRLEPEDFAV YYCSQSTLVP 100
LTFGGGTKVE IKRTVAAPSV FIFPPSDEQL KSGTASVVCL LNNFYPREAK 150
VQWKVDNALQ SGNSQESVTE QDSKDSTYSL SSTLTLSKAD YEKHKVYACE 200
VTHQGLSSPV TKSFNRGEC                                   219
```

Post-translational modifications
Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro
Intra-H (C23-C104) 22-96 143-199 257-317 363-421
22"-96" 143"-199" 257"-317" 363"-421"
Intra-L (C23-C104) 23'-93' 139'-199'
23'"-93'" 139'"-199'"
Inter-H-L (CH1 10-CL 126) 130-219' 130"-219'"
Inter-H-H (h 8, h 11) 222-222" 225-225"

N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación
H CH2 N84.4:
293, 293"
Fucosylated complex bi-antennary CHO-type glycans / glycanes de type CHO bi-antennaires complexes fucosylés / glicanos de tipo CHO biantenarios complejos fucosilados

Recommended International Nonproprietary Names (Rec. INN): List 85
Dénominations communes internationales recommandées (DCI Rec.): Liste 85
Denominaciones Comunes Internacionales Recomendadas (DCI Rec.): Lista 85
(WHO Drug Information, Vol. 35, No. 1, 2021)

p.200 **radgocitabinum**
radgocitabine *replace the structure by the following one*
radgocitabine *remplacer la structure par la suivante*
radgocitabina *sustitúyase la estructura por la siguiente*



p.233 **zanidatamabum zovodotinum #**

-235 zanidatamab zovodotin *replace the description and the structure by the following ones*

zanidatamab zovodotine *remplacer la description et la structure par les suivantes*

zanidatamab zovodotina *sustitúyase la descripción y la estructura por las siguientes*

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 **a derivative of** 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 an auristatin E derivative, via a cleavable 1-maleimido-3,6,9-trioxadodecan-12-oyl-valyl-citrullyl-*p*-aminobenzenesulfonyl linker**

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 **un dérivé de** 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, à **un dérivé de l'auristatine E**, via un linker clivable **1-maléimido-3,6,9-trioxadodécan-12-oyl-valyl-citrullyl-*p*-aminobenzènesulfonyle**.

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 un derivado de 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 cisteinilo en término medio, con **un derivado de auristatina E**, mediante un conector escindible **1-maleimido-3,6,9-trioxadodecan-12-oil-valil-citrullil-*p*-aminobencenesulfonilo.**

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"

***The inter-chain disulfide bridges are partially reduced, an average of 2 to 3 cysteinyl being conjugated each via a thioether bond to a drug linker. * Les ponts disulfure inter-chaînes sont partiellement réduits, une moyenne de 2 à 3 cystéinyl étant chacun conjugué via une liaison thioéther à un linker-principe actif. * Los puentes disulfuro inter-catenarios están parcialmente reducidos, una media de 2 a 3 cisteinil está conjugada a conectores de principio activo a través de un enlace tioeter.**

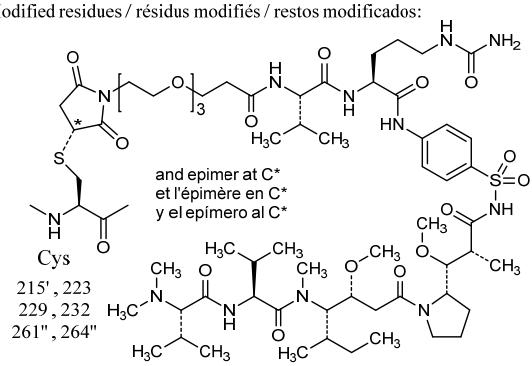
N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación

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:



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.

ヨビパス皮下注 168μg ペン
ヨビパス皮下注 294μg ペン
ヨビパス皮下注 420μg ペン

第 1 部（モジュール 1）

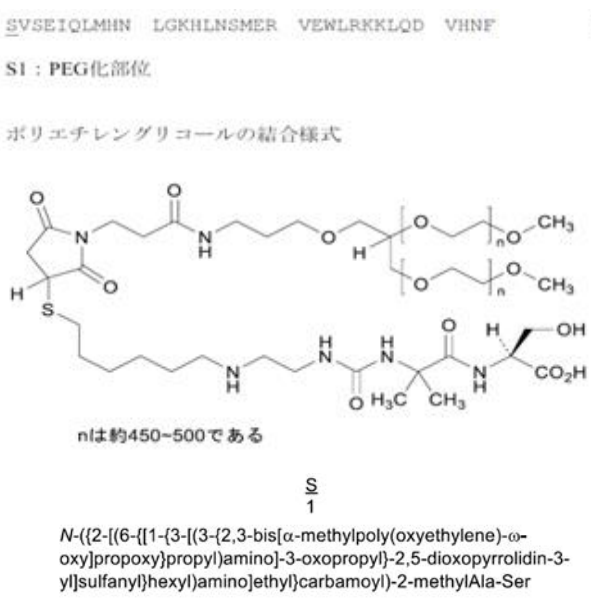
1.10　毒薬・劇薬等の指定審査資料のまとめ

帝人ファーマ株式会社

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1.10　毒薬・劇薬等の指定審査資料のまとめ..... 3

1.10　毒薬・劇薬等の指定審査資料のまとめ

化学名・別名	JAN（日本名）　パロペグテリパラチド JAN（英　名）　Palopegteriparatide
構　造　式	 S 1 *N*-({2-[(6-{[1-{3-[(3-{2,3-bis[α-methylpoly(oxyethylene)-ω-oxy]propoxy}propyl)amino]-3-oxopropyl}-2,5-dioxopyrrolidin-3-yl]sulfanyl}hexyl)amino]ethyl}carbamoyl)-2-methylAla-Ser
効能・効果	副甲状腺機能低下症
用法・用量	通常、成人には、パロペグテリパラチドを、PTH（1-34）として 1 回 18 μｇを開始用量とし、1 日 1 回、皮下注射する。以後、患者の血清カルシウム濃度の十分な管理のもとに、1 日 1 回 6～60 μｇの範囲で適宜用量を増減して皮下投与するが、増量又は減量は 3 μｇずつ行うこと。
劇薬等の指定	原薬：毒薬
販売名及び有効成分・分量	原体：パロペグテリパラチド 製剤： ヨビパス®皮下注 168 μg ペン：1 カートリッジ中 0.56 mL に PTH(1-34) 注1）　168 μg に相当するパロペグテリパラチドを含有する。 ヨビパス®皮下注 294 μg ペン：1 カートリッジ中 0.98 mL に PTH(1-34) 注1）　294 μg に相当するパロペグテリパラチドを含有する。 ヨビパス®皮下注 420 μg ペン：1 カートリッジ中 1.4 mL に PTH(1-34) 注1）　420 μg に相当するパロペグテリパラチドを含有する。 注 1) 副甲状腺ホルモンの N 末端 1～34 番目のアミノ酸に相当するペプチドである。
毒　　性	概略の致死量： ICH M3(R2)に基づき、急性毒性は反復投与毒性試験で適切に評価可能と考えられるため、パロペグテリパラチドの単回投与毒性試験は実施していない。 概略の致死量は、反復投与毒性試験（用量設定試験を含む）での投与期間初期に生じた死亡事例をもとに検討／算定した。 ラット：投与開始後初期（投与開始後 4 日目）に認められた全身状態の悪化及び安楽殺、死亡個体の発生状況を踏まえ、雌 60 μg PTH(1-34)/kg/day、雄 120 μg PTH(1-34)/kg/day と判断した。用量依存的な血清カルシウム濃度の増加が認められており、病理組織学的検査で心臓及び腎臓に石灰化、尿細管変性が確認された。大動脈を含む他の組織でも石灰化が認められた。すなわち、高カルシウム血症及びそれに引き続く組織石灰化が、死亡または安楽殺の原因となったと考えられた。

サル：反復投与毒性試験（用量設定試験含む）での最大耐量及び死亡個体の発生タイミングとその所見を考慮し、雌雄ともに 2.0 μg PTH(1-34)/kg/day より大きいと判断した。用量設定試験では最大投与量を 2.0 μg PTH(1-34)/kg/日として試験を開始したものの、投与 4 日目までに雌雄（各 1 例/群）ともに重篤な血清カルシウム値増加を示したことから、高カルシウム血症による死亡を回避することを目的に、投与 5 日目以降、投与量を 1.5 μg PTH(1-34)/kg/日に変更した。なお、26 週間反復投与毒性試験で 1.5 μg PTH(1-34)/kg/日群の雌 1 例で死亡しているものの、急性期の毒性変化に基づく死亡ではなく投与 24 日目に認められたこと、及び 4 週間反復投与毒性試験において 1.5 μg PTH(1-34)/kg/日まで死亡は認められなかったことから、概略の致死量には該当しないと考えた。

	概略の致死量	
	PTH(1-34)相当量	パロペグテリパラチド投与総量*
ラット	雌：60 μg PTH(1-34)/kg/day 雄：120 μg PTH(1-34)/kg/day	雌：691.2 μg/kg/day 雄：1382.4 μg/kg/day
サル	雌雄：>2.0 μg PTH(1-34)/kg/day	雌雄：>23.0 μg/kg/day

*: 換算係数 11.52（CTD 3.2.S.1.3）

反復投与毒性試験：
以下に記載する投与量は、PTH(1-34)相当量で記載している。PTH(1-34)の含量または濃度等価量をパロペグテリパラチドに対応する含量または濃度等価量に換算するためには、11.52 の理論換算係数を用いる。
ラット及びサルにおいて、26 週間反復投与毒性試験において、いずれの動物種も最高用量まで、オフターゲット毒性は認められなかった。
以下の毒性試験におけるすべての毒性所見は、副甲状腺機能が正常な動物が生理的濃度を超える PTH に持続的に曝露されたことによる用量依存的な薬理作用の過剰発現と考えられた。
反復投与により、用量依存的かつ可逆的な血清カルシウム濃度の増加が認められた一方、尿中カルシウム排泄量は維持された。試験に使用したすべての動物種において、最高用量では、薬理作用の過剰発現による血清カルシウム濃度の増加が用量制限毒性であった。

【ラット】
用量制限毒性として死亡又は安楽殺に至る顕著な持続性高カルシウム血症、一般状態変化（活動性の低下、呼吸異常、脱水、円背位、筋緊張低下）、体重減少及び軟部組織の石灰化が認められた。軟部組織の石灰化は、主に腎臓で認められ、大動脈、副腎、心筋、肝臓、肺、膵臓、胃、小腸及び大腸でも認められた。カルシウムの恒常性に対する影響は可逆的と考えられ、すべての試験で回復期間中に血清カルシウム濃度は正常化した。
用量依存的かつ可逆的な所見が骨端軟骨（成長板）に認められた。26 週反復投与毒性試験では、毒性所見として骨端軟骨の異形成が、非毒性所見として骨端軟骨の肥厚が認められた。20 μg PTH(1-34)/kg/日群で認められた骨端軟骨の異形成に基づき、無毒性量（NOAEL）は 10 μg PTH(1-34)/kg/日と判断した。26 週間反復投与毒性試験において、6 週間の回復期間終了時にこれら変化の発生頻度及び重篤度が低かったことから、骨端軟骨への影響は可逆的と考えられた。
薬理作用に関連した変化として、用量依存的で可逆的な骨代謝の増加が認められた。この骨代謝の増加は、主に、低用量[最大推奨臨床用量投与時の遊離 PTH の 2 倍（AUC 比）]では正味の骨異化作用（骨吸収）を、高用量[最大推奨臨床

用量投与時の遊離 PTH の 5 倍（AUC 比）]は正味の骨同化作用（骨形成）をもたらした。その他の変化として、赤血球数の減少（貧血）及び脾臓及び肝臓における髄外造血の亢進が認められた。この貧血及び造血系への影響は、主として骨同化作用及びそれに伴う骨髄腔の狭小化に関連した二次的変化と考えられた。

【サル】
4 週間反復投与毒性試験では、1.5 μg PTH(1-34)/kg/日まで投与に関連する死亡・瀕死は認められなかった。
26 週間反復投与毒性試験では、死亡を回避するための予防的措置として投与 25/26 日に最高投与量を 1.0 μg PTH(1-34)/kg/日に減量した。1.5 μg PTH(1-34)/kg/日投与時に認められた動物の死亡（雌 1 例、投与 24 日目）、1.5/1.0 μg PTH(1-34)/kg/日投与時に認められた血清カルシウム濃度の顕著かつ持続的な増加及び 1 例に認められたパロペグテリパラチド投与と関連する可能性がある重度の変性関節病変に基づき、NOAEL は 0.5 μg PTH(1-34)/kg/日と判断した。

動物種/系統 性、動物数（主群）	投与期間	投与方法	投与量	無毒性量
ラット/ Crl:CD（SD） 雌雄、10 匹/性/群	4 週間	皮下	0, 10, 30, 60 μg PTH(1-34)/kg/日	10 μg PTH(1-34)/kg/日
ラット/ Crl:CD（SD） 雌雄、12 匹/性/群	26 週間	皮下	0, 2, 5, 10, 20 μg PTH(1-34)/kg/日	10 μg PTH(1-34)/kg/日
カニクイザル 雌雄、3 又は 5 匹/性/群	4 週間	皮下	0, 0.2, 0.5, 1.5 μg PTH(1-34)/kg/日	1.5 μg PTH(1-34)/kg/日
カニクイザル 雌雄、6 匹/性/群	26 週間	皮下	0, 0.2, 0.5, 1.0/1.5* μg PTH(1-34)/kg/日	0.5 μg PTH(1-34)/kg/日

*: 投与 25/26 日目以降に高カルシウム血症による死亡回避の予防的措置として投与量を減量した

副　作　用	CCSI 及び海外第Ⅲ相臨床試験及び国内第Ⅲ相臨床試験（TCP-304 試験及び TCP-305 試験）の結果に基づき記載した。 副作用発現率（臨床検査異常を含む）　30／74（40.5%） 副作用の種類（臨床検査値異常を含む）　例数（%） 注射部位反応（紅斑、内出血、発疹等）　25（33.8） 頭痛　6（8.1） 高カルシウム血症　7（9.5） 悪心　5（6.8） 下痢　3（4.1） 浮動性めまい　1（1.4） 体位性めまい　1（1.4） 動悸　1（1.4）
会　　社	帝人ファーマ株式会社　製剤：製造

ヨビパス皮下注 168 μg ペン
ヨビパス皮下注 294 μg ペン
ヨビパス皮下注 420 μg ペン

第 1 部（モジュール 1）

1.12　添付資料一覧

帝人ファーマ株式会社

1.12　添付資料一覧

第 3 部（モジュール 3）品質に関する文書　添付資料一覧

CTD No.- 資料番号	著者	表題	実施場所 （国内／海外）	掲載誌・ その他	評価／ 参考
3.1　TABLE OF CONTENTS OF MODULE 3					
3.2　BODY OF DATA					

3.2.S　原薬（パロペグテリパラチド）

CTD No.- 資料番号	著者	表題	実施場所 （国内／海外）	掲載誌・ その他	評価／ 参考
3.2.S　DRUG SUBSTANCE (Palopegteriparatide, [redacted])					
3.2.S.1	General Information (Palopegteriparatide, [redacted])				
3.2.S.1.1	帝人ファーマ株式会社	Nomenclature (Palopegteriparatide, [redacted])	海外	社内資料	評価
3.2.S.1.2	帝人ファーマ株式会社	Structure (Palopegteriparatide, [redacted])	海外	社内資料	評価
3.2.S.1.3	帝人ファーマ株式会社	General Properties (Palopegteriparatide, [redacted])	海外	社内資料	評価
3.2.S.2	Manufacture (Palopegteriparatide, [redacted])				
3.2.S.2.1	帝人ファーマ株式会社	Manufacturers (Palopegteriparatide, [redacted])	国内／海外	社内資料	評価
3.2.S.2.2	帝人ファーマ株式会社	Introduction to Manufacturing Process and Process Controls (Palopegteriparatide, [redacted])	国内／海外	社内資料	評価
3.2.S.2.2	帝人ファーマ株式会社	Manufacturing Process for mPEG-maleimide (Palopegteriparatide, [redacted])	国内	社内資料	評価
3.2.S.2.2	帝人ファーマ株式会社	Manufacturing Process for PTH(1-34) Linker Thiol (Palopegteriparatide, [redacted])	海外	社内資料	評価
3.2.S.2.2	帝人ファーマ株式会社	Manufacturing Process for Palopegteriparatide Drug Substance (Palopegteriparatide, [redacted])	海外	社内資料	評価
3.2.S.2.3	帝人ファーマ株式会社	Control of Materials (Palopegteriparatide, [redacted]) Introduction to Control of Starting Materials	国内／海外	社内資料	評価

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3.2.S.2.3	帝人ファーマ株式会社	Control of Materials (Palopegteriparatide, [redacted]) Manufacturing and Control of Amino Acid Derivatives	海外	社内資料	評価
3.2.S.2.3	帝人ファーマ株式会社	Control of Materials (Palopegteriparatide, [redacted]) Manufacturing and Control of Amino Acid Derivatives - Appendix 1	海外	社内資料	評価
3.2.S.2.3	帝人ファーマ株式会社	Control of Materials (Palopegteriparatide, [redacted]) Manufacturing and Control of Linker Reagent F	海外	社内資料	評価
3.2.S.2.3	帝人ファーマ株式会社	Control of Materials (Palopegteriparatide, [redacted]) Manufacturing and Control of mPEG-propylamine	国内／海外	社内資料	評価
3.2.S.2.3	帝人ファーマ株式会社	Control of Materials (Palopegteriparatide, [redacted]) Raw Materials for Manufacture of mPEG-maleimide	国内	社内資料	評価
3.2.S.2.3	帝人ファーマ株式会社	Control of Materials (Palopegteriparatide, [redacted]) Raw Materials for Manufacture of Palopegteriparatide	海外	社内資料	評価
3.2.S.2.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Palopegteriparatide, [redacted]) Critical In-Process Controls for PTH(1-34) Linker Thiol	海外	社内資料	評価
3.2.S.2.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Palopegteriparatide, [redacted]) Analytical Procedures for PTH(1-34) Linker Thiol In-Process Controls	海外	社内資料	評価
3.2.S.2.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Palopegteriparatide, [redacted]) Critical In-Process Controls for Palopegteriparatide Drug Substance	海外	社内資料	評価
3.2.S.2.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Palopegteriparatide, [redacted]) Analytical Procedures for Palopegteriparatide Drug Substance In-Process Controls	海外	社内資料	評価
3.2.S.2.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Palopegteriparatide, [redacted]) Control of PTH(1-34) Linker Thiol	海外	社内資料	評価

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3.2.S.2.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Palopegteriparatide, [redacted]) A-PTH-041, ESI-MS and ESI-MS/MS Analysis for Identity, PTH(1-34) Linker Thiol	海外	社内資料	評価
3.2.S.2.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Palopegteriparatide, [redacted]) A-PTH-015, Amino Acid Analysis for Identity, PTH(1-34) Linker Thiol	海外	社内資料	評価
3.2.S.2.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Palopegteriparatide, [redacted]) A-PTH-027, Elemental Analysis for Content, PTH(1-34) Linker Thiol	海外	社内資料	評価
3.2.S.2.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Palopegteriparatide, [redacted]) A-PTH-007, HPLC Analysis for Purity and Impurities, PTH(1-34) Linker Thiol	海外	社内資料	評価
3.2.S.2.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Palopegteriparatide, [redacted]) A-PTH-019, SE-HPLC Analysis for HMWS, PTH(1-34) Linker Thiol	海外	社内資料	評価
3.2.S.2.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Palopegteriparatide, [redacted]) Control of mPEG-maleimide	国内／海外	社内資料	評価
3.2.S.2.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Palopegteriparatide, [redacted]) A-PTH-038, MALDI-TOF-MS Analysis for Average MW, mPEG-maleimide	国内	社内資料	評価
3.2.S.2.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Palopegteriparatide, [redacted]) A-PTH-029, GPC Analysis for Purity, HMWS and polydispersity, mPEG-maleimide	国内	社内資料	評価
3.2.S.2.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Palopegteriparatide, [redacted])	国内	社内資料	評価

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		A-PTH-002, IEX-HPLC Analysis for Terminal Activity, mPEG-maleimide			
3.2.S.2.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Palopegteriparatide, [redacted]) A-PTH-021 HPLC Analysis for N-SMP, mPEG-maleimide	国内	社内資料	評価
3.2.S.2.5	帝人ファーマ株式会社	Process Validation and/or Evaluation (Palopegteriparatide, [redacted]) Process Validation	国内／海外	社内資料	評価
3.2.S.2.6	帝人ファーマ株式会社	Manufacturing Process Development (Palopegteriparatide, [redacted])	国内／海外	社内資料	評価
3.2.S.3	Characterisation (Palopegteriparatide, [redacted])				
3.2.S.3.1	帝人ファーマ株式会社	Elucidation of Structure and Other Characteristics (Palopegteriparatide, [redacted])	海外	社内資料	評価
3.2.S.3.2	帝人ファーマ株式会社	Impurities (Palopegteriparatide, [redacted])	海外	社内資料	評価
3.2.S.4	Control of Drug Substance (Palopegteriparatide, [redacted])				
3.2.S.4.1	帝人ファーマ株式会社	Specification (Palopegteriparatide, [redacted])	海外	社内資料	評価
3.2.S.4.2	帝人ファーマ株式会社	Analytical Procedures (Palopegteriparatide, [redacted]) Analytical Procedures	海外	社内資料	評価
3.2.S.4.2	帝人ファーマ株式会社	Analytical Procedures (Palopegteriparatide, [redacted]) Analytical Development	海外	社内資料	評価
3.2.S.4.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Palopegteriparatide, [redacted]) Validation Statement	海外	社内資料	評価
3.2.S.4.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Palopegteriparatide, [redacted]) A-PTH-031, HPLC Analysis for Identity, Purity and Related Impurities	海外	社内資料	評価
3.2.S.4.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Palopegteriparatide, [redacted]) A-PTH-040, MALDI-MS Analysis for Identity	海外	社内資料	評価
3.2.S.4.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Palopegteriparatide, [redacted]) A-PTH-052, HPLC Analysis for Content	海外	社内資料	評価
3.2.S.4.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Palopegteriparatide, [redacted])	海外	社内資料	評価

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		A-PTH-013, SE-HPLC Analysis for HMWS			
3.2.S.4.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Palopegteriparatide, [redacted]) A-PTH-037, HPLC Analysis for Purity and Related Impurities of Released PTH(1-34)	海外	社内資料	評価
3.2.S.4.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Palopegteriparatide, [redacted]) A-PTH-008, HPLC-CAD Analysis for Total Free PEG	海外	社内資料	評価
3.2.S.4.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Palopegteriparatide, [redacted]) A-PTH-018, IC Analysis for Acetic Acid Content	海外	社内資料	評価
3.2.S.4.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Palopegteriparatide, [redacted]) A-PTH-036, IC Analysis for TFA Content	海外	社内資料	評価
3.2.S.4.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Palopegteriparatide, [redacted]) A-PTH-001, GC Analysis for Residual Organic Solvents	海外	社内資料	評価
3.2.S.4.4	帝人ファーマ株式会社	Batch Analyses (Palopegteriparatide, [redacted])	海外	社内資料	評価
3.2.S.4.5	帝人ファーマ株式会社	Justification of Specification (Palopegteriparatide, [redacted]) Justification of Specification	海外	社内資料	評価
3.2.S.4.5	帝人ファーマ株式会社	Justification of Specification (Palopegteriparatide, [redacted]) Control Strategy	海外	社内資料	評価
3.2.S.5	Reference Standards or Materials (Palopegteriparatide, [redacted])				
3.2.S.5	帝人ファーマ株式会社	Reference Standards or Materials (Palopegteriparatide, [redacted]) Palopegteriparatide Primary Reference Standards	海外	社内資料	評価
3.2.S.5	帝人ファーマ株式会社	Reference Standards or Materials (Palopegteriparatide, [redacted]) Protocol for Establishment of Palopegteriparatide Reference Standards	海外	社内資料	評価
3.2.S.6	Container Closure System (Palopegteriparatide, [redacted])				
3.2.S.6	帝人ファーマ株式会社	Container Closure System (Palopegteriparatide, [redacted])	海外	社内資料	評価
3.2.S.7	Stability (Palopegteriparatide, [redacted])				
3.2.S.7.1	帝人ファーマ株式会社	Stability Summary and Conclusions (Palopegteriparatide, [redacted])	海外	社内資料	評価

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3.2.S.7.2	帝人ファーマ株式会社	Post-Approval Stability Protocol and Stability Commitment (Palopegteriparatide, [redacted])	海外	社内資料	評価
3.2.S.7.3	帝人ファーマ株式会社	Stability Data (Palopegteriparatide, [redacted]) Forced Degradation Studies	海外	社内資料	評価
3.2.S.7.3	帝人ファーマ株式会社	Stability Data (Palopegteriparatide, [redacted]) Stability Data – Primary and Supportive	海外	社内資料	評価
3.2.S.7.3	帝人ファーマ株式会社	Stability Data (Palopegteriparatide, [redacted]) Stability Data – PPQ	海外	社内資料	評価

3.2.P　製剤（ヨビパス皮下注 168 μg ペン、ヨビパス皮下注 294 μg ペン、ヨビパス皮下注 420 μg ペン）

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3.2.P　DRUG PRODUCT (Yorvipath Subcutaneous Injection, Injections)					
3.2.P.1	Description and Composition of the Drug Product (Yorvipath Subcutaneous Injection, Injections)				
3.2.P.1	帝人ファーマ株式会社	Description and Composition of the Drug Product (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.2	Pharmaceutical Development (Yorvipath Subcutaneous Injection, Injections)				
3.2.P.2.1	帝人ファーマ株式会社	Components of the Drug Product (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.2.2	帝人ファーマ株式会社	Drug Product (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.2.3	帝人ファーマ株式会社	Manufacturing Process Development (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.2.4	帝人ファーマ株式会社	Container Closure System Primary Container Closure (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.2.4	帝人ファーマ株式会社	Container Closure System Functional Secondary Container Closure (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.2.5	帝人ファーマ株式会社	Microbiological Attributes (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.2.6	帝人ファーマ株式会社	Compatibility (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.3	Manufacture (Yorvipath Subcutaneous Injection, Injections)				
3.2.P.3.1	帝人ファーマ株式会社	Manufacturers (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.3.2	帝人ファーマ株式会社	Batch Formula (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.3.3	帝人ファーマ株式会社	Description of Manufacturing Process and Process Controls (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.3.4	帝人ファーマ株式会社	Control of Critical Steps and Intermediates (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.3.5	帝人ファーマ株式会社	Process Validation Strategy and Overview (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価

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3.2.P.3.5	帝人ファーマ株式会社	Process Performance Qualification (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.3.5	帝人ファーマ株式会社	Process Performance Qualification of Final Assembly Process (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.3.5	帝人ファーマ株式会社	Process Justification Summary (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.3.5	帝人ファーマ株式会社	Validation of Aseptic Processing (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.3.5	帝人ファーマ株式会社	Validation of Sterilizing Filter (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.4	Control of Excipients (Yorvipath Subcutaneous Injection, Injections)				
3.2.P.4	帝人ファーマ株式会社	Control of Excipients (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.5	Control of Drug Product (Yorvipath Subcutaneous Injection, Injections)				
3.2.P.5.1	帝人ファーマ株式会社	Specifications (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.5.2	帝人ファーマ株式会社	Analytical Procedures (Yorvipath Subcutaneous Injection, Injections) Analytical procedure	海外	社内資料	評価
3.2.P.5.2	帝人ファーマ株式会社	Analytical Procedures (Yorvipath Subcutaneous Injection, Injections) Analytical Development	海外	社内資料	評価
3.2.P.5.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Yorvipath Subcutaneous Injection, Injections) Validation Statement	海外	社内資料	評価
3.2.P.5.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Yorvipath Subcutaneous Injection, Injections) A-PTH-043, HPLC Analysis for Identity, Content and Related Impurities	海外	社内資料	評価
3.2.P.5.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Yorvipath Subcutaneous Injection, Injections) A-PTH-024, MALDI-MS Analysis for Identity	海外	社内資料	評価

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3.2.P.5.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Yorvipath Subcutaneous Injection, Injections) A-PTH-033, HPLC Analysis for PTH(1-34) Release Profile	海外	社内資料	評価
3.2.P.5.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Yorvipath Subcutaneous Injection, Injections) A-PTH-003, HPLC Analysis for Related Impurities of Released PTH(1-34)	海外	社内資料	評価
3.2.P.5.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Yorvipath Subcutaneous Injection, Injections) A-PTH-032, HPLC Analysis for Identity and Content of Metacresol	海外	社内資料	評価
3.2.P.5.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Yorvipath Subcutaneous Injection, Injections) Compendial Test, Bacterial Endotoxins Test	海外	社内資料	評価
3.2.P.5.3	帝人ファーマ株式会社	Validation of Analytical Procedures (Yorvipath Subcutaneous Injection, Injections) Compendial Test, Sterility	海外	社内資料	評価
3.2.P.5.4	帝人ファーマ株式会社	Batch Analyses (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.5.5	帝人ファーマ株式会社	Characterization of Impurities (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.5.5	帝人ファーマ株式会社	Characterization of Impurities (Yorvipath Subcutaneous Injection, Injections) Biological Activity	海外	社内資料	評価
3.2.P.5.5	帝人ファーマ株式会社	Characterization of Impurities (Yorvipath Subcutaneous Injection, Injections) Nitrosamine Risk Assessment	海外	社内資料	評価
3.2.P.5.5	帝人ファーマ株式会社	Characterization of Impurities (Yorvipath Subcutaneous Injection, Injections) Elemental Impurities	海外	社内資料	評価

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3.2.P.5.5	帝人ファーマ株式会社	Characterization of Impurities (Yorvipath Subcutaneous Injection, Injections) Forced Degradation Studies	海外	社内資料	評価
3.2.P.5.6	帝人ファーマ株式会社	Justification of Specifications (Yorvipath Subcutaneous Injection, Injections) Justification of Specifications	海外	社内資料	評価
3.2.P.5.6	帝人ファーマ株式会社	Justification of Specifications (Yorvipath Subcutaneous Injection, Injections) Control Strategy	海外	社内資料	評価
3.2.P.6	Reference Standards or Materials (Yorvipath Subcutaneous Injection, Injections)				
3.2.P.6	帝人ファーマ株式会社	Reference Standards or Materials (Yorvipath Subcutaneous Injection, Injections) Palopegteriparatide Reference Standards	海外	社内資料	評価
3.2.P.7	Container Closure System (Yorvipath Subcutaneous Injection, Injections)				
3.2.P.7	帝人ファーマ株式会社	Container Closure System, Primary Packaging (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.7	帝人ファーマ株式会社	Container Closure System, Secondary Packaging (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.7	帝人ファーマ株式会社	DEVICE Design and Development (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.7	帝人ファーマ株式会社	DEVICE Relevant Standards (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.7	帝人ファーマ株式会社	DEVICE Ypsomed Manufacturing and Assembly (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.7	帝人ファーマ株式会社	DEVICE Design Verifications (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.7	帝人ファーマ株式会社	DEVICE HFE Studies and Design Validation (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価

CTD No.- 資料番号	著者	表題	実施場所 （国内／海外）	掲載誌・ その他	評価／ 参考
3.2.P.7	帝人ファーマ株式会社	DEVICE Risk Management (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.8	Stability (Yorvipath Subcutaneous Injection, Injections)				
3.2.P.8.1	帝人ファーマ株式会社	Stability Summary and Conclusions (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.8.2	帝人ファーマ株式会社	Post-Approval Stability Protocol and Stability Commitment (Yorvipath Subcutaneous Injection, Injections)	海外	社内資料	評価
3.2.P.8.3	帝人ファーマ株式会社	Stability Data (Yorvipath Subcutaneous Injection, Injections) Primary Stability Data	海外	社内資料	評価
3.2.P.8.3	帝人ファーマ株式会社	Stability Data (Yorvipath Subcutaneous Injection, Injections) Supportive Stability Data	海外	社内資料	評価
3.2.P.8.3	帝人ファーマ株式会社	Stability Data (Yorvipath Subcutaneous Injection, Injections) PPQ Stability Data	海外	社内資料	評価
3.2.P.8.3	帝人ファーマ株式会社	Stability Data (Yorvipath Subcutaneous Injection, Injections) In-Use Stability Data	海外	社内資料	評価
3.2.P.8.3	帝人ファーマ株式会社	Stability Data (Yorvipath Subcutaneous Injection, Injections) Stability Testing After Pen Assembly	海外	社内資料	評価
3.2.P.8.3	帝人ファーマ株式会社	Stability Data (Yorvipath Subcutaneous Injection, Injections) Photostability	海外	社内資料	評価
3.2.P.8.3	帝人ファーマ株式会社	Stability Data (Yorvipath Subcutaneous Injection, Injections) Analytical Procedure, Stability Testing, Break Loose and Gliding Force	海外	社内資料	評価

3.2.A　その他

CTD No.- 資料番号	著者	表題	実施場所 （国内／海外）	掲載誌・ その他	評価／ 参考
3.2.A　その他					
3.2.A.1	帝人ファーマ株式会社	Facilities and Equipment (Yorvipath Subcutaneous Injection, [redacted])	海外	社内資料	評価
3.2.A.2	帝人ファーマ株式会社	Adventitious Agents Safety Evaluation (Yorvipath Subcutaneous Injection, Injections, [redacted] and [redacted])	海外	社内資料	評価
3.2.A.3	帝人ファーマ株式会社	Excipients	該当なし		

3.2.R　各極の要求資料

CTD No.- 資料番号	著者	表題	実施場所 （国内／海外）	掲載誌・ その他	評価／ 参考
3.2.R	帝人ファーマ株式会社	Regional Information	該当なし		

3.3　参考文献

CTD No.- 資料番号	著者	表題	実施場所 （国内／海外）	掲載誌・ その他	評価／ 参考
3.3	帝人ファーマ株式会社	Literature References	－	－	参考
－	Allen PV, Dukes GR, Gerger ME.	Determination of release limits: a general methodology.	－	Pharm Res. 1991; 8(9):1210–1213.	参考
－	Marx UC, Adermann K, Bayer P, et al.	Solution structures of human parathyroid hormone fragments hPTH(1-34) and hPTH(1-39) and bovine parathyroid hormone fragment bPTH(1-37).	－	Biochem Biophys Res Commun.	参考

				2000;267(1):213–220.	
－	Kaiser E, Colescott RL, Bossinger CD, et al.	Color test for detection of free terminal amino groups in the solid-phase synthesis of peptides.	－	Anal Biochem. 1970; 34(2):595–598	参考
－	Hancock WS, Battersby JE.	A new micro-test for the detection of incomplete coupling reactions in solid-phase peptide synthesis using 2,4,6-trinitrobenzenesulphonic acid.	－	Anal Biochem. 1976; 71(1):260–264.	参考
－	Vázquez J, Qushair G, Albericio F.	Qualitative colorimetric tests for solid phase synthesis.	－	Methods Enzymol. 2003;369:21–35.	参考

4.2.1　薬理試験

CTD No.-資料番号	著者	表題	実施場所（国内／海外）	掲載誌・その他	評価／参考
4.2.1.1　効力を裏付ける試験					
4.2.1.1-1	[redacted]	Analysis of Binding of TransCon PTH to PTH Receptor1 by Surface Plasmon Resonance	海外	社内資料	評価
4.2.1.1-2	Ascendis Pharma, GmbH	BIOPOTENCY TESTING OF PTH(1-33)	海外	社内資料	評価
4.2.1.1-3	[redacted]	Pharmacokinetics of TransCon PTH (ACP-014) in the Male Sprague Dawley Rat Following Intravenous and Subcutaneous Administration	海外	社内資料	評価
4.2.1.1-4	[redacted]	Pharmacokinetics of TransCon PTH in the Male Cynomolgus Monkey	海外	社内資料	評価

CTD No.- 資料番号	著者	表題	実施場所 （国内／海外）	掲載誌・ その他	評価／ 参考
	[redacted]	Following Subcutaneous and Intravenous Administration			
4.2.1.1-5	[redacted]	A 28-Day Subcutaneous Injection Comparative Study of Positive Control and TransCon PTH in TPTx Rats	海外	社内資料	評価
4.2.1.3　安全性薬理試験					
4.2.1.3-1	[redacted]	A Pharmacological Assessment of the Effect of ACP-014 on the Central Nervous System of Sprague Dawley Rats	海外	社内資料	評価
4.2.1.3-2	[redacted]	A Pharmacological Assessment of the Effect of TransCon PTH (ACP-014) on the Respiratory System of Sprague Dawley Rats	海外	社内資料	評価
4.2.1.3-3	[redacted]	A Pharmacological Assessment of the Effects of TransCon (ACP-014) on the Cardiovascular System of the Cynomolgus Monkey Using Telemetry	海外	社内資料	評価

4.2.2　薬物動態試験

CTD No.- 資料番号	著者	表題	実施場所 （国内／海外）	掲載誌・ その他	評価／ 参考
4.2.2.1　分析法及びバリデーション報告書					
4.2.2.1-1	[redacted]	Validation of a method for the determination of mPEG in rat EDTA plasma samples by LC-MS/MS (API6500)	海外	社内資料	評価
4.2.2.1-2	[redacted]	Validation of a method for the determination of mPEG and mPEG-linker in rat EDTA plasma samples by LC-MS/MS (API 6500)	海外	社内資料	評価

CTD No.- 資料番号	著者	表題	実施場所 （国内／海外）	掲載誌・ その他	評価／ 参考
4.2.2.1-3	[redacted]	Validation of a method for the determination of Total PTH in rat EDTA plasma samples by LC-MS/MS (Triple Quad 6500)	海外	社内資料	評価
4.2.2.1-4	[redacted]	Validation of a method for the determination of Free PTH(1-34) and Free PTH(1-33) in acidified rat EDTA plasma samples by LC-MS/MS (Triple Quad 6500)	海外	社内資料	評価
4.2.2.1-5	[redacted]	Additional Validation of a Method for the Determination of Free PTH(1-34) and Free PTH(1-33) in Acidified Rat EDTA Plasma Samples by LC-MS/MS	海外	社内資料	評価
4.2.2.1-6	[redacted]	Qualification of a method for the determination of endogenous PTH(1-84) concentrations in rat plasma samples by ELISA	海外	社内資料	評価
4.2.2.1-7	[redacted]	Qualification of a method for the determination of PTH(1-84) in rat plasma samples by ELISA	海外	社内資料	評価
4.2.2.1-8	[redacted]	Scientific validation of an analytical method for the determination of Total PTH in rabbit plasma samples by LC-MS/MS (Triple Quad 6500)	海外	社内資料	評価
4.2.2.1-9	[redacted]	Validation of a method for the determination of Free PTH(1-34) and Free PTH(1-33) in acidified rabbit EDTA plasma samples by LC-MS/MS (Triple Quad 6500)	海外	社内資料	評価

CTD No.- 資料番号	著者	表題	実施場所 （国内／海外）	掲載誌・ その他	評価／ 参考
4.2.2.1-10	[redacted]	Validation of a method for the determination of mPEG in monkey EDTA plasma samples by LC-MS/MS (API6500)	海外	社内資料	評価
4.2.2.1-11	[redacted]	Validation of a method for the determination of mPEG and mPEG-linker in monkey EDTA plasma samples by LC-MS/MS (API 6500)	海外	社内資料	評価
4.2.2.1-12	[redacted]	Validation of a method for the determination of mPEG and mPEG-linker in monkey EDTA plasma samples by LC-MS/MS (Triple Quad 6500)	海外	社内資料	評価
4.2.2.1-13	[redacted]	Validation of a method for the determination of Total PTH in monkey EDTA plasma samples by LC-MS/MS (Triple Quad 6500)	海外	社内資料	評価
4.2.2.1-14	[redacted]	Validation of a method for the determination of Free PTH(1-34) and Free PTH(1-33) in acidified cynomolgus monkey EDTA plasma samples by LC-MS/MS (Triple Quad 6500)	海外	社内資料	評価
4.2.2.1-15	[redacted]	Qualification of a method for the determination of PTH(1-84) in monkey plasma samples by ELISA.	海外	社内資料	評価
4.2.2.1-16	[redacted]	Validation of an Immunoassay for the Detection of Parathyroid Hormone Antibodies in Rat Serum	海外	社内資料	評価
4.2.2.1-17	[redacted]	Qualification of an Immunoassay for the Detection of Anti-Parathyroid Hormone Antibodies in Rabbit Serum	海外	社内資料	評価

CTD No.- 資料番号	著者	表題	実施場所 （国内／海外）	掲載誌・ その他	評価／ 参考
4.2.2.1-18	[redacted]	Validation of an Immunoassay for the Detection of Parathyroid Hormone Antibodies in Cynomolgus Monkey Serum	海外	社内資料	評価
4.2.2.1-19	[redacted]	Validation of an Immunoassay for the Detection of Antibodies to Polyethylene Glycol in response to ACP-014 in Cynomolgus Monkey Serum	海外	社内資料	評価
4.2.2.2　吸収					
4.2.2.2-1	Ascendis Pharma, GmbH	INFLUENCE OF PH ON LINKER CLEAVAGE AT 37 °C OF ACP-014	海外	社内資料	評価
4.2.2.2-2	Ascendis Pharma, GmbH	INFLUENCE OF TEMPERATURE ON ACP-014 LINKER CLEAVAGE AT PH 7.40	海外	社内資料	評価
4.2.2.2-3 (4.2.1.1-3 参照)	[redacted]	Pharmacokinetics of TransCon PTH (ACP-014) in the Male Sprague Dawley Rat Following Intravenous and Subcutaneous Administration	海外	社内資料	評価
4.2.2.2-4 (4.2.1.1-4 参照)	[redacted]	Pharmacokinetics of TransCon PTH in the Male Cynomolgus Monkey Following Subcutaneous and Intravenous Administration	海外	社内資料	評価
4.2.2.2-5	Ascendis Pharma, GmbH	Determination of plasma concentrations and pharmacokinetic evaluation of TransCon PTH measured as Total PTH, Total PTH(1-34), mPEG and Free PTH(1-34) in plasma samples from Study No. [redacted] (Pharmacokinetics of TransCon PEG PTH in the Male Cynomolgus Monkey Following Subcutaneous and Intravenous Administration)	海外	社内資料	評価
4.2.2.2-6 (4.2.3.2-1 参照)	[redacted]	A Subcutaneous Range Finding Injection Toxicity Study of TransCon PTH (ACP-014) in the Albino Rat	海外	社内資料	評価

CTD No.- 資料番号	著者	表題	実施場所 （国内／海外）	掲載誌・ その他	評価／ 参考
4.2.2.2-7 (4.2.3.2-2 参照)	[redacted]	A 28-Day Subcutaneous Injection Toxicity Study Of TransCon PTH (ACP-014) In The Albino Rat with a 2-Week Recovery Period	海外	社内資料	評価
4.2.2.2-8 (4.2.3.2-3 参照)	[redacted]	A 26-Week Subcutaneous Injection Toxicity Study Of TransCon PTH (ACP-014) in The Albino Rat Followed By A 6-Week Recovery Period	海外	社内資料	評価
4.2.2.2-9 (4.2.3.2-4 参照)	[redacted]	28-Day Range Finding Subcutaneous Injection Toxicity Study Of TransCon PTH In The Cynomolgus Monkey	海外	社内資料	評価
4.2.2.2-10 (4.2.3.2-5 参照)	[redacted]	A 28-Day Subcutaneous Injection Toxicity Study of TransCon PTH (ACP-014) in the Cynomolgus Monkey with a 2-Week Recovery Period	海外	社内資料	評価
4.2.2.2-11 (4.2.3.2-6 参照)	[redacted]	A 26-Week Subcutaneous Injection Toxicity Study of TransCon PTH (ACP-014) in The Cynomolgus Monkey Followed by a 13-Week Recovery Period	海外	社内資料	評価
4.2.2.2-12 (4.2.3.5.2-1 参照)	[redacted]	A Dosage Range-finding Embryo-fetal Development Study of TransCon PTH (ACP-014) by Subcutaneous Injection in Rats	海外	社内資料	評価
4.2.2.2-13 (4.2.3.5.2-3 参照)	[redacted]	An Dosage Range-finding Embryo-fetal Development Study of TransCon PTH (ACP-014) by Subcutaneous Injection in Rabbits	海外	社内資料	評価
4.2.2.2-14 (4.2.3.5.2-4 参照)	[redacted]	An Embryo-fetal Development Study of TransCon PTH (ACP-014) by Daily Subcutaneous Injection in Rabbits	海外	社内資料	評価
4.2.2.2-15 (4.2.3.5.3-1 参照)	[redacted]	A Pre and Postnatal Development Study of TransCon PTH (ACP-014) by Daily Subcutaneous Injection in Rats	海外	社内資料	評価
4.2.2.4　代謝					
4.2.2.4-1	Ascendis Pharma, GmbH	METABOLITE ASSESSMENT OF TRANSCON PTH (ACP-014) IN PLASMA FROM HUMANS, CYNOMOLGUS MONKEYS AND SPRAGUE DAWLEY RATS	海外	社内資料	評価

4.2.3 毒性試験

CTD No.- 資料番号	著者	表題	実施場所 （国内／海外）	掲載誌・ その他	評価／ 参考
4.2.3.2 反復投与毒性試験					
4.2.3.2-1	[redacted]	A Subcutaneous Range Finding Injection Toxicity Study of TransCon PTH(ACP-014) in the Albino Rat	海外	社内資料	参考
4.2.3.2-2	[redacted]	A 28-Day Subcutaneous Injection Toxicity Study of TransCon PTH (ACP-014) in the Albino Rat with a 2-Week Recovery Period	海外	社内資料	評価
4.2.3.2-3	[redacted]	A 26-Week Subcutaneous Injection Toxicity Study of TransCon PTH (ACP-014) in the Albino Rat Followed by a 6-Week Recovery Period	海外	社内資料	評価
4.2.3.2-4	[redacted]	28-Day Range Finding Subcutaneous Injection Toxicity Study of TransCon PTH in the Cynomolgus Monkey	海外	社内資料	参考
4.2.3.2-5	[redacted]	A 28-Day Subcutaneous Injection Toxicity Study of TransCon PTH (ACP-014) in the Cynomolgus Monkey with a 2-Week Recovery Period	海外	社内資料	評価
4.2.3.2-6	[redacted]	A 26-Week Subcutaneous Injection Toxicity Study of TransCon PTH (ACP-014) in the Cynomolgus Monkey Followed by a 13-Week Recovery Period	海外	社内資料	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	[redacted]	Partly Hydrolyzed TransCon PTH (ACP-014): Bacterial Reverse Mutation Test in Salmonella Typhimurium and Escherichia Coli	海外	社内資料	評価

CTD No.- 資料番号	著者	表題	実施場所 （国内／海外）	掲載誌・ その他	評価／ 参考
4.2.3.3.1-2	[redacted]	Partly Hydrolyzed TransCon PTH (ACP-014): In Vitro Mammalian Chromosome Aberration Test in Human Peripheral Blood Lymphocytes	海外	社内資料	評価
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					
4.2.3.5.1-1	[redacted]	A Subcutaneous Injection Fertility and Early Embryonic Development Study of TransCon PTH (ACP-014) in the Female Rat	海外	社内資料	評価
4.2.3.5.1-2	[redacted]	A Subcutaneous Injection Fertility and Early Embryonic Development Study of TransCon PTH (ACP-014) in the Male Rat	海外	社内資料	評価
4.2.3.5.2 胚・胎児発生に関する試験					
4.2.3.5.2-1	[redacted]	A Dosage Range-finding Embryo-fetal Development Study of TransCon PTH (ACP-014) by Subcutaneous Injection in Rats	海外	社内資料	参考
4.2.3.5.2-2	[redacted]	An Embryo-Fetal Development Study of TransCon PTH (ACP-014) by Subcutaneous Injection in Rats	海外	社内資料	評価
4.2.3.5.2-3	[redacted]	An Dosage Range-finding Embryo-fetal Development Study of TransCon PTH (ACP-014) by Subcutaneous Injection in Rabbits	海外	社内資料	参考
4.2.3.5.2-4	[redacted]	An Embryo-Fetal Development Study of TransCon PTH (ACP-014) by Daily Subcutaneous Injection in Rabbits	海外	社内資料	評価
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					
4.2.3.5.3-1	[redacted]	A Pre and Postnatal Development Study of TransCon PTH (ACP-014) by Daily Subcutaneous Injection in Rats	海外	社内資料	評価
4.2.3.7　その他の毒性試験					
4.2.3.7.7 その他の試験					

CTD No.- 資料番号	著者	表題	実施場所 （国内／海外）	掲載誌・ その他	評価／ 参考
4.2.3.7.7-1	[redacted]	Computational assessment and evaluation of potential for genotoxic and nongenotoxic carcinogenicity, genotoxicity, teratogenicity, hepato-, renal-, cardio-,reproductive-, developmental- and systemic toxicity of non-cyclized linker, PEG-linker, non-cyclized linker including branching point for 2x20 kDa PEG attachment and PEG-linker including branching point for 2x20 kDa PEG attachment	海外	社内資料	参考

4.3 参考文献

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-24-001	Takasu H, Bringhurst FR.	Type-1 parathyroid hormone (PTH)/PTH-related peptide (PTHrP) receptors activate phospholipase C in response to carboxyl-truncated analogs of PTH(1-34).	Endocrinology. 1998;139(10):4293-4299.	2.4.1
4.3-24-002	Morley P, Whitfield JF, Willick GE.	Design and applications of parathyroid hormone analogues.	Curr Med Chem. 1999;6(11):1095-1106.	2.4.1
4.3-24-003	Abate EG, Clarke BL.	Review of Hypoparathyroidism.	Front Endocrinol (Lausanne). 2017;7:172.	2.4.1
4.3-24-004	Hadjidakis DJ, Androulakis II.	Bone remodeling.	Ann N Y Acad Sci. 2006;1092:385-396.	2.4.1

CTD No.-資料番号	著者	表題	掲載誌・その他	引用CTD No.
4.3-24-005	Bilezikian JP, Cusano NE, Khan AA, et al.	Primary hyperparathyroidism.	Nat Rev Dis Primers. 2016;2:16033.	2.4.1
4.3-24-006	Brandi ML, Bilezikian JP, Shoback Roger DB, et al.	Management of hypoparathyroidism: summary statement and guidelines.	J Clin Endocrinol Metab. 2016;101(6):2273-2283.	2.4.1
4.3-24-007	Uzawa T, Hori M, Ejiri S, et al.	Comparison of the effects of intermittent and continuous administration of human parathyroid hormone(1-34) on rat bone.	Bone. 1995;16(4):477-484.	2.4.2.1.2
4.3-24-008	Lotinun S, Evans GL, Bronk JT, et al.	Continuous parathyroid hormone induces cortical porosity in the rat: effects on bone turnover and mechanical properties.	J Bone Miner Res. 2004;19(7):1165-1171.	2.4.2.1.2
4.3-24-009	Horwitz MJ, Tedesco MB, Sereika SM, et al.	A 7-day continuous infusion of PTH or PTHrP suppresses bone formation and uncouples bone turnover.	J Bone Miner Res. 2011;26(9):2287-2297.	2.4.2.1.2
4.3-24-010	Vargas HM, Bass AS, Breidenbach A, et al.	Scientific review and recommendations on preclinical cardiovascular safety evaluation of biologics.	J Pharmacol Toxicol Methods. 2008;58(2):72-76.	2.4.2.2
4.3-24-011	Murray TM, Rao LG, Divieti P, et al.	Parathyroid hormone secretion and action: evidence for discrete receptors for the carboxyl-terminal region and related biological actions of carboxyl- terminal ligands.	Endocr Rev. 2005;26(1):78-113.	2.4.2.2

CTD No.-資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-24-012	Webster R, Didier E, Harris P, et al.	PEGylated proteins: evaluation of their safety in the absence of definitive metabolism studies.	Drug Metab Dispos. 2007;35(1):9-16.	2.4.3.2, 2.4.4.3
4.3-24-013	Webster R, Elliott V, Park BK, et al.	PEG and PEG conjugates toxicity: towards an understanding of the toxicity of PEG and its relevance to PEGylated biologicals.	PEGylated Protein Drugs: Basic Science and Clinical Applications. 2009;127-146.	2.4.3.2
4.3-24-014	Hock JM, Gera I.	Effects of continuous and intermittent administration and inhibition of resorption on the anabolic response of bone to parathyroid hormone.	J Bone Miner Res. 1992;7(1):65-72.	2.4.4.1.1
4.3-24-015	Lotinun S, Sibonga JD, Turner RT.	Evidence that the cells responsible for marrow fibrosis in a rat model for hyperparathyroidism are preosteoblasts.	Endocrinology. 2005;146(9):4074-4081.	2.4.4.1.1
4.3-24-016	European Medicines Agency	Natpar EPAR - Public Assessment Report, 2017.	https://www.ema.europa.eu/en/documents/assessment-report/natpar-epar-public-assessment-report_en.pdf	2.4.4.1.1, 2.4.4.3
4.3-24-017	Food and Drug Administration	BLA #125511-Natpara. Center for Drug Evaluation and Research	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2015	2.4.4.1.1.

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
			/125511Orig1s000AdminCorres.pdf	
4.3-24-018	European Medicines Agency	Forsteo EPAR. Scientific Discussion, 2005.	https://www.ema.europa.eu/en/documents/scientific-discussion/forsteo-epar-scientific-discussion_en.pdf	2.4.4.1.1, 2.4.4.3
4.3-24-019	Food and Drug Administration	NDA #21-318-Forteo [teriparatide]. Center for Drug Evaluation and Research. Food & Drug Administration. 2002.	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2002/21-318_Forteo.cfm	2.4.4.1.1 2.4.4.1.3
4.3-24-020	Iwamoto M, Jikko A, Murakami H, et al.	Changes in parathyroid hormone receptors during chondrocyte cytodifferentiation.	J Biol Chem. 1994;269(25):17245-17251.	2.4.4.1.2
4.3-24-021	Chen X, Macica CM, Nasiri A, et al.	Regulation of articular chondrocyte proliferation and differentiation by indian hedgehog and parathyroid hormone-related protein in mice.	Arthritis Rheum. 2008;58(12):3788-97.	2.4.4.1.2
4.3-24-022	Qiu T, Xian L, Crane J, et al.	PTHreceptor signaling in osteoblasts regulates endochondral vascularization in maintenance of postnatal growth plate.	J Bone Miner Res. 2015;30(2):309317.	2.4.4.1.2

CTD No.-資料番号	著者	表題	掲載誌・その他	引用CTD No.
4.3-24-023	Ma YL, Cain RL, Halladay DL, et al.	Catabolic effects of continuous humanPTH(1--38) in vivo is associated with sustained stimulation of RANKL and inhibition of osteoprotegerin and gene-associated bone formation.	Endocrinology. 2001;142:4047-4054.	2.4.4.1.3
4.3-24-024	Babey M, Brandi ML, Shoback D.	Conventional Treatment of Hypoparathyroidism.	Endocrinol Metab Clin North Am. 2018;47(4):889-900.	2.4.4.1.3
4.3-24-025	Goodman HM.	Hormonal Regulation of Calcium Metabolism. Basic Medical Endocrinology (Third Edition).	Academic Press. 2003;8:255-289.	2.4.4.1.3
4.3-24-026	Wang YH, Liu Y, Buhl K, et al.	Comparison of the action of transient and continuousPTHon primary osteoblast cultures expressing differentiation stage-specific GFP.	J Bone Miner Res. 2005;20(1):5-14.	2.4.4.1.3
4.3-24-027	Wang YH, Liu Y, Rowe DW.	Effects of transientPTHon early proliferation, apoptosis, and subsequent differentiation of osteoblast in primary osteoblast cultures.	Am J Physiol Endocrinol Metab. 2007;292(2):E594-E603.	2.4.4.1.3
4.3-24-028	Food and Drug Administration	Natpara USPI. Prescribing Information for Natpara:	https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125511s028lbl.pdf	2.4.4.3
4.3-24-029	Food and Drug Administration	Forteo USPI (recent major change 2020, accessed 16 Jun 2022). Prescribing Information for Forteo:	https://www.accessdata.fda.gov/drugsa	2.4.4.3

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
			tfda_docs/label/2020/021318s054lbl.pdf	
4.3-24-030	Jimenez C, Yang Y, Kim HW, et al.	Primary hyperparathyroidism and osteosarcoma: examination of a large cohort identifies three cases of fibroblastic osteosarcoma.	J Bone Miner Res. 2005;20(9):1562-1568.	2.4.4.3
4.3-24-031	Cinamon U, Turcotte RE.	Primary hyperparathyroidism and malignancy: “studies by nature”.	Bone. 2006;39(2):420-423.	2.4.4.3
4.3-24-032	Andrews EB, Gilsenan AW, Midkiff K, et al.	The US postmarketing surveillance study of adult osteosarcoma and teriparatide: study design and findings from the first 7 years.	J Bone Miner Res. 2012;27(12):2429-37.	2.4.4.3
4.3-24-033	Cipriani C, Irani D, Bilezikian JP.	Safety of osteoanabolic therapy: a decade of experience.	J Bone Miner Res. 2012;27(12):2419-2428.	2.4.4.1.3
4.3-24-034	Nishikawa A, Yoshiki F, Taketsuna M, et al.	Safety and effectiveness of daily teriparatide for osteoporosis in patients with severe stages of chronic kidney disease: post hoc analysis of a postmarketing observational study.	Clin Interv Aging. 2016;11:1653-1659.	2.4.4.3
4.3-24-035	Gilsenan A, Harding A, Kellier-Steele N, et al.	The Forteo Patient Registry linkage to multiple state cancer registries: study design and results from the first 8 years.	Osteoporos Int. 2018;29(10):2335-2343.	2.4.4.3
4.3-24-036	Gilsenan A, Harris D, Reynolds M, et al.	Long-Term Cancer Surveillance: Results from the Forteo Patient Registry Surveillance Study.	Osteoporos Int. 2021;32:645-651.	2.4.4.3

CTD No.-資料番号	著者	表題	掲載誌・その他	引用CTD No.
4.3-24-037	Gilsenan A, Midkiff K, Harris D, et al.	Teriparatide Did Not Increase Adult Osteosarcoma Incidence in a 15-Year US Postmarketing Surveillance Study.	J Bone Miner Res. 2021;36(2):244-251.	2.4.4.3
4.3-24-038	RTI Health Solutions.	Forteo Patient Registry.	https://www.rtihs.org/publications/long-term-cancer-surveillance-five-year-update-forteo-patient-registry-surveillance	2.4.4.3
4.3-24-039	Palombo M, Deshmukh M, Myers D, et al.	Pharmaceutical and toxicological properties of engineered nanomaterials for drug delivery.	Annu. Rev. Pharmacol. Toxicol. 2014;54:581-598.	2.4.4.3
4.3-24-040	Ivens IA, Achanzar W, Baumann A, et al.	PEGylated biopharmaceuticals: current experience and considerations for nonclinical development.	Toxicol Pathol. 2015;43(7):959-983.	2.4.4.3, 2.4.5
4.3-24-041	Stidl R, Denne M, Goldstine J, et al.	Polyethylene Glycol Exposure with Antihemophilic Factor (Recombinant), PEGylated (rurioctocog alfa pegol) and Other Therapies Indicated for the Pediatric Population: History and Safety.	Pharmaceuticals (Basel). 2018;11(3):75.	2.4.4.3
4.3-24-042	Zhu Z, Gao P, Hu Y, et al.	PEGylated versus non-PEGylated drugs: A cross-sectional analysis of adverse events in the FDA Adverse Event Reporting System (FAERS) Database.	Int J Clin Pharmacol Ther.	2.4.4.3

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
			2020;58(6):332-342.	
4.3-24-043	European Medicines Agency	Apidra SmPC (latest renewal 2024).	https://www.ema.europa.eu/en/documents/product-information/apidra-epar-product-information_en.pdf	2.4.4.6
4.3-24-044	Food and Drug Administration	Apidra USPI (latest renewal 2022).	https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/021629s042lbl.pdf	2.4.4.6
4.3-24-045	European Medicines Agency	CHMP Safety Working Party's response to the PDCO regarding the use of PEGylated drug products in the paediatric population. 2012.	EMA/CHMP/SWP/647258/2012.	2.4.5
4.3-24-046	Food and Drug Administration	BPAC Briefing Document. BLA 125611 Coagulation Factor IX (Recombinant), GlycoPEGylated N9-GPN9-GP.	https://public4.pagefreezer.com/content/FDA/26-05-2022T13:14/https://www.fda.gov/media/104091/download	2.4.5

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-24-047	Baumann A.	PEGylated biologics in haemophilia treatment: Current understanding of their long-term safety.	Haemophilia. 2020;26(1):e11-e13.	2.4.5
4.3-261-001	Takasu H, Bringhurst FR.	Type-1 parathyroid hormone (PTH)/PTH-related peptide (PTHrP) receptors activate phospholipase C in response to carboxyl-truncated analogs of PTH(1-34).	Endocrinology. 1998;139(10):4293-4299.	2.6.1.1.2
4.3-261-002	Morley P, Whitfield JF, Willick GE.	Design and applications of parathyroid hormone analogues.	Curr Med Chem. 1999;6(11):1095-1106.	2.6.1.1.2
4.3-261-003	Habener JF, Rosenblatt M, Potts JT Jr.	Parathyroid hormone: biochemical aspects of biosynthesis, secretion, action, and metabolism.	Physiol Rev. 1984;64(3):985-1053.	2.6.1.1.2
4.3-261-004	Lee C, Luck MD, Jüppner H, et al.	Homolog-scanning mutagenesis of the parathyroid hormone (PTH) receptor reveals PTH-(1-34) binding determinants in the third extracellular loop.	Mol Endocrinol. 1995;9(10):1269-1278.	2.6.1.1.2
4.3-261-005	Abate EG, Clarke BL.	Review of Hypoparathyroidism.	Front Endocrinol (Lausanne). 2017; 7:172.	2.6.1.1.2
4.3-261-006	Hadjidakis DJ, Androulakis II.	Bone remodeling.	Ann N Y Acad Sci. 2006; 1092:385-396.	2.6.1.1.2
4.3-261-007	Bilezikian JP, Brandi ML, Cusano NE, et al.	Management of Hypoparathyroidism: Present and Future.	J Clin Endocrinol Metab.	2.6.1.1.2

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
			2016;101(6):2313-2324.	
4.3-261-008	Brandi ML, Bilezikian JP, Shoback D, et al.	Management of hypoparathyroidism: summary statement and guidelines.	J Clin Endocrinol Metab. 2016;101(6):2273-2283.	2.6.1.1.2
4.3-262-001	Abate EG, Clarke BL.	Review of Hypoparathyroidism.	Front Endocrinol (Lausanne). 2017;7:172.	2.6.2.1
4.3-262-002	Hadjidakis DJ, Androulakis II.	Bone remodeling.	Ann N Y Acad Sci. 2006;1092:385-396.	2.6.2.1
4.3-262-003	Bilezikian JP, Brandi ML, Cusano NE, et al.	Management of Hypoparathyroidism: Present and Future.	J Clin Endocrinol Metab. 2016;101(6):2313-2324.	2.6.2.1, 2.6.2.2.1
4.3-262-004	Brandi ML, Bilezikian JP, Shoback D, et al.	Management of hypoparathyroidism: summary statement and guidelines.	J Clin Endocrinol Metab. 2016;101(6):2273-2283.	2.6.2.1 2.6.2.2.1
4.3-262-005	Takasu H, Bringhurst RF.	Type-1 Parathyroid Hormone (PTH)/PTH-Related Peptide (PTHrP) Receptors Activate Phospholipase C in Response to Carboxyl-Truncated Analogs of PTH(1–34).	Endocrinology 1998;139(10):4293-4299.	2.6.2.1 2.6.2.2

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-262-006	Morley P, Whitfield JF, Willick GE.	Design and applications of parathyroid hormone analogues.	Curr Med Chem. 1999;6(11):1095-1106.	2.6.2.1 2.6.2.2
4.3-262-007	Holten-Andersen L, Pihl S, Rasmussen CE, et al.	Design and Preclinical Development of TransCon PTH, an Investigational Sustained-Release PTHR eplacement Therapy for Hypoparathyroidism.	J Bone Miner Res. 2019; 34(11):2075-2086.	2.6.2.1
4.3-262-008	Uzawa T, Hori M, Ejiri S, et al.	Comparison of the effects of intermittent and continuous administration of human parathyroid hormone(1-34) on rat bone.	Bone. 1995;16(4):477-484.	2.6.2.1 2.6.2.2
4.3-262-009	Lotinun S, Evans GL, Bronk JT, et al.	Continuous parathyroid hormone induces cortical porosity in the rat: effects on bone turnover and mechanical properties.	J Bone Miner Res. 2004;19(7):1165-1171.	2.6.2.1
4.3-262-010	Horwitz MJ, Tedesco MB, Sereika SM, et al.	A 7-day continuous infusion of PTH or PTHrP suppresses bone formation and uncouples bone turnover.	J Bone Miner Res. 2011;26(9):2287-2297.	2.6.2.1 2.6.2.2
4.3-262-011	Vargas HM, Bass AS, Breidenbach A, et al.	Scientific review and recommendations on preclinical cardiovascular safety evaluation of biologics.	J Pharmacol Toxicol Methods. 2008;58(2):72-76.	2.6.2.1 2.6.2.1.1 2.6.2.5.1
4.3-262-012	Murray TM, Rao LG, Divieti P, at el.	Parathyroid hormone secretion and action: evidence for discrete receptors for the carboxyl-terminal region and related biological actions of carboxyl- terminal ligands.	Endocr Rev. 2005;26(1):78-113.	2.6.2.1 2.6.2.5.1
4.3-262-013	Goodman WG.	Calcium-sensing receptors.	Seminars in Nephrology.	2.6.2.2

CTD No.-資料番号	著者	表題	掲載誌・その他	引用CTD No.
			2004;24(1):17-24.	
4.3-262-014	Samuels MH, Veldhuis J, Cawley C, et al.	Pulsatile secretion of parathyroid hormone in normal young subjects: assessment by deconvolution analysis.	J Clin Endocrinol Metab. 1993;77(2):399-403.	2.6.2.2
4.3-262-015	el-Hajj Fuleihan G, Klerman EB, Brown EN, et al.	The parathyroid hormone circadian rhythm is truly endogenous—a general clinical research center study.	J Clin Endocrinol Metab. 1997;82(1):281-286.	2.6.2.2
4.3-262-016	Ureña P, Kong XF, Abou-Samra AB, et al.	Parathyroid hormone (PTH)/PTH-related peptide receptor messenger ribonucleic acids are widely distributed in rat tissues.	Endocrinology. 1993;133(2):617-23.	2.6.2.2
4.3-262-017	Reppe S, Stilgren L, Abrahamsen B, et al.	Abnormal muscle and hematopoietic gene expression may be important for clinical morbidity in primary hyperparathyroidism.	Am J Physiol Endocrinol Metab. 2007 May;292(5):E1465-73.	2.6.2.2
4.3-262-018	Datta NS, Abou-Samra AB.	PTH and PTHrP signaling in osteoblasts.	Cell Signal. 2009. 21(8): 1245-1254.	2.6.2.2
4.3-262-019	Lee M, Partridge NC.	Parathyroid hormone signaling in bone and kidney.	Curr Opin Nephrol Hypertens.	2.6.2.2

CTD No.-資料番号	著者	表題	掲載誌・その他	引用 CTD No.
			2009;18(4):298-302.	
4.3-262-020	Lupp A, Klenk C, Röcken C, et al.	Immunohistochemical identification of the PTHR1 parathyroid hormone receptor in normal and neoplastic human tissues.	Eur J Endocrinol. 2010;162(5):979-86.	2.6.2.2
4.3-262-021	Drechsler N, Fröbel J, Jahreis G, et al.	Binding specificity of the ectodomain of the parathyroid hormone receptor.	Biophys Chem. 2011;154(2-3):66-72.	2.6.2.2
4.3-262-022	Henry HL.	Regulation of vitamin D metabolism.	Best Pract Res Clin Endocrinol Metab. 2011;25(4):531-541.	2.6.2.2
4.3-262-023	Martin TJ, Sims NA, Seeman E.	Physiological and Pharmacological Roles of PTH and PTHrP in Bone Using Their Shared Receptor, PTH1R.	Endocr Rev. 2021;42(4):383-406.	2.6.2.2
4.3-262-024	Parfitt AM.	Misconceptions (2): turnover is always higher in cancellous than in cortical bone	Bone. 2002;30(6): 807-809.	2.6.2.2
4.3-262-025	Goodman HM.	Hormonal Regulation of Calcium Metabolism. Basic Medical Endocrinology (Third Edition).	Academic Press. 2003;8:255-289.	2.6.2.2 2.6.2.7.1.2
4.3-262-026	Huang JC, Sakata T, Pfleger LL, et al.	PTH differentially regulates expression of RANKL and OPG.	J Bone Miner Res. 2004;19(2):235-244.	2.6.2.2

CTD No.-資料番号	著者	表題	掲載誌・その他	引用CTD No.
4.3-262-027	Fu Q, Manolagas SC, O'Brien CA.	Parathyroid hormone controls receptor activator of NF-kappaB ligand gene expression via a distant transcriptional enhancer.	Mol Cell Biol. 2006;26(17):6453-6468.	2.6.2.2
4.3-262-028	Ducy P, Zhang R, Geoffroy V, et al.	Osf2/Cbfa1: a transcriptional activator of osteoblast differentiation.	Cell. 1997;89(5):747-754.	2.6.2.2
4.3-262-029	Wang YH, Liu Y, Rowe DW.	Effects of transientPTHon early proliferation, apoptosis, and subsequent differentiation of osteoblast in primary osteoblast cultures.	Am J Physiol Endocrinol Metab. 2007;292(2):E594-603.	2.6.2.2
4.3-262-030	Silva BC, Bilezikian JP.	Parathyroid hormone: anabolic and catabolic actions on the skeleton.	Curr Opin Pharmacol. 2015;22:41-50.	2.6.2.2
4.3-262-031	Crane JL, Cao X.	Function of matrix IGF-1 in coupling bone resorption and formation.	J Mol Med. 2014;92(2):107-15.	2.6.2.2
4.3-262-032	Bellido T, Ali AA, Plotkin LI, et al.	Proteasomal degradation of Runx2 shortens parathyroid hormone-induced anti-apoptotic signaling in osteoblasts. A putative explanation for why intermittent administration is needed for bone anabolism.	J Biol Chem. 2003;278(50):50259-50272.	2.6.2.2
4.3-262-033	Fonseca H, Moreira-Gonçalves D, Coriolano HJ, et al.	Bone quality: the determinants of bone strength and fragility.	Sports Med. 2014;44(1):37-53.	2.6.2.2 2.6.2.7.1.2

CTD No.-資料番号	著者	表題	掲載誌・その他	引用CTD No.
4.3-262-034	Langdahl BL, Mortensen L, Vesterby A, et al.	Bone histomorphometry in hypoparathyroid patients treated with vitamin D.	Bone 1996;18(2): 103-108.	2.6.2.2
4.3-262-035	Neer, RM. Arnaud CD, Zanchetta JR, et al.	Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis.	N Engl J Med. 2001;344 (19):1434-1441.	2.6.2.2
4.3-262-036	Jiang, Y, Zhao JJ, Mitlak BH, et al.	Recombinant human parathyroid hormone (1-34) [teriparatide] improves both cortical and cancellous bone structure	J Bone Miner Res 2003;18 (11):1932-1941.	2.6.2.2
4.3-262-037	Wang YH, Liu Y, Buhl K, et al.	Comparison of the action of transient and continuous PTH on primary osteoblast cultures expressing differentiation stage-specific GFP.	J Bone Miner Res. 2005;20(1):5-14.	2.6.2.2
4.3-262-038	Tawfeek H, Bedi B, Li JY, et al.	Disruption of PTH receptor 1 in T cells protects against PTH-induced bone loss.	PLoS One. 2010;5(8):e12290.	2.6.2.2
4.3-262-039	Li JY, D'Amelio P, Robinson J, et al.	IL-17A Is Increased in Humans with Primary Hyperparathyroidism and Mediates PTH-Induced Bone Loss in Mice.	Cell Metab 2015;22(5): 799-810.	2.6.2.2
4.3-262-040	Terauchi M, Li JY, Bedi B, et al.	T lymphocytes amplify the anabolic activity of parathyroid hormone through Wnt10b signaling.	Cell Metab. 2009;10(3):229-240.	2.6.2.2
4.3-262-041	Li JY, Walker LD, Tyagi AM, Adams J, et al.	The sclerostin-independent bone anabolic activity of intermittent PTH treatment is mediated by T-cell-produced Wnt10b.	J Bone Miner Res. 2014;29(1):43-54.	2.6.2.2

CTD No.-資料番号	著者	表題	掲載誌・その他	引用CTD No.
4.3-262-042	Yu M, D'Amelio P, Tyagi AM, et al.	Regulatory T cells are expanded by Teriparatide treatment in humans and mediate intermittent PTH-induced bone anabolism in mice.	EMBO Rep. 2018;19(1): 156-171.	2.6.2.2
4.3-262-043	Li JY, Yu M, Tyagi AM, et al.	IL-17 Receptor Signaling in Osteoblasts/Osteocytes Mediates PTH-Induced Bone Loss and Enhances Osteocytic RANKL Production.	J Bone Miner Res. 2019;34(2):349-360.	2.6.2.2
4.3-262-044	Nakashima T, Kobayashi Y, Yamasaki, S et al.	Protein Expression and Functional Difference of Membrane-Bound and Soluble Receptor Activator of NF-κB Ligand: Modulation of the Expression by Osteotropic Factors and Cytokines.	Biochemical and Biophysical Research Communications. 2000;275(3): 768-775.	2.6.2.2
4.3-262-045	Clarke BL, Brown EM, Collins MT, et al.	Epidemiology and Diagnosis of Hypoparathyroidism.	J Clin Endocrinol Metab. 2016;101(6): 2284-2299.	2.6.2.2.1
4.3-262-046	Mannstadt M, Clarke BL, Vokes T, et al.	Efficacy and safety of recombinant human parathyroid hormone (1-84) in hypoparathyroidism (REPLACE): a double-blind, placebo-controlled, randomised, phase 3 study	Lancet Diabetes Endocrinol. 2013;1(4):275-283.	2.6.2.2.1
4.3-262-047	Shoback DM, Bilezikian JP, Costa AG, et al.	Presentation of Hypoparathyroidism: Etiologies and Clinical Features.	J Clin Endocrinol Metab. 2016;101(6):2300-2312.	2.6.2.2.1

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-262-048	Shoback D.	Hypoparathyroidism.	N Engl J Med. 2008;359(4):391-403.	2.6.2.2.1
4.3-262-049	Sikjaer T, Rejnmark L, Mosekilde L.	PTH treatment in hypoparathyroidism.	Curr Drug Saf. 2011;6(2):89-99.	2.6.2.2.1
4.3-262-050	Underbjerg L, Sikjaer T, Mosekilde L, et al.	Postsurgical hypoparathyroidism—risk of fractures, psychiatric diseases, cancer, cataract, and infections.	Journal of Bone and Mineral Research. 2014;29(11):2504-2510.	2.6.2.2.1
4.3-262-051	Rubin MR, Dempster DW, Zhou H, et al.	Dynamic and structural properties of the skeleton in hypoparathyroidism	J Bone Miner Res. 2008;23(12):2018-2024.	2.6.2.2.1
4.3-262-052	Langdahl B, Ferrari S, Dempster DW.	Bone modeling and remodeling: potential as therapeutic targets for the treatment of osteoporosis.	Ther Adv Musculoskelet Dis. 2016;8(6):225-235.	2.6.2.2.1 2.6.2.7.1.2
4.3-262-053	Boivin G, Meunier PJ.	Changes in bone remodeling rate influence the degree of mineralization of bone.	Connect Tissue Res. 2002;43(2–3):535-537.	2.6.2.2.1
4.3-262-054	Rubin MR, Dempster DW, Kohler T, et al.	Three dimensional cancellous bone structure in hypoparathyroidism.	Bone. 2010;46(1):190-195.	2.6.2.2.1
4.3-262-055	Food and Drug Administration	Natpara advisory Committee, 2014	https://www.accessdata.fda.gov/drugsa	2.6.2.2.1

CTD No.-資料番号	著者	表題	掲載誌・その他	引用 CTD No.
			tfda_docs/nda/2015/125511Orig1s000AdminCorres.pdf	
4.3-262-056	Bilezikian JP.	Hypoparathyroidism.	J Clin Endocrinol Metab. 2020;105(6): 1722-1736.	2.6.2.2.1, 2.6.2.7.2
4.3-262-057	Cheloha RW, Maeda A, Dean T, et al.	Backbone modification of a polypeptide drug alters duration of action in vivo.	Nat Biotechnol. 2014; 32(7):653-655.	2.6.2.3.1, 2.6.2.7.2
4.3-262-058	European Medicines Agency	Forsteo EPAR – Scientific Discussion, 2005.	https://www.ema.europa.eu/en/documents/scientific-discussion/forsteo-epar-scientific-discussion_en.pdf	2.6.2.3.1 2.6.2.5.1 2.6.2.7.2
4.3-262-059	Food and Drug Administration	NDA #21-318-Forteo [teriparatide]. Center for Drug Evaluation and Research. Food & Drug Administration. 2002.	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2002/21-318_Forteo.cfm	2.6.2.3.1 2.6.2.5.1 2.6.2.7.2
4.3-262-060	European Medicines Agency	Natpar EPAR - Public Assessment Report, 2017.	https://www.ema.europa.eu/en/documents/assessment-	2.6.2.3.1 2.6.2.5.1 2.6.2.7.2

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
			report/natpar-epar-public-assessment-report_en.pdf	
4.3-262-061	Food and Drug Administration	BLA #125511-Natpara. Center for Drug Evaluation and Research, Food & Drug Administration. 2015.	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/125511Orig1s000TOC.cfm	2.6.2.3.1 2.6.2.5.1 2.6.2.7.2
4.3-262-062	Ferreira JC, Ferrari GO, Neves KR, et al.	Effects of Dietary Phosphate on Adynamic Bone Disease in Rats with Chronic Kidney Disease – Role of Sclerostin?	PLoS One. 2013;8(11): e79721.	2.6.2.3.1.1
4.3-262-063	Jung SY, Kim HY, Park HS, et al.	Standardization of A Physiologic Hypoparathyroidism Animal Model.	PLoS One. 2016;11(10): e0163911.	2.6.2.3.1.1
4.3-262-064	Shimizu M, Joyashiki E, Noda H, et al.	Pharmacodynamic Actions of a Long-ActingPTHAnalog (LA-PTH) in Thyroparathyroidectomized (TPTX) Rats and Normal Monkeys.	J Bone Miner Res. 2016;31(7):1405-1412.	2.6.2.3.1.1 2.6.2.7.1.2
4.3-262-065	Krishnan V, Ma YL, Chen CZ, et al.	Repurposing a novel parathyroid hormone analogue to treat hypoparathyroidism.	Br J Pharmacol. 2018;175(2):262-271.	2.6.2.3.1.1
4.3-262-066	Vasikaran S, Eastell R, Bruyère O, et al.	Markers of bone turnover for the prediction of fracture risk and monitoring of osteoporosis treatment: a need for international reference standards.	Osteoporos Int. 2011;22(2):391-420.	2.6.2.3.2

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-262-067	Dempster DW, Compston JE, Drezner MK, et al.	Standardized nomenclature, symbols, and units for bone histomorphometry: a 2012 update of the report of the ASBMR Histomorphometry Nomenclature Committee.	Journal of Bone and Mineral Research. 2013;28(1): 2-17.	2.6.2.3.2
4.3-262-068	Food and Drug Administration	Osteoporosis: Nonclinical Evaluation of Drugs Intended for Treatment Guidance for Industry, 2019.	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/osteoporosis-nonclinical-evaluation-drugs-intended-treatment-guidance-industry	2.6.2.3.2
4.3-262-069	National Research Council.	Nutrient requirements of nonhuman primates. Minerals. 2nd Revised Edition.	National Academy of Sciences. 2003;6:94-112.	2.6.2.3.4.2, 2.6.2.3.4.3
4.3-262-070	Brandi ML, Bilezikian JP, Shoback D, et al.	Management of hypoparathyroidism: summary statement and guidelines.	J Clin Endocrinol Metab. 2016; 101(6); 2273‐2283.	2.6.2.3.4.3
4.3-262-071	Qu Y, Fang M, Gao B, et al.	BeKm-1, a peptide inhibitor of human ether-a-go-go-related gene potassium currents, prolongs QTc intervals in isolated rabbit heart.	J Pharmacol Exp Ther. 2011;337(1):2-8.	2.6.2.5.1

CTD No.-資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-262-072	Leifert A, Pan A, Kinkeldey A, et al.	Differential hERG ion channel activity of ultrasmall gold nanoparticles.	Proc Natl Acad Sci USA. 2013;110(20):8004-8009.	2.6.2.5.1
4.3-262-073	Kim TW, Kim KS, Seo JW, et al.	Antisense oligonucleotides on neurobehavior, respiratory, and cardiovascular function, and hERG channel current studies.	J Pharmacol Toxicol Methods. 2014; 69(1):49-60.	2.6.2.5.1
4.3-262-074	Yue Y, Castrichini M, Srivastava U, et al.	Pathogenesis of the Novel Autoimmune-Associated Long-QT Syndrome.	Circulation. 2015;132(4):230-240.	2.6.2.5.1
4.3-262-075	Piscopo S, Brown ER.	Zinc Oxide Nanoparticles and Voltage-Gated Human Kv 11.1 Potassium Channels Interact through a Novel Mechanism.	Small. 2018;14(15):e1703403.	2.6.2.5.1
4.3-262-076	Holzgrefe H, Ferber G, Champeroux P, et al.	Preclinical QT safety assessment: Cross-species comparisons and human translation from an industry consortium.	J Pharmcol Toxicol Methods. 2014:69(1):61-101.	2.6.2.5.2.2
4.3-262-077	European Medicines Agency	Forsteo SmPC (latest renewal 2022).	https://www.ema.europa.eu/en/documents/product-information/forsteo-epar-product-information_en.pdf	2.6.2.6

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-262-078	Food and Drug Administration	Forteo USPI (latest renewal 2024).	https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/021318s057lbl.pdf	2.6.2.6
4.3-262-079	European Medicines Agency	Natpar SmPC (latest renewal 2023).	https://www.ema.europa.eu/en/documents/product-information/natpar-epar-product-information_en.pdf	2.6.2.6
4.3-262-080	Food and Drug Administration	Natpara USPI (latest renewal 2022).	https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125511s028lbl.pdf	2.6.2.6
4.3-262-081	Food and Drug Administration	Lanoxin USPI (latest renewal 2024).	https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/020405Orig1s017lbl.pdf	2.6.2.6
4.3-262-082	Webster R, Didier E, Harris P, et al.	PEGylated proteins: evaluation of their safety in the absence of definitive metabolism studies.	Drug Metab Dispos. 2007;35(1):9-16.	2.6.2.6

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-262-083	Peterson MC, Riggs MM.	A physiologically based mathematical model of integrated calcium homeostasis and bone remodeling.	Bone. 2010;46(1):49-63.	2.6.2.7.1.1
4.3-262-084	Silverberg SJ.	Vitamin D deficiency and primary hyperparathyroidism.	J Bone Miner Res. 2007;22 Suppl 2:V100-V104.	2.6.2.7.1.1
4.3-262-085	DeLuca HF.	he Kidney as an Endocrine Organ for the Production of 1,25-Dihydroxyvitamin D3, a Calcium-Mobilizing Hormone.	New England Journal of Medicine. 1973;289(7):359-365.	2.6.2.7.1.1
4.3-262-086	Panda DK, Miao D, Bolivar I, et al.	Inactivation of the 25-hydroxyvitamin D 1alpha-hydroxylase and vitamin D receptor demonstrates independent and interdependent effects of calcium and vitamin D on skeletal and mineral homeostasis.	J Biol Chem. 2004;279(16): 16754-16766.	2.6.2.7.1.1
4.3-262-087	Prié D, Friedlander G.	Reciprocal Control of 1,25-Dihydroxyvitamin D and FGF23 Formation Involving the FGF23/Klotho System.	Clinical Journal of the American Society of Nephrology. 2010;5(9):1717-1722.	2.6.2.7.1.1
4.3-262-088	Chambers TJ, Athanasou NA, Fuller K.	Effect of parathyroid hormone and calcitonin on the cytoplasmic spreading of isolated osteoclasts.	J Endocrinol 1984;102:281-286.	2.6.2.7.1.2

CTD No.-資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-262-089	Hsiao C-Y, Chen TH, Chu TH, et al.	Calcitonin Induces Bone Formation by Increasing Expression of Wnt10b in Osteoclasts in Ovariectomy-Induced Osteoporotic Rats.	Frontiers in Endocrinology. 2020;11:613.	2.6.2.7.1.2
4.3-262-090	Hoff AO, Catala-Lehnen P, Thomas PM, et al.	Increased bone mass is an unexpected phenotype associated with deletion of the calcitonin gene.	J. Clin. Invest. 2002;110(12):1849-1857.	2.6.2.7.1.2
4.3-262-091	Cooper CW, Hirsch PF, Munson PL.	Importance of endogenous thyrocalcitonin for protection against hypercalcemia in the rat.	Endocrinology. 1970;86(2):406-415.	2.6.2.7.1.2
4.3-262-092	Rodriguez, M, Felsenfeld AJ, Torres A, et al.	Calcitonin, an important factor in the calcemic response to parathyroid hormone in the rat.	Kidney Int. 1991;40(2): 219-225.	2.6.2.7.1.2
4.3-262-093	Hirsch PF, Lester GE, Talmage RV.	Calcitonin, an enigmatic hormone: does it have a function?	J Musculoskelet Neuronal Interact 2001;1(4):299-305.	2.6.2.7.1.2
4.3-262-094	Hurley DL, Tiegs RD, Wahner HW, et al.	Axial and appendicular bone mineral density in patients with long-term deficiency or excess of calcitonin.	N Engl J Med. 1987;317(9): 537-541.	2.6.2.7.1.2
4.3-262-095	Baran DT, Braverman LE.	Editorial: thyroid hormones and bone mass.	J Clin Endocrinol Metab 1991; 72:1182-1183.	2.6.2.7.1.2

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-262-096	Gonzalez DC, Mautalen CA, Correa PH, et al.	Bone mass in totally thyroidectomized patients. Role of calcitonin deficiency and exogenous thyroid treatment.	Acta Endocrinol. 1991;124(5): 521-525.	2.6.2.7.1.2
4.3-262-097	Giannini S, Nobile M, Sartori L, et al.	Bone density and mineral metabolism in thyroidectomized patients treated with long-term L-thyroxine.	Clin Sci. 1994;87(5): 593-597.	2.6.2.7.1.2
4.3-262-098	Felsenfeld AJ, Levine BS.	Calcitonin, the forgotten hormone: does it deserve to be forgotten?	Clin Kidney J 2015;8(2):180-187.	2.6.2.7.1.2
4.3-262-099	Rubin MR, Cusano NE, Fan WW, et al.	Therapy of hypoparathyroidism with PTH(1-84): a prospective six year investigation of efficacy and safety.	J Clin Endocrinol Metab. 2016;101(7):2742-2750.	2.6.2.7.1.2
4.3-262-100	Lelovas PP, Xanthos TT, Thoma SE, et al.	The laboratory rat as an animal model for osteoporosis research.	Comparative medicine. 2008;58(5): 424-430.	2.6.2.7.1.2
4.3-262-101	Burr DB, Turner CH, Naick P, et al.	Does microdamage accumulation affect the mechanical properties of bone?	J Biomech. 1998;31(4):337-345.	2.6.2.7.1.2
4.3-262-102	Yerramshetty JS, Akkus O.	The associations between mineral crystallinity and the mechanical properties of human cortical bone.	Bone. 2008;42(3): 476-482.	2.6.2.7.1.2

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-264-001	Food and Drug Administration	Guidance for Industry: Bioanalytical method validation – General Considerations. 2001.	－	2.6.4.2.1
4.3-264-002	Food and Drug Administration	Guidance for Industry: Bioanalytical method validation – General Considerations. 2018.	－	2.6.4.2.1
4.3-264-003	Viswanathan CT, Bansal S, Booth B, et al.	Quantitative bioanalytical methods validation and implementation: best practices for chromatographic and ligand binding assays.	Pharm Res. 2007;24(10):1962-1973.	2.6.4.2.1
4.3-264-004	European Medicines Agency	Guideline on bioanalytical method validation. 21 July 2011	－	2.6.4.2.1
4.3-264-005	Knutsson M, Schmidt R, Timmerman P.	LC-MS/MS of large molecules in a regulated bioanalytical environment - which acceptance criteria to apply?	Bioanalysis. 2013;5(18):2211-2214.	2.6.4.2.1
4.3-264-006	Mire-Sluis AR, Barrett YC, Devanarayan V, et al.	Recommendations for the design and optimization of immunoassays used in the detection of host antibodies against biotechnology products.	J Immunol Methods. 2004;289(1-2):1-16.	2.6.4.2.2
4.3-264-007	Shankar G, Devanarayan V, Amaravadi L, et al.	Recommendations for the validation of immunoassays used for detection of host antibodies against biotechnology products.	J Pharm Biomed Anal. 2008;48(5):1267-1281.	2.6.4.2.2
4.3-264-008	Food and Drug Administration	Guidance for Industry: Immunogenicity Testing of Therapeutic Protein Products - Developing and Validating Assays for Anti-Drug Antibody Detection. 2019.	－	2.6.4.2.2

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-264-009	European Medicines Agency	Guideline on Immunogenicity assessment of therapeutic proteins. 18 May 2017.	－	2.6.4.2.2
4.3-264-010	－	Immunogenicity Assays - Design and Validation of Immunoassays to Detect Anti-Drug Antibodies. 2013.	USP General Chapter 1106	2.6.4.2.2
4.3-264-011	－	Immunogenicity Assays - Design and Validation of Assays to Detect Anti-Drug Neutralising Antibody. 2015.	USP General Chapter 1106-1	2.6.4.2.2
4.3-264-012	Eli Lilly and Company	Forteo USPI	recent major change 2024	2.6.4.4
4.3-264-013	Takeda Pharmaceutical Company Limited	Natpara USPI	recent major change 2022	2.6.4.4
4.3-264-014	Yamaoka T, Tabata Y, Ikada Y.	Distribution and tissue uptake of poly(ethylene glycol) with different molecular weights after intravenous administration to mice.	J Pharm Sci. 1994;83(4):601-606.	2.6.4.4 2.6.4.6
4.3-264-015	Harris JM, Chess RB.	Effect of pegylation on pharmaceuticals.	Nat Rev Drug Discov. 2003;2(3):214-221.	2.6.4.4
4.3-264-016	Fishburn CS	The pharmacology of PEGylation: balancing PD with PK to generate novel therapeutics.	J Pharm Sci. 2008;97(10):4167-4183.	2.6.4.4
4.3-264-017	Markovsky E, Baabur-Cohen H, Eldar-Boock A, et al.	Administration, distribution, metabolism and elimination of polymer therapeutics.	J Control Release. 2012;161(2):446-460.	2.6.4.4

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-264-018	Woodburn KW, Holmes CP, Wilson SD, et al.	Absorption, distribution, metabolism and excretion of peginesatide, a novel erythropoiesis-stimulating agent, in rats.	Xenobiotica. 2012;42(7):660-670.	2.6.4.4
4.3-264-019	Baumann A, Piel I, Hucke F, et al.	Pharmacokinetics, excretion, distribution, and metabolism of 60-kDa polyethylene glycol used in BAY 94-9027 in rats and its value for human prediction.	Eur J Pharm Sci. 2019;130:11-20.	2.6.4.4
4.3-264-020	Corvilain J, Manderlier T, Struyven J, et al.	Metabolism of human PTH by the kidney and the liver.	Horm Metab Res. 1977;9(3):239-242.	2.6.4.5
4.3-264-021	Oldham SB, Finck EJ, Singer FR.	Parathyroid hormone clearance in man.	Metabolism. 1978;27(8):993-1001.	2.6.4.5
4.3-264-022	European Medicines Agency	Forsteo EPAR – Scientific Discussion, 2005.	－	2.6.4.5 2.6.4.6
4.3-264-023	Food and Drug Administration	Forteo NDA 21-318	Approval date: 11/26/2002	2.6.4.5 2.6.4.6
4.3-264-024	European Medicines Agency	Natpar EPAR - Public Assessment Report, 2017.	－	2.6.4.5 2.6.4.6
4.3-264-025	Food and Drug Administration	Natpara BLA 125511	Approval date: 1/23/2015	2.6.4.5 2.6.4.6
4.3-264-026	Takasu H, Bringhurst FR.	Type-1 parathyroid hormone (PTH)/PTH-related peptide (PTHrP) receptors activate phospholipase C in response to carboxyl-truncated analogs of PTH(1-34).	Endocrinology. 1998;139(10):4293-4299.	2.6.4.5

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-264-027	Morley P, Whitfield JF, Willick GE.	Design and applications of parathyroid hormone analogues.	Curr Med Chem. 1999;6(11):1095-1106.	2.6.4.5
4.3-264-028	Webster R, Didier E, Harris P, et al.	PEGylated proteins: evaluation of their safety in the absence of definitive metabolism studies.	Drug Metab Dispos. 2007;35(1):9-16.	2.6.4.5 2.6.4.6
4.3-264-029	Webster R, Elliott V, Park BK, et al.	PEG and PEG conjugates toxicity: towards an understanding of the toxicity of PEG and its relevance to PEGylated biologicals.	PEGylated Protein Drugs: Basic Science and Clinical Applications. 2009;127-146.	2.6.4.5
4.3-264-030	Bringhurst FR, Stern AM, Yotts M, et al.	Peripheral metabolism of PTH: fate of biologically active amino terminus in vivo.	Am J Physiol Endocrinol Metab. 1988;255(6):E886–E893.	2.6.4.6
4.3-264-031	Xu J, Bussiere J, Yie J, et al.	Polyethylene glycol modified FGF21 engineered to maximize potency and minimize vacuole formation.	Bioconjug Chem. 2013;24(6):915-925.	2.6.4.6
4.3-264-032	Rudmann DG, Alston JT, Hanson JC, et al.	High molecular weight polyethylene glycol cellular distribution and PEG-associated cytoplasmic vacuolation is molecular weight dependent and does not require conjugation to proteins.	Toxicol Pathol. 2013;41: 970-983.	2.6.4.6

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-264-033	Bjørnsdottir I, Sternebring O, Kappers WA, et al.	Pharmacokinetics, tissue distribution and excretion of 40kDa PEG and PEGylated rFVIII (N8-GP) in rats.	Eur J Pharm Sci. 2016;87:58-68.	2.6.4.6
4.3-266-001	Takasu H, Bringhurst FR.	Type-1 parathyroid hormone (PTH)/PTH-related peptide (PTHrP) receptors activate phospholipase C in response to carboxyl-truncated analogs of PTH(1-34).	Endocrinology. 1998;139(10):4293-4299.	2.6.6.1
4.3-266-002	Morley P, Whitfield JF, Willick GE	Design and applications of parathyroid hormone analogues.	Curr Med Chem. 1999;6(11):1095-1106.	2.6.6.1
4.3-266-003	European Medicines Agency	Natpar EPAR - Public Assessment Report, 2017.	－	2.6.6.1 2.6.6.3 2.6.6.3.2.2 2.6.6.4.3 2.6.6.5 2.6.6.10.1
4.3-266-004	Food and Drug Administration	BLA #125511-Natpara. Center for Drug Evaluation and Research, Food & Drug Administration. 2015.	Approval date: 1/23/2015	2.6.6.1 2.6.6.3 2.6.6.3.2.2 2.6.6.4.3 2.6.6.10.1 2.6.6.10.4
4.3-266-005	European Medicines Agency	Forsteo EPAR – Scientific Discussion, 2005.	－	2.6.6.1 2.6.6.3

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				2.6.6.3.2.2 2.6.6.4.3 2.6.6.5 2.6.6.10.1
4.3-266-006	Food and Drug Administration	NDA #21-318-Forteo [teriparatide]. Center for Drug Evaluation and Research. Food & Drug Administration. 2002.	Approval date: 11/26/2002	2.6.6.1 2.6.6.3 2.6.6.3.2.2 2.6.6.4.3 2.6.6.10.1 2.6.6.10.4
4.3-266-007	Iwamoto M, Jikko A, Murakami H, et al.	Changes in parathyroid hormone receptors during chondrocyte cytodifferentiation.	J Biol Chem. 1994;269(25):17245-17251.	2.6.6.1
4.3-266-008	Chen X, Macica CM, Nasiri A, et al.	Regulation of articular chondrocyte proliferation and differentiation by indian hedgehog and parathyroid hormone-related protein in mice.	Arthritis Rheum. 2008;58(12):3788-3797.	2.6.6.1
4.3-266-009	Qiu T, Xian L, Crane J, et al.	PTHreceptor signaling in osteoblasts regulates endochondral vascularization in maintenance of postnatal growth plate.	J Bone Miner Res. 2015;30(2):309-317.	2.6.6.1
4.3-266-010	Ma YL, Cain RL, Halladay DL, et al.	Catabolic effects of continuous humanPTH(1--38) in vivo is associated with sustained stimulation of RANKL and inhibition of osteoprotegerin and gene-associated bone formation.	Endocrinology. 2001;142:4047-4054.	2.6.6.1 2.6.6.10.4

CTD No.-資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-266-011	Babey M, Brandi ML, Shoback D.	Conventional treatment of hypoparathyroidism.	Endocrinol Metab Clin North Am. 2018;47(4):889-900.	2.6.6.1 2.6.6.10.4
4.3-266-012	Huang JC, Sakata T, Pfleger LL, et al.	PTH differentially regulates expression of RANKL and OPG.	J Bone Miner Res. 2004;19(2):235-244.	2.6.6.1 2.6.6.10.4
4.3-266-013	Fan Y, Hanai JI, Le PT, et al.	Parathyroid Hormone Directs Bone Marrow Mesenchymal Cell Fate.	Cell Metab. 2017;25(3):661-672.	2.6.6.1 2.6.6.10.4
4.3-266-014	Ivens IA, Achanzar W, Baumann A, et al.	PEGylated biopharmaceuticals: current experience and considerations for non-clinical development.	Toxicol Pathol. 2015;43(7):959-983.	2.6.6.1 2.6.6.5 2.6.6.10.3
4.3-266-015	Clarke J, Hurst C, Martin P, et al.	Duration of chronic toxicity studies for biotechnology-derived pharmaceuticals: is 6 months still appropriate?	Regul Toxicol Pharmacol. 2008;50(1):2-22.	2.6.6.3
4.3-266-016	Evans GO.	Fluid Balance, Electrolytes and Mineral Metabolsim.	A Practical handbook for toxicologists and biomedical researchers, second edition, Chapter 6, 2009;115-144.	2.6.6.3.1.1

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-266-017	Uzawa T, Hori M, Ejiri S, et al.	Comparison of the effects of intermittent and continuous administration of human parathyroid hormone(1-34) on rat bone.	Bone. 1995;16(4):477-484.	2.6.6.3.1.3 2.6.6.5 2.6.6.10.1 2.6.6.10.2 2.6.6.10.4
4.3-266-018	Lotinun S, Sibonga JD, Turner RT.	Evidence that the cells responsible for marrow fibrosis in a rat model for hyperparathyroidism are preosteoblasts.	Endocrinology. 2005;146(9):4074-4081.	2.6.6.3.1.3 2.6.6.5 2.6.6.10.1 2.6.6.10.4
4.3-266-019	Rutkovskiy A, Stensløkken KO, Vaage IJ.	Osteoblast Differentiation at a Glance.	Med Sci Monit Basic Res. 2016;22:95-106.	2.6.6.3.1.3
4.3-266-020	Gasser JA, Kneissel, M.	Bone physiology and biology.	Bone Toxicology. Springer. 2017;2:27-94.	2.6.6.3.1.3
4.3-266-021	Fossey S, Vahle J, Long P, et al.	Nonproliferative and proliferative lesions of the rat and ouse skeletal tissues (Bones, Joints, and Teeth).	J Toxicol Pathol. 2016;29(3 Suppl):49S-103S.	2.6.6.3.1 2.6.6.10.4
4.3-266-022	National Research Council.	Nutrient requirements of nonhuman primates.	Minerals. 2nd Revised Edition. National Academy of Sciences. 2003;6:94-112.	2.6.6.3.2

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4.3-266-023	Carlson CS, Loeser RF, Jayo MJ, et al.	Osteoarthritis in cynomolgus macaques: a primate model of naturally occurring disease.	J Orthop Res. 1994;12(3):331-339.	2.6.6.3.2.2
4.3-266-024	Carlson CS, Loeser RF, Purser CB, et al.	Osteoarthritis in cynomolgus macaques. III: Effects of age, gender, and subchondral bone thickness on the severity of disease.	J Bone Miner Res. 1996;11(9):1209-1217.	2.6.6.3.2.2
4.3-266-025	Miller LM, Novatt JT, Hamerman D, et al.	Alterations in mineral composition observed in osteoarthritic joints of cynomolgus monkeys.	Bone. 2004;35(2):498-506.	2.6.6.3.2.2
4.3-266-026	McCoy AM.	Animal models of osteoarthritis: comparisons and key considerations.	Vet Pathol. 2015;52(5):803-818.	2.6.6.3.2.2
4.3-266-027	Liao S, Qie JK, Xue M, et al.	Metabolic stability of human parathyroid hormone peptide hPTH (1-34) in rat tissue homogenates: kinetics and products of proteolytic degradation.	Amino Acids. 2010;38(5):1595-1605.	2.6.6.4.1.1
4.3-266-028	Aeschbacher HU, Finot PA, Wolleb U.	Interactions of histidine-containing test substances and extraction methods with the Ames mutagenicity test.	Mutation Research – Fundamental and Molecular Mechanisms of Mutagenesis. 1983;113(2):103-116.	2.6.6.4.1.1

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-266-029	Gatehouse D.	Critical features of bacterial mutation assays.	Mutagenesis. 1987;2(5):397-409.	2.6.6.4.1.1
4.3-266-030	Thompson C, Morley P, Kirkland D, et al.	Modified bacterial mutation test procedures for evaluation of peptides and amino acid-containing material.	Mutagenesis. 2005;20(5):345-350.	2.6.6.4.1.1
4.3-266-031	-	Natpara USPI (recent major change 2018)	https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125511s020lbl.pdf	2.6.6.5 2.6.6.10.5.2
4.3-266-032	-	Forteo USPI (recent major change 2020)	https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/021318s054lbl.pdf	2.6.6.5 2.6.6.4.3
4.3-266-033	-	Forsteo SmPC (latest renewal 2013)	https://www.ema.europa.eu/en/documents/product-information/forsteo-epar-product-information_en.pdf	2.6.6.5
4.3-266-034	-	Natpar SmPC (latest renewal 2021)	https://www.ema.europa.eu/en/docume	2.6.6.5 2.6.6.10.5.2

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
			nts/product-information/natpar-epar-product-information_en.pdf	
4.3-266-035	Jolette J, Wilker CE, Smith SY, et al.	Defining a noncarcinogenic dose of recombinant human parathyroid hormone 1-84 in a 2-year study in Fischer 344 rats.	Toxicol Pathol. 2006;34(7):929-940.	2.6.6.5
4.3-266-036	Vahle JL, Sato M, Long GG, et al.	Skeletal changes in rats given daily subcutaneous injections of recombinant human parathyroid hormone (1-34) for 2 years and relevance to human safety.	Toxicol Pathol. 2002;30(3):312-321.	2.6.6.5
4.3-266-037	Vahle JL, Long GG, Sandusky G, et al.	Bone neoplasms in F344 rats given teriparatide [rhPTH(1-34)] are dependent on duration of treatment and dose.	Toxicol Pathol. 2004;32(4):426-438.	2.6.6.5
4.3-266-038	Tashjian AH Jr, Chabner BA.	Commentary on clinical safety of recombinant human parathyroid hormone 1-34 in the treatment of osteoporosis in men and postmenopausal women.	J Bone Miner Res. 2002;17(7):1151-1161.	2.6.6.5
4.3-266-039	Tashjian AH Jr, Goltzman D.	On the interpretation of rat carcinogenicity studies for human PTH(1-34) and human PTH(1-84).	J Bone Miner Res. 2008;23(6):803-811.	2.6.6.5
4.3-266-040	Jerome CP, Burr DB, Van Bibber T, et al.	Treatment with human parathyroid hormone (1-34) for 18 months increases cancellous bone volume and improves	Bone. 2001;28(2):150-159.	2.6.6.5

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
		trabecular architecture in ovariectomized cynomolgus monkeys (Macaca fascicularis).		
4.3-266-041	Jimenez C, Yang Y, Kim HW, et al.	Primary hyperparathyroidism and osteosarcoma: examination of a large cohort identifies three cases of fibroblastic osteosarcoma.	J Bone Miner Res. 2005;20(9):1562-1568.	2.6.6.5
4.3-266-042	Cinamon U, Turcotte RE.	Primary Hyperparathyroidism and malignancy: “Studies by nature”.	Bone. 2006;39(2):420-423.	2.6.6.5
4.3-266-043	Fox J, Miller MA, Newman MK, et al.	Treatment of skeletally mature ovariectomized rhesus monkeys with PTH(1-84) for 16 months increases bone formation and density and improves trabecular architecture and biomechanical properties at the lumbar spine.	J Bone Miner Res. 2007;22(2):260-273.	2.6.6.5
4.3-266-044	Vahle J, Zuehlke U, Schmidt A et al.	Lack of bone neoplasms and persistence of bone efficacy in cynomolgus macaques after long-term treatment with teriparatide [rhPTH(1-34)].	J Bone Miner Res. 2008;23(12): 2033-2039.	2.6.6.5
4.3-266-045	Andrews EB, Gilsenan AW, Midkiff K, et al.	The US postmarketing surveillance study of adult osteosarcoma and teriparatide: study design and findings from the first 7 years.	J Bone Miner Res. 2012;27(12):2429-2437.	2.6.6.5
4.3-266-046	Cipriani C, Irani D, Bilezikian JP.	Safety of osteoanabolic therapy: a decade of experience.	J Bone Miner Res. 2012;27(12):2419-2428.	2.6.6.5

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-266-047	Nishikawa A, Yoshiki F, Taketsuna M, et al.	Safety and effectiveness of daily teriparatide for osteoporosis in patients with severe stages of chronic kidney disease: post hoc analysis of a postmarketing observational study.	Clin Interv Aging. 2016;11:1653-1659.	2.6.6.5
4.3-266-048	Gilsenan A, Harding A, Kellier-Steele N, et al.	The Forteo Patient Registry linkage to multiple state cancer registries: study design and results from the first 8 years.	Osteoporos Int. 2018;29(10):2335-2343.	2.6.6.5
4.3-266-049	Gilsenan A, Harris D, Reynolds M, et al.	Long-Term Cancer Surveillance: Results from the Forteo Patient Registry Surveillance Study.	Osteoporos Int. 2021a;32:645-651.	2.6.6.5
4.3-266-050	Gilsenan A, Midkiff K, Harris D, et al.	Teriparatide did not Increase Adult Osteosarcoma Incidence in a 15-Year US Postmarketing Surveillance Study.	J Bone Miner Res. 2021b;36(2):244-251.	2.6.6.5
4.3-266-051	-	Forteo Patient Registry 2015. Accessed 15 May 2022.	https://www.rtihs.org/publications/long-term-cancer-surveillance-five-year-update-Forteo-patient-registry-surveillance	2.6.6.5
4.3-266-052	Hock JM, Gera I.	Effects of continuous and intermittent administration and inhibition of resorption on the anabolic response of bone to parathyroid hormone.	J Bone Miner Res. 1992;7(1):65-72.	2.6.6.5 2.6.6.10.1 2.6.6.10.4

CTD No.-資料番号	著者	表題	掲載誌・その他	引用CTD No.
4.3-266-053	Parisien M, Cosman F, Mellish RW, et al.	Bone structure in postmenopausal hyperparathyroid, osteoporotic, and normal women.	J Bone Miner Res. 1995;10(9):1393-1399.	2.6.6.5 2.6.6.10.4
4.3-266-054	Vogel M, Hahn M, Delling G.	Trabecular bone structure in patients with primary hyperparathyroidism.	Virchows Arch. 1995;426(2):127-134.	2.6.6.5 2.6.6.10.4
4.3-266-055	Bellido T, Ali AA, Plotkin LI, et al.	Proteasomal degradation of Runx2 shortens parathyroid hormone-induced anti-apoptotic signaling in osteoblasts. A putative explanation for why intermittent administration is needed for bone anabolism.	J Biol Chem. 2003;278(50):50259-50272.	2.6.6.5
4.3-266-056	Frolik CA, Black EC, Cain RL, et al.	Anabolic and catabolic bone effects of human parathyroid hormone (1-34) are predicted by duration of hormone exposure.	Bone. 2003;33(3):372-379.	2.6.6.5
4.3-266-057	Li JY, Walker LD, Tyagi AM, et al.	The sclerostin-independent bone anabolic activity of intermittent PTH treatment is mediated by T-cell-produced Wnt10b.	J Bone Miner Res. 2014;29(1):43-54.	2.6.6.5
4.3-266-058	Morimoto A, Kikuta J, Nishikawa K, et al.	SLPI is a critical mediator that controls PTH-induced bone formation.	Nat Commun. 2021;12(1):2136.	2.6.6.5
4.3-266-059	Moonga BS, Moss DW, Patchell A, et al.	Intracellular regulation of enzyme secretion from rat osteoclasts and evidence for a functional role in bone resorption.	J Physiol. 1990;429:29-45.	2.6.6.5
4.3-266-060	Feng Y, Zhou M, Zhang Q, et al.	Synergistic effects of high dietary calcium and exogenous parathyroid hormone in promoting osteoblastic bone formation in mice.	Br J Nutr. 2015;113(6):909-922.	2.6.6.5

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-266-061	Stidl R, Denne M, Goldstine J, et al.	Polyethylene Glycol Exposure with Antihemophilic Factor (Recombinant), PEGylated (rurioctocog alfa pegol) and Other Therapies Indicated for the Pediatric Population: History and Safety.	Pharmaceuticals (Basel). 2018;11(3).	2.6.6.5 2.6.6.10.3
4.3-266-062	Webster R, Didier E, Harris P, et al.	PEGylated proteins: evaluation of their safety in the absence of definitive metabolism studies.	Drug Metab Dispos. 2007;35(1):9-16.	2.6.6.5 2.6.6.10.5.1
4.3-266-063	Palombo M, Deshmukh M, Myers D, et al.	Pharmaceutical and toxicological properties of engineered nanomaterials for drug delivery.	Annu Rev Pharmacol Toxicol. 2014;54:581-598.	2.6.6.5
4.3-266-064	-	Apidra SmPC (latest renewal 2009 pidra SmPC)	https://www.ema.europa.eu/en/documents/product-information/apidra-epar-product-information_en.pdf	2.6.6.9
4.3-266-065	-	Apidra USPI (recent major change 2022)	https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/021629s042lbl.pdf	2.6.6.9

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-266-066	-	FDA Guidance on Immunogenicity Assessment for Therapeutic Protein Products. CDER/CBER. FDA-2013-D-0092. August 2014.	https://www.fda.gov/media/85017/download	2.6.6.9.2
4.3-266-067	Cooper CW, Hirsch PF, Munson PL.	Importance of endogenous thyrocalcitonin for protection against hypercalcemia in the rat.	Endocrinology. 1970;86(2):406-415.	2.6.6.10.1
4.3-266-068	Kozhemyakina E, Lassar AB, Zelzer E.	A pathway to bone: signaling molecules and transcription factors involved in chondrocyte development and maturation.	Development. 2015;142(5):817-831.	2.6.6.10.2
4.3-266-069	Jüppner H, Abou-Samra AB, Freeman M, et al.	A G protein-linked receptor for parathyroid hormone and parathyroid hormone-related peptide.	Science. 1991;254(5034):1024-1026.	2.6.6.10.2
4.3-266-070	Karp S, Schipani E, St-Jacques B, et al.	Pregnancy Outcomes After Exposure to Certolizumab Pegol: Updated Results From a Pharmacovigilance Safety Database.	Development 2000;127(3):543-548.	2.6.6.10.2
4.3-266-071	Miao D, Li J, Xue Y, et al.	Parathyroid hormone-related peptide is required for increased trabecular bone volume in parathyroid hormone-null mice.	Endocrinology. 2004;145(8):3554-3562.	2.6.6.10.2
4.3-266-072	Vortkamp A, Lee K, Lanske B, et al.	Regulation of rate of cartilage differentiation by Indian hedgehog and PTH-related protein.	Science. 1996;273(5275):613-622.	2.6.6.10.2

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-266-073	Koyama E, Mundy C, Saunders, et al.	Premature growth plate closure caused by a Hedgehog cancer drug is preventable by co-administration of a retinoid antagonist in mice.	J Bone Min Res 2021,36(7):1387-1402.	2.6.6.10.2
4.3-266-074	Kilborn SH, Trudel G, Uhthoff H.	Review of growth plate closure compared with age at sexual maturity and lifespan in laboratory animals.	Contemp Top Lab Anim Sci. 2002;41(5):21-26.	2.6.6.10.2
4.3-266-075	-	CHMP Safety Working Party's response to the PDCO regarding the use of PEGylated drug products in the paediatric population.	16 November 2012. EMA/CHMP/SWP/647258/2012.	2.6.6.10.3
4.3-266-076	Conover C, Lejeune L, Linberg R, et al.	Transitional vacuole formation following a bolus infusion of PEG-hemoglobin in the rat.	Artif Cells Blood Substit Immobil Biotechnol. 1996;24(6):599-611.	2.6.6.10.3
4.3-266-077	Bendele A, Seely J, Richey C, et al.	Short communication: renal tubular vacuolation in animals treated with polyethylene-glycol-conjugated proteins.	Toxicol Sci. 1998;42:152-157.	2.6.6.10.3
4.3-266-078	Webster R, Elliott V, Park BK, et al.	PEG and PEG conjugates toxicity: towards an understanding of the toxicity of PEG and its relevance to PEGylated biologicals.	PEGylated Protein Drugs: Basic Science and Clinical Applications. 2009;127-146.	2.6.6.10.3

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-266-079	Rudmann D, Alston J, Hanson J, et al.	High molecular weight polyethylene glycol cellular distribution and PEG-associated cytoplasmic vacuolation is molecular weight dependent and does not require conjugation to proteins.	Toxicol Pathol. 2013; 41(7):970-983.	2.6.6.10.3
4.3-266-080	Irizarry Rovira AR, Bennet BM, Bolon B, et al.	Scientific and Regulatory Policy Committee Points to Consider: Histopathologic Evaluation in Safety Assessment Studies for PEGylated Pharmaceutical Products.	Toxicol Pathol. 2018;46(6):616-635.	2.6.6.10.3
4.3-266-081	Fang JL, Vanlandingham MM, Beland FA, et al.	Toxicity of high-molecular-weight polyethylene glycols in Sprague Dawley rats.	Toxicol Lett. 2022;359:22-30.	2.6.6.10.3
4.3-266-082	Zhu Z, Gao P, Hu Y, et al.	PEGylated versus non-PEGylated drugs: A cross-sectional analysis of adverse events in the FDA Adverse Event Reporting System (FAERS) Database.	Int J Clin Pharmacol Ther. 2020;58(6):332-342.	2.6.6.10.3
4.3-266-083	-	BPAC Briefing Document. BLA 125611 Coagulation Factor IX (Recombinant), GlycoPEGylated N9-GPN9-GP.	FDA Blood Products Advisory Committee. April 4, 2017.	2.6.6.10.3
4.3-266-084	Baumann A.	PEGylated biologics in haemophilia treatment: Current understanding of their long-term safety.	Haemophilia. 2020;26(1):e11-e13.	2.6.6.10.3
4.3-266-085	Andreollo NA, Santos EF, Araújo MR, et al.	Rat’s age versus human’s age: what is the relationship?	ABCD Arq Bras Cir Dig. 2012;25(1):49-51.	2.6.6.10.3

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-266-086	Sengupta P.	The laboratory rat: relating its age with human's.	Int J Prev Med. 2013;4(6):624-630.	2.6.6.10.3
4.3-266-087	Khan A, Bilezikian J.	Primary hyperparathyroidism: pathophysiology and impact on bone.	CMAJ. 2000;163(2):184-187.	2.6.6.10.4
4.3-266-088	Silva BC, Costa AG, Cusano NE, et al.	Catabolic and anabolic actions of parathyroid hormone on the skeleton.	J Endocrinol Invest. 2011;34(10):801-810.	2.6.6.10.4
4.3-266-089	Lotinun S, Evans GL, Bronk JT, et al.	Continuous parathyroid hormone induces cortical porosity in the rat: effects on bone turnover and mechanical properties.	J Bone Miner Res. 2004;19(7):1165-1171.	2.6.6.10.4
4.3-266-090	Horwitz MJ, Tedesco MB, Sereika SM, et al.	A 7-day continuous infusion of PTH or PTHrP suppresses bone formation and uncouples bone turnover.	J Bone Miner Res. 2011;26(9):2287-2297.	2.6.6.10.4
4.3-266-091	Baron R, Tross R, Vignery A.	Evidence of sequential remodeling in rat trabecular bone: Morphology, dynamic histomorphometry, and changes during skeletal maturation.	Anat Rec.1984; 208(1):137–145.	2.6.6.10.4
4.3-266-092	Wang YH, Liu Y, Buhl K, et al.	Comparison of the action of transient and continuous PTH on primary osteoblast cultures expressing differentiation stage-specific GFP.	J Bone Miner Res. 2005;20(1):5-14.	2.6.6.10.4
4.3-266-093	Goodman HM.	Hormonal Regulation of Calcium Metabolism.	Basic Medical Endocrinology (Third Edition).	2.6.6.10.4

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
			Academic Press. 2003;8:255-289.	
4.3-266-094	Jolette J, Attalla B, Varela A, et al.	Comparing the incidence of bone tumors in rats chronically exposed to the selective PTH type 1 receptor agonist abaloparatide or PTH(1-34).	Regul Toxicol Pharmacol. 2017;86:356-365.	2.6.6.10.4
4.3-266-095	Syme MR, Paxton JW, Keelan JA.	Drug transfer and metabolism by the human placenta.	Clin Pharmacokinet. 2004;43(8):487-514.	2.6.6.10.5.1 2.6.6..10.5.2
4.3-266-096	Martin PL, Breslin W, Rocca M, et al.	Considerations in assessing the developmental and reproductive toxicity potential of biopharmaceuticals.	Birth Defects Res B Dev Reprod Toxicol. 2009;86(3):176-203.	2.6.6.10.5.1 2.6.6.10.5.2
4.3-266-097	Harris JM, Chess RB.	Effect of pegylation on pharmaceuticals.	Nat Rev Drug Discov. 2003;2(3):214-221.	2.6.6.10.5.1
4.3-266-098	Mahadevan U, Wolf DC, Dubinsky M, et al.	Placental transfer of anti-tumor necrosis factor agents in pregnant patients with inflammatory bowel disease.	Clin Gastroenterol Hepatol. 2013;11(3):286-292.	2.6.6.10.5.1

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-266-099	Mariette X, Förger F, Abraham B, et al.	Lack of placental transfer of certolizumab pegol during pregnancy: results from CRIB, a prospective, postmarketing, pharmacokinetic study.	Ann Rheum Dis. 2018;77(2):228-233.	2.6.6.10.5.1
4.3-266-100	Clowse MEB, Scheuerle AE, Chambers C, et al.	Pregnancy Outcomes After Exposure to Certolizumab Pegol: Updated Results From a Pharmacovigilance Safety Database.	Arthritis Rheumatol. 2018;70(9):1399-1407.	2.6.6.10.5.1
4.3-266-101	-	Cimzia SmPC (latest renewal 2023,).	https://www.ema.europa.eu/en/documents/product-information/cimzia-epar-product-information_en.pdf	2.6.6.10.5.1
4.3-266-102	-	Cimzia BLA 125160. Center for Drug Evaluation and Research, Food & Drug Administration. Approved 04-22-2008.	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2008/125160s000TOC2.cfm	2.6.6.10.5.1
4.3-266-103	-	Cimzia BLA 125160. Center for Drug Evaluation and Research, Food & Drug Administration. Approved 04-22-2008.	https://www.ema.europa.eu/en/documents/assessment-report/cimzia-epar-	2.6.6.10.5.1

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
			public-assessment-report_en.pdf	
4.3-266-104	-	Cimzia USPI	https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/125160s000lbl.pdf	2.6.6.10.5.1
4.3-266-105	Northrop G, Misenhimer HR, Becker FO.	Failure of parathyroid hormone to cross the nonhuman primate placenta.	Am J Obstet Gynecol. 1977;129(4):449-453.	2.6.6.10.5.2
4.3-266-106	Leone-Bay A, Sato M, Paton D, et al.	Oral Delivery of Biologically Active Parathyroid Hormone.	Pharm Res. 2001;18:964-970.	2.6.6.10.5.2
4.3-266-107	Hwang SR, Seo DH, Byun Y, et. al.	Preparation and in vivo evaluation of an orally available enteric-microencapsulated parathyroid hormone (1-34)-deoxycholic acid nanocomplex.	Int J Nanomedicine. 2016;11:4231-4246.	2.6.6.10.5.2
4.3-266-108	Krysiak R, Wilk M, Okopien B.	Recurrent pancreatitis induced by hyperparathyroidism in pregnancy.	Arch Gynecol Obstet. 2011;284:531-534.	2.6.6.10.5.3
4.3-266-109	Kovacs CS.	Bone development and mineral homeostasis in the fetus and neonate: roles of the calciotropic and phosphotropic hormones.	Physiol Rev. 2014;94(4):1143-1218.	2.6.6.10.5.3

CTD No.- 資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-266-110	Dochez V, Ducarme G.	Primary hyperparathyroidism during pregnancy.	Arch Gynecol Obstet. 2015;291:259-263.	2.6.6.10.5,3
4.3-266-111	McCarthy A, Howarth S, Khoo S, et al.	Management of primary hyperparathyroidism in pregnancy: a case series.	Endocrinol Diabetes Metab Case Rep. 2019;2019:19-0039.	2.6.6.10.5.3
4.3-266-112	Ali DS, Dandurand K, Khan AA.	Primary Hyperparathyroidism in Pregnancy: Literature Review of the Diagnosis and Management.	J Clin Med. 2021;10(13):2956.	2.6.6.10.5.3
4.3-266-113	Norman J, Politz D, Politz L.	Hyperparathyroidism during pregnancy and the effect of rising calcium on pregnancy loss: a call for earlier intervention.	Clin Endocrinol (Oxf). 2009;71(1):104-109.	2.6.6.10.5.3
4.3-266-114	Qamar H, Perumal N, Papp E, et al.	Higher maternal parathyroid hormone concentration at delivery is not associated with smaller newborn size.	Endocr Connect. 2021;10(3):345-357.	2.6.6.10.5.3
4.3-266-115	Ilany J, Vered I, Cohen O.	The effect of continuous subcutaneous recombinantPTH(1-34) infusion during pregnancy on calcium homeostasis - a case report.	Gynecol Endocrinol. 2013;29(9):807-810.	2.6.6.10.5.3

CTD No.-資料番号	著者	表題	掲載誌・その他	引用 CTD No.
4.3-266-116	Shulman D.	Subcutaneous infusion of rhPTH1-34 during pregnancy and nursing in a woman with autosomal dominant hypoparathyroidism 1.	J Endocr Soc. 2022;6(5):bvac031.	2.6.6.10.5.3

第 5 部（モジュール 5）臨床試験報告書　添付資料一覧

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他	評価／参考	電子データの提出有無
5.2　全臨床試験一覧表 5.3　試験報告書及び関連情報 5.3.1　生物薬剤学試験報告書								
5.3.1.4　生物学的及び理化学的分析法検討報告書								
5.3.1.4-1	[redacted]	[redacted]	Validation of a method for the determination of Total PTH and Total PTH(1-34) in human EDTA plasma samples by LC-MS/MS (Triple Quad 6500)	20[redacted] 年[redacted] 月～ 20[redacted] 年[redacted] 月	海外	社内資料	評価	－
5.3.1.4-2	[redacted]	[redacted]	Validation of a method for the determination of Free PTH(1-34) and Free PTH(1-33) in acidified human EDTA plasma samples by LC-MS/MS (Triple Quad 6500)	20[redacted] 年[redacted] 月～ 20[redacted] 年[redacted] 月	海外	社内資料	評価	－

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他	評価／参考	電子データの提出有無
5.3.1.4-3	[redacted]	[redacted]	Validation of a method for the determination of mPEG in human EDTA plasma samples by LC-MS/MS (Triple Quad 6500)	20[redacted] 年[redacted] 月～ 20[redacted] 年[redacted] 月	海外	社内資料	評価	－
5.3.1.4-4	[redacted]	[redacted]	Validation of a method for the determination of mPEG in human EDTA plasma samples by LC-MS/MS (Triple Quad 6500)	20[redacted] 年[redacted] 月～ 20[redacted] 年[redacted] 月	海外	社内資料	評価	－
5.3.1.4-5	[redacted]	[redacted]	Validation of an Immunoassay for the Detection of Parathyroid Hormone (PTH) Antibodies in Human Serum	20[redacted] 年[redacted] 月～ 20[redacted] 年[redacted] 月	海外	社内資料	評価	－
5.3.1.4-6	[redacted]	[redacted]	Validation of an Immunoassay for the Detection of Antibodies to TransCon PTH Preexisting and in response to TransCon PTH (ACP-014) in Human Serum	20[redacted] 年[redacted] 月～ 20[redacted] 年[redacted] 月	海外	社内資料	評価	－
5.3.1.4-7	[redacted]	[redacted]	Validation of a Cell-Based Assay to Detect Neutralizing Antibodies (NAb) to Parathyroid Hormone (PTH) in Human Serum using Electrochemiluminescent Detection of Cyclic Adenosine Monophosphate	20[redacted] 年[redacted] 月～ 20[redacted] 年[redacted] 月	海外	社内資料	評価	－

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他	評価／参考	電子データの提出有無
5.3.1.4-8	[redacted]	[redacted]	Validation of an Immunoassay for the Detection of Antibodies to Polyethylene Glycol Preexisting and in response to TransCon PTH (ACP-014) in Human Serum	20[redacted] 年[redacted] 月～20[redacted] 年[redacted] 月	海外	社内資料	評価	－
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								
5.3.3.1-1	CT-103	Ascendis Pharma Bone Diseases A/S	A Phase 1, Randomized, Placebo-Controlled, Single and Multiple Ascending Dose Trial to Evaluate the Safety, Tolerability, Pharmacodynamics, and Pharmacokinetics of TransCon PTH in Healthy Adult Subjects (TransCon PTH-Phase 1)	20[redacted] 年[redacted] 月[redacted] 日（FPI）～20[redacted] 年[redacted] 月[redacted] 日	海外	社内資料	評価	○
5.3.3.1-2	TCP-105	Ascendis Pharma Bone Diseases A/S	A Single Center, Phase 1, Randomized, Double-Blind Study Comparing the PK and PD of Transcon PTH Administered as a Single Subcutaneous Dose in Healthy Adult Japanese and Non-Japanese Volunteers	20[redacted] 年[redacted] 月[redacted] 日（FPI）～20[redacted] 年[redacted] 月[redacted] 日	海外	社内資料	評価	○
5.3.3.3　内因性要因を検討した PK 試験報告書								

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他	評価／参考	電子データの提出有無
5.3.3.3-1	TCP-104	Ascendis Pharma Bone Diseases A/S	A Multicenter, Open-Label, Single-Dose, Parallel-Group Trial to Investigate the Effect of Varying Degrees of Renal Function on the Pharmacokinetics of TransCon PTH	20[redacted]年[redacted]月[redacted]日（FPI）～20[redacted]年[redacted]月[redacted]日	海外	社内資料	評価	○
5.3.3.5　ポピュレーション PK 試験報告書								
5.3.3.5-1	[redacted]	[redacted]	Population PK of TransCon PTH in healthy and in subjects with hypoparathyroidism in trials CT-103, TCP-104, TCP-105 and TCP-201	－	海外	社内資料	評価	－
5.3.3.5-2	[redacted]	[redacted]	Population PK of TransCon PTH in healthy and in subjects with hypoparathyroidism in trials CT-103, TCP-104, TCP-105, TCP-201 and TCP-304	－	海外	社内資料	評価	○
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	TCP-201	Ascendis Pharma A/S	PaTH Forward: A Phase 2, Multicenter, Randomized,Double-Blind, Placebo-Controlled, Parallel Group Trial with an Open-Label Extension, Investigating the Safety, Tolerability and Efficacy of TransCon PTH Administered Subcutaneously Daily in Adults with Hypoparathyroidism	20[redacted]年[redacted]月[redacted]日（FPI）～20[redacted]年[redacted]月[redacted]日	海外	社内資料	評価	○

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他	評価／参考	電子データの提出有無
5.3.5.1-2	TCP-304	Ascendis Pharma A/S	PaTHway TRIAL: A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Trial, with an Open-Label Extension, Investigating the Safety, Tolerability and Efficacy of TransCon PTH Administered Subcutaneously Daily in Adults with Hypoparathyroidism	20[redacted]年[redacted]月[redacted]日（FPI）～20[redacted]年[redacted]月[redacted]日	海外	社内資料	評価	○
5.3.5.2 非対照試験報告書								
5.3.5.2-1	TCP-305	Ascendis Pharma A/S	PaTHway Japan Trial: A Phase 3, Multicenter, Singlearm, Open-label Trial, Investigating the Safety, Tolerability and Efficacy of TransCon PTH Administered Subcutaneously Daily in Adults with Hypoparathyroidism	20[redacted]年[redacted]月[redacted]日（FPI）～20[redacted]年[redacted]月[redacted]日	国内	社内資料	評価	○
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	CT-103 TCP-104 TCP-201 TCP-304	Ascendis Pharma A/S	Integrated Summary of Immunogenicity for Palopegteriparatide	－	海外	社内資料	評価	－
5.3.5.3-2	ACP-014-CTD_Safety	帝人ファーマ株式会社	ACP-014 CTD 統計解析図表_第 01.00 版	－	国内	社内資料	参考	○
5.3.5.4 その他の臨床試験報告書								

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他	評価／参考	電子データの提出有無
5.3.5.4-1	TCP-304	Lars Rejnmark 他	Palopegteriparatide Treatment Improves Renal Function in Adults with Chronic Hypoparathyroidism_1-Year Results from the Phase 3 PaTHway Trial	－	海外	Advances in Therapy	評価	－
5.3.5.4-2	TCP-201	帝人ファーマ株式会社	TCP-201-SubgroupAnalysis.pdf	－	海外	社内資料	評価	－
5.3.5.4-3	TCP-305	帝人ファーマ株式会社	TCP-305-SubgroupAnalysis.pdf	－	海外	社内資料	評価	－
5.3.6　市販後の使用経験に関する報告書								
5.3.6-1	－	Ascendis Pharma Bone Diseases A/S	Periodic Benefit-Risk Evaluation Report (PBRER)（期間：2023 年 11 月 17 日～2024 年 5 月 16 日）	－	－	社内資料	参考	－
5.3.7　患者データ一覧表及び症例記録								
5.3.7.1　主要な試験の症例一覧表								
5.3.7.1-1	CT-103	Ascendis Pharma Bone Diseases A/S	A Phase 1, Randomized, Placebo-Controlled, Single and Multiple Ascending Dose Trial to Evaluate the Safety, Tolerability, Pharmacodynamics, and Pharmacokinetics of TransCon PTH in Healthy Adult Subjects (TransCon PTH-Phase 1)	20[redacted] 年[redacted] 月[redacted] 日（FPI）～ 20[redacted] 年[redacted] 月[redacted] 日	海外	社内資料	評価	○

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他	評価／参考	電子データの提出有無
5.3.7.1-2	TCP-105	Ascendis Pharma Bone Diseases A/S	A Single Center, Phase 1, Randomized, Double-Blind Study Comparing the PK and PD of Transcon PTH Administered as a Single Subcutaneous Dose in Healthy Adult Japanese and Non-Japanese Volunteers	20■ 年 ■ 月 ■ 日（FPI）～ 20■ 年■ 月 ■ 日	海外	社内資料	評価	○
5.3.7.1-3	TCP-104	Ascendis Pharma Bone Diseases A/S	A Multicenter, Open-Label, Single-Dose, Parallel-Group Trial to Investigate the Effect of Varying Degrees of Renal Function on the Pharmacokinetics of TransCon PTH	20■ 年■ 月■ 日（FPI）～ 20■ 年■ 月■ 日	海外	社内資料	評価	○
5.3.7.1-4	TCP-201	Ascendis Pharma A/S	PaTH Forward: A Phase 2, Multicenter, Randomized,Double-Blind, Placebo-Controlled, Parallel Group Trial with an Open-Label Extension, Investigating the Safety, Tolerability and Efficacy of TransCon PTH Administered Subcutaneously Daily in Adults with Hypoparathyroidism	20■ 年■月■ 日（FPI）～ 20■ 年■月■ 日	海外	社内資料	評価	○
5.3.7.1-5	TCP-304	Ascendis Pharma A/S	PaTHway TRIAL: A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Trial, with an Open-Label Extension, Investigating the Safety, Tolerability and Efficacy of TransCon PTH Administered	20■ 年■月■ 日（FPI）～ 20■ 年■月■ 日	海外	社内資料	評価	○

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他	評価／参考	電子データの提出有無
			Subcutaneously Daily in Adults with Hypoparathyroidism					
5.3.7.1-6	TCP-305	Ascendis Pharma A/S	PaTHway Japan Trial: A Phase 3, Multicenter, Singlearm, Open-label Trial, Investigating the Safety, Tolerability and Efficacy of TransCon PTH Administered Subcutaneously Daily in Adults with Hypoparathyroidism	20[redacted]年[redacted]月[redacted]日（FPI）～ 20[redacted]年[redacted]月[redacted]日	国内	社内資料	評価	○
5.3.7.2　有害事象症例一覧表								
5.3.7.2-1	CT-103	Ascendis Pharma Bone Diseases A/S	A Phase 1, Randomized, Placebo-Controlled, Single and Multiple Ascending Dose Trial to Evaluate the Safety, Tolerability, Pharmacodynamics, and Pharmacokinetics of TransCon PTH in Healthy Adult Subjects (TransCon PTH-Phase 1)	20[redacted]年[redacted]月[redacted]日（FPI）～ 20[redacted]年[redacted]月[redacted]日	海外	社内資料	評価	○
5.3.7.2-2	TCP-105	Ascendis Pharma Bone Diseases A/S	A Single Center, Phase 1, Randomized, Double-Blind Study Comparing the PK and PD of Transcon PTH Administered as a Single Subcutaneous Dose in Healthy Adult Japanese and Non-Japanese Volunteers	20[redacted]年[redacted]月[redacted]日（FPI）～ 20[redacted]年[redacted]月[redacted]日	海外	社内資料	評価	○
5.3.7.2-3	TCP-104	Ascendis Pharma Bone Diseases A/S	A Multicenter, Open-Label, Single-Dose, Parallel-Group Trial to Investigate the Effect of Varying	20[redacted]年[redacted]月[redacted]日（FPI）～	海外	社内資料	評価	○

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他	評価／参考	電子データの提出有無
			Degrees of Renal Function on the Pharmacokinetics of TransCon PTH	20■ 年■ 月■ 日				
5.3.7.2-4	TCP-201	Ascendis Pharma A/S	PaTH Forward: A Phase 2, Multicenter, Randomized,Double-Blind, Placebo-Controlled, Parallel Group Trial with an Open-Label Extension, Investigating the Safety, Tolerability and Efficacy of TransCon PTH Administered Subcutaneously Daily in Adults with Hypoparathyroidism	20■ 年■ 月■ 日（FPI）～ 20■ 年■ 月■ 日	海外	社内資料	評価	○
5.3.7.2-5	TCP-304	Ascendis Pharma A/S	PaTHway TRIAL: A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Trial, with an Open-Label Extension, Investigating the Safety, Tolerability and Efficacy of TransCon PTH Administered Subcutaneously Daily in Adults with Hypoparathyroidism	20■ 年■ 月■ 日（FPI）～ 20■ 年■ 月■ 日	海外	社内資料	評価	○
5.3.7.2-6	TCP-305	Ascendis Pharma A/S	PaTHway Japan Trial: A Phase 3, Multicenter, Singlearm, Open-label Trial, Investigating the Safety, Tolerability and Efficacy of TransCon PTH Administered Subcutaneously Daily in Adults with Hypoparathyroidism	20■ 年■ 月■ 日（FPI）～ 20■ 年■ 月■ 日	国内	社内資料	評価	○
5.3.7.3　重篤な有害事象症例一覧表								

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他	評価／参考	電子データの提出有無
5.3.7.3-1	CT-103	Ascendis Pharma Bone Diseases A/S	A Phase 1, Randomized, Placebo-Controlled, Single and Multiple Ascending Dose Trial to Evaluate the Safety, Tolerability, Pharmacodynamics, and Pharmacokinetics of TransCon PTH in Healthy Adult Subjects (TransCon PTH-Phase 1)	20[redacted]年[redacted]月[redacted]日（FPI）～ 20[redacted]年[redacted]月[redacted]日	海外	社内資料	評価	○
5.3.7.3-2	TCP-201	Ascendis Pharma A/S	PaTH Forward: A Phase 2, Multicenter, Randomized,Double-Blind, Placebo-Controlled, Parallel Group Trial with an Open-Label Extension, Investigating the Safety, Tolerability and Efficacy of TransCon PTH Administered Subcutaneously Daily in Adults with Hypoparathyroidism	20[redacted]年[redacted]月[redacted]日（FPI）～ 20[redacted]年[redacted]月[redacted]日	海外	社内資料	評価	○
5.3.7.3-3	TCP-304	Ascendis Pharma A/S	PaTHway TRIAL: A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Trial, with an Open-Label Extension, Investigating the Safety, Tolerability and Efficacy of TransCon PTH Administered Subcutaneously Daily in Adults with Hypoparathyroidism	20[redacted]年[redacted]月[redacted]日（FPI）～ 20[redacted]年[redacted]月[redacted]日	海外	社内資料	評価	○
5.3.7.3-4	TCP-305	Ascendis Pharma A/S	PaTHway Japan Trial: A Phase 3, Multicenter, Singlearm, Open-label Trial, Investigating the	20[redacted]年[redacted]月[redacted]日（FPI）～	国内	社内資料	評価	○

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他	評価／参考	電子データの提出有無
			Safety, Tolerability and Efficacy of TransCon PTH Administered Subcutaneously Daily in Adults with Hypoparathyroidism	20■ 年■月■日				
5.3.7.4　臨床検査値異常変動症例一覧表								
5.3.7.4-1	CT-103	Ascendis Pharma Bone Diseases A/S	A Phase 1, Randomized, Placebo-Controlled, Single and Multiple Ascending Dose Trial to Evaluate the Safety, Tolerability, Pharmacodynamics, and Pharmacokinetics of TransCon PTH in Healthy Adult Subjects (TransCon PTH-Phase 1)	20■ 年■月■日（FPI）～ 20■ 年■月■日	海外	社内資料	評価	○
5.3.7.4-2	TCP-105	Ascendis Pharma Bone Diseases A/S	A Single Center, Phase 1, Randomized, Double-Blind Study Comparing the PK and PD of Transcon PTH Administered as a Single Subcutaneous Dose in Healthy Adult Japanese and Non-Japanese Volunteers	20■ 年■月■日（FPI）～ 20■ 年■月■日	海外	社内資料	評価	○
5.3.7.4-3	TCP-104	Ascendis Pharma Bone Diseases A/S	A Multicenter, Open-Label, Single-Dose, Parallel-Group Trial to Investigate the Effect of Varying Degrees of Renal Function on the Pharmacokinetics of TransCon PTH	20■年■月■日（FPI）～ 20■ 年■月■日	海外	社内資料	評価	○
5.3.7.4-4	TCP-201	Ascendis Pharma A/S	PaTH Forward: A Phase 2, Multicenter, Randomized,Double-Blind, Placebo-Controlled, Parallel Group Trial with an Open-Label	20■ 年■月■日（FPI）～	海外	社内資料	評価	○

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他	評価／参考	電子データの提出有無
			Extension, Investigating the Safety, Tolerability and Efficacy of TransCon PTH Administered Subcutaneously Daily in Adults with Hypoparathyroidism	20[redacted]年[redacted]月[redacted]日				
5.3.7.4-5	TCP-304	Ascendis Pharma A/S	PaTHway TRIAL: A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Trial, with an Open-Label Extension, Investigating the Safety, Tolerability and Efficacy of TransCon PTH Administered Subcutaneously Daily in Adults with Hypoparathyroidism	20[redacted]年[redacted]月[redacted]日（FPI）～20[redacted]年[redacted]月[redacted]日	海外	社内資料	評価	○
5.3.7.4-6	TCP-305	Ascendis Pharma A/S	PaTHway Japan Trial: A Phase 3, Multicenter, Singlearm, Open-label Trial, Investigating the Safety, Tolerability and Efficacy of TransCon PTH Administered Subcutaneously Daily in Adults with Hypoparathyroidism	20[redacted]年[redacted]月[redacted]日（FPI）～20[redacted]年[redacted]月[redacted]日	国内	社内資料	評価	○

5.4 参考文献

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他
5.4-25-001	—	Brown EM, Juppner H.	Parathyroid hormone: synthesis, secretion, and action.	—	—	Primer on the metabolic bone diseases and

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他
						disorders of mineral metabolism. 2006:90-99.
5.4-25-002	—	Gilsenan A, Harding A, Kellier-Steele N, et al.	The Forteo Patient Registry linkage to multiple state cancer registries: study design and results from the first 8 years.	—	—	Osteoporos Int. 2018;29(10):2335-2343.
5.4-25-003	—	DeLuca HF.	The kidney as an endocrine organ for the production of 1,25-dihydroxyvitamin D 3, a calcium-mobilizing hormone.	—	—	N Engl J Med. 1973;289(7):359-365.
5.4-25-004	—	Haussler MR, McCain TA.	Basic and clinical concepts related to vitamin D metabolism and action (First of two parts).	—	—	N Engl J Med. 1977a;297(18):974-983.
5.4-25-005	—	Haussler MR, McCain TA.	Basic and clinical concepts related to vitamin D metabolism and action (Second of two parts).	—	—	N Engl J Med. 1977b;297(19):1041-1050.
5.4-25-006	—	Reichel H, Koeffler HP, Norman AW.	The role of the vitamin D endocrine system in health and disease.	—	—	N Engl J Med. 1989;320(15):980-991.
5.4-25-007	—	Lupp A, Klenk C, Röcken C, et al.	Immunohistochemical identification of the PTHR1 parathyroid hormone receptor in normal and neoplastic human tissues.	—	—	Eur J Endocrinol. 2010;162(5):979-986.
5.4-25-008	—	Reppe S, Stilgren L, Abrahamsen B, et al.	Abnormal muscle and hematopoietic gene expression may be important for clinical morbidity in primary hyperparathyroidism.	—	—	Am J Physiol Endocrinol Metab. 2007;292(5):E1465-1473.

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5.4-25-009	—	Cheloha RW, Gellman SH, Vilardaga JP, et al.	PTH receptor-1 signalling-mechanistic insights and therapeutic prospects.	—	—	Nat Rev Endocrinol. 2015;11(12):712-724.
5.4-25-010	—	Clemens TL, Cormier S, Eichinger A, et al.	Parathyroid hormone-related protein and its receptors: nuclear functions and roles in the renal and cardiovascular systems, the placental trophoblasts and the pancreatic islets.	—	—	Br J Pharmacol. 2001;134(6):1113-1136.
5.4-25-011	—	Brandi ML, Bilezikian JP, Shoback D, et al.	Management of hypoparathyroidism: summary statement and guidelines.	—	—	J Clin Endocrinol Metab. 2016;101(6):2273-2283.
5.4-25-012	—	Clarke BL, Brown EM, Collins MT, et al.	Epidemiology and diagnosis of hypoparathyroidism.	—	—	J Clin Endocrinol Metab. 2016;101(6):2284-2299.
5.4-25-013	—	Shoback DM, Bilezikian JP, Costa AG, et al.	Presentation of Hypoparathyroidism: Etiologies and Clinical Features.	—	—	J Clin Endocrinol Metab. 2016;101(6):2300-2312.
5.4-25-014	—	Astor MC, Løvås K, Debowska A, et al.	Epidemiology and Health-Related Quality of Life in Hypoparathyroidism in Norway.	—	—	J Clin Endocrinol Metab. 2016;101(8):3045-3053.

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他
5.4-25-015	—	Cianferotti L, Parri S, Gronchi G, et al.	Prevalence of Chronic Hypoparathyroidism in a Mediterranean Region as Estimated by the Analysis of Anonymous Healthcare Database.	—	—	Calcif Tissue Int. 2018;103(2):144-150.
5.4-25-016	—	Clarke BL, Leibson C, Emerson J, et al.	Co-morbid-medical conditions associated with prevalent hypoparathyroidism: a population-based study.	—	—	Journal of Bone and Mineral Research. 2011;S182:26 (Abstract SA1070).
5.4-25-017	—	Powers J, Joy K, Ruscio A, et al.	Prevalence and incidence of hypoparathyroidism in the United States using a large claims database.	—	—	J Bone Miner Res. 2013;28(12):2570-2576.
5.4-25-018	—	Underbjerg L, Sikjaer T, Mosekilde L, et al.	Cardiovascular and renal complications to postsurgical hypoparathyroidism: a Danish nationwide controlled historic follow-up study.	—	—	J Bone Miner Res. 2013;28(11):2277-2285.
5.4-25-019	—	Underbjerg L, Sikjaer T, Mosekilde L, et al.	The Epidemiology of Nonsurgical Hypoparathyroidism in Denmark: A Nationwide Case Finding Study.	—	—	J Bone Miner Res. 2015;30(9):1738-1744.
5.4-25-020	—	Vadiveloo T, Donnan PT, Leese GP.	A Population-Based Study of the Epidemiology of Chronic Hypoparathyroidism.	—	—	J Bone Miner Res. 2018;33(3):478-485.
5.4-25-021	—	Shishiba Y, Imai T, Kanmori M, et al.	Prevalence of postsurgical hypoparathyroidism in Japan: Estimated from the data of multiple institutes.	—	—	J JAES JSTS. 2017;34(1):51-56.

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5.4-25-022	—	Takatani R, Kubota T, Minagawa M, et al.	Prevalence of Pseudohypoparathyroidism and Nonsurgical Hypoparathyroidism in Japan in 2017: A Nationwide Survey.	—	—	J Epidemiol. 2023;33(11):569-573.
5.4-25-023	—	Shoback D.	Clinical practice. Hypoparathyroidism.	—	—	N Engl J Med. 2008;359(4):391-403.
5.4-25-024	—	Khan AA, Bilezikian JP, Brandi ML, et al.	Evaluation and Management of Hypoparathyroidism Summary Statement and Guidelines from the Second International Workshop.	—	—	J Bone Miner Res. 2022 Dec;37(12):2568-2585. doi: 10.1002/jbmr.4691. Epub 2022 Nov 14. PMID: 36054621.
5.4-25-025	—	Almquist M, Ivarsson K, Nordenström E, et al.	Mortality in patients with permanent hypoparathyroidism after total thyroidectomy.	—	—	Br J Surg. 2018;105(10):1313-1318.
5.4-25-026	—	Mannstadt M, Clarke BL, Vokes T, et al.	Efficacy and safety of recombinant human parathyroid hormone (1-84) in hypoparathyroidism (REPLACE): a double-blind, placebo-controlled, randomised, phase 3 study.	—	—	Lancet Diabetes Endocrinol. 2013;1(4):275-283.
5.4-25-027	—	Mannstadt M, Bilezikian JP, Thakker RV, et al.	Hypoparathyroidism.	—	—	Nat Rev Dis Primers. 2017;3:17080.

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他
5.4-25-028	—	Cipriani C, Minisola S, Bilezikian JP, et al.	Vertebral Fracture Assessment in Postmenopausal Women With Postsurgical Hypoparathyroidism.	—	—	J Clin Endocrinol Metab. 2021;106(5):1303-1311.
5.4-25-029	—	Büttner M, Musholt TJ, Singer S.	Quality of life in patients with hypoparathyroidism receiving standard treatment: a systematic review.	—	—	Endocrine. 2017;58(1):14-20.
5.4-25-030	—	山内美香.	低カルシウム血症と内分泌疾患.	—	—	日本内科学会雑誌. 109 (4), 733-739, 2020-04-10.
5.4-25-031	—	Mitchell DM, Regan S, Cooley MR, et al.	Long-Term Follow-Up of Patients with Hypoparathyroidism.	—	—	J Clin Endocrinol Metab. 2012;97(12):4507-4514.
5.4-25-032	—	Bilezikian JP, Cusano NE, Khan AA, et al.	Primary hyperparathyroidism.	—	—	Nat Rev Dis Primers. 2016;2:16033.
5.4-25-033	—	Abate EG, Clarke BL.	Review of Hypoparathyroidism.	—	—	Front Endocrinol (Lausanne). 2017;7:172.
5.4-25-034	—	Takeda Statement, 04 October 2022.	Takeda to Discontinue Manufacturing of NATPAR® / NATPARA® for Patients with Hypoparathyroidism at the End of 2024	—	—	https://www.takeda.com/en-us/newsroom/statements/2022/takeda-to-discontinue-manufacturing-of-natpar-natpara/#:~:text=OSAKA

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他
						%2C%20Japan%20and%20CAMBRIDGE%2C%20Massachusetts,issues%20that%20are%20specific%20to
5.4-25-035	—	Winer KK, Yanovski JA, Sarani B, et al.	A randomized, cross-over trial of once-daily versus twice-daily parathyroid hormone 1-34 in treatment of hypoparathyroidism.	—	—	J Clin Endocrinol Metab. 1998;83(10):3480-3486.
5.4-25-036	—	Winer KK, Sinaii N, Peterson D, et al.	Effects of once versus twice-daily parathyroid hormone 1-34 therapy in children with hypoparathyroidism.	—	—	J Clin Endocrinol Metab. 2008;93(9):3389-3395.
5.4-25-037	—	Winer KK, Zhang B, Shrader JA, et al.	Synthetic human parathyroid hormone 1-34 replacement therapy: a randomized crossover trial comparing pump versus injections in the treatment of chronic hypoparathyroidism.	—	—	J Clin Endocrinol Metab. 2012;97(2):391-399.
5.4-25-038	—	Winer KK, Kelly A, Johns A, et al.	Long-Term Parathyroid Hormone 1-34 Replacement Therapy in Children with Hypoparathyroidism.	—	—	J Pediatr. 2018;203:391-399.
5.4-25-039	—	Iida-Klein A, Lu SS, Kapadia R, et al.	Short-term continuous infusion of human parathyroid hormone 1-34 fragment is catabolic with decreased trabecular connectivity density accompanied by hypercalcemia in C57BL/J6 mice.	—	—	J Endocrinol. 2005;186(3):549-557.

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5.4-25-040	—	Takasu H, Bringhurst FR.	Type-1 parathyroid hormone (PTH)/PTH-related peptide (PTHrP) receptors activate phospholipase C in response to carboxyl-truncated analogs of PTH (1-34).	—	—	Endocrinology. 1998;139(10):4293-4299.
5.4-25-041	—	Morley P, Whitfield JF, Willick GE.	Design and applications of parathyroid hormone analogues.	—	—	Curr Med Chem. 1999;6(11):1095-1106.
5.4-25-042	—	Habener JF, Rosenblatt M, Potts JT Jr.	Parathyroid hormone: biochemical aspects of biosynthesis, secretion, action, and metabolism.	—	—	Physiol Rev. 1984;64(3):985-1053.
5.4-25-043	—	Lee C, Luck MD, Jüppner H, et al.	Homolog-scanning mutagenesis of the parathyroid hormone (PTH) receptor reveals PTH-(1-34) binding determinants in the third extracellular loop.	—	—	Mol Endocrinol. 1995;9(10):1269-1278.
5.4-25-044	—	Drechsler N, Fröbel J, Jahreis G, et al.	Binding specificity of the ectodomain of the parathyroid hormone receptor.	—	—	Biophys Chem. 2011;154(2-3):66-72.
5.4-25-045	—	Food and Drug Administration.	FDA Guidance for Industry, Bioanalytical Method Validation. 2001.	—	—	https://www.federalregister.gov/documents/2001/05/23/01-12908/guidance-for-industry-on-bioanalytical-method-validation-availability.

CTD No.-資料番号	試験番号又は報告書番号	著者	表題	実施期間	実施場所（国内／海外）	掲載誌・その他
5.4-25-046	—	Food and Drug Administration.	FDA Guidance for Industry, Bioanalytical Method Validation. May 2018.	—	—	
5.4-25-047	—	European Medicines Agency.	Guideline on Bioanalytical Method Validation. EMEA/Committee for Medicinal Products for Human Use. 2011.	—	—	
5.4-25-048	—	Viswanathan CT, Bansal S, Booth B, et al.	Quantitative bioanalytical methods validation and implementation: best practices for chromatographic and ligand binding assays.	—	—	Pharm Res. 2007;24(10):1962-1973.
5.4-25-049	—	Knutsson M, Schmidt R, Timmerman P.	LC-MS/MS of large molecules in a regulated bioanalytical environment - which acceptance criteria to apply?	—	—	Bioanalysis. 2013;5(18):2211-2214.
5.4-25-050	—	Corvilain J, Manderlier T, Struyven J, et al.	Metabolism of Human PTH by the Kidney and the liver.	—	—	Horm Metab Res. 1977;9:239-242.
5.4-25-051	—	Horwitz MJ, Tedesco MB, Sereika SM, et al.	A 7-day continuous infusion of PTH or PTHrP suppresses bone formation and uncouples bone turnover.	—	—	J Bone Miner Res. 2011;26(9):2287-2297.
5.4-25-052	—	Rubin MR, Cusano NE, Fan WW, et al.	Therapy of hypoparathyroidism with PTH(1-84): a prospective six year investigation of efficacy and safety.	—	—	J Clin Endocrinol Metab. 2016;101(7):2742-2750.

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5.4-25-053	—	Mannstadt M, Clarke BL, Bilezikian JP, et al.	Safety and Efficacy of 5 Years of Treatment With Recombinant Human Parathyroid Hormone in Adults With Hypoparathyroidism.	—	—	J Clin Endocrinol Metab. 2019;104(11):5136-5147.
5.4-25-054	—	Winer KK, Fulton KA, Albert PS, et al.	Effects of pump versus twice-daily injection delivery of synthetic parathyroid hormone 1-34 in children with severe congenital hypoparathyroidism.	—	—	J Pediatr. 2014;165(3):556-563.
5.4-25-055	—	Herdman M.	Using Patient Reported Outcome measures in a cross-cultural context: conceptual and linguistic issues.	—	—	ISPOR 2023.
5.4-25-056	—	Bioclinica.	Charter for Independent Imaging Assessment, Dual-energy X-ray Absorptiometry (DXA). 2021.	—	—	
5.4-25-057	—	Clarke J, Hurst C, Martin P, et al.	Duration of chronic toxicity studies for biotechnology-derived pharmaceuticals: is 6 months still appropriate?	—	—	Regul Toxicol Pharmacol. 2008;50(1):2-22.
5.4-25-058	—	Parfitt AM.	Misconceptions (2): turnover is always higher in cancellous than in cortical bone.	—	—	Bone. 2002;30(6):807-809.
5.4-25-059	—	Rejnmark L, Gosmanova EO, Khan AA, et al.	Palopegteriparatide treatment improves renal function in adults with chronic hypoparathyroidism: 1-year results from the Phase 3 PaTHway Trial.	—	—	Adv Ther. 2024;41(6):2500-2518.

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5.4-25-060	—	Natpara USPI.	Prescribing Information for Natpara:	—	—	https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125511s028lbl.pdf
5.4-25-061	—	Forteo USPI (recent major change 2020, accessed 30 Aug 2024).	-	—	—	https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/021318s054lbl.pdf
5.4-25-062	—	Forsteo EPAR	Scientific Discussion. 2005.	—	—	https://www.ema.europa.eu/en/documents/scientific-discussion/forsteo-epar-scientific-discussion_en.pdf
5.4-25-063	—	Natpar EPAR	Public Assessment Report, 2017. Accessed 30-Aug-2024.	—	—	https://www.ema.europa.eu/en/documents/assessment-report/natpar-epar-public-assessment-report_en.pdf
5.4-25-064	—	Jerome CP, Burr DB, Van Bibber T, et al.	Treatment with human parathyroid hormone (1-34) for 18 months increases cancellous bone volume and improves trabecular architecture in ovariectomized cynomolgus monkeys (Macaca fascicularis).	—	—	Bone. 2001;28(2):150-159.

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5.4-25-065	—	Jimenez C, Yang Y, Kim HW, et al.	Primary hyperparathyroidism and osteosarcoma: examination of a large cohort identifies three cases of fibroblastic osteosarcoma.	—	—	J Bone Miner Res. 2005;20(9):1562-1568.
5.4-25-066	—	Cinamon U, Turcotte RE.	Primary hyperparathyroidism and malignancy: “studies by nature”.	—	—	Bone. 2006;39(2):420-423.
5.4-25-067	—	Fox J, Miller MA, Newman MK, et al.	Treatment of skeletally mature ovariectomized rhesus monkeys with PTH(1-84) for 16 months increases bone formation and density and improves trabecular architecture and biomechanical properties at the lumbar spine.	—	—	J Bone Miner Res. 2007;22(2):260-273.
5.4-25-068	—	Vahle JL, Zuehlke U, Schmidt A et al.	Lack of bone neoplasms and persistence of bone efficacy in cynomolgus macaques after long-term treatment with teriparatide [rhPTH(1-34)].	—	—	J Bone Miner Res. 2008;23(12):2033-2039.
5.4-25-069	—	Andrews EB, Gilsenan AW, Midkiff K, et al.	The US postmarketing surveillance study of adult osteosarcoma and teriparatide: study design and findings from the first 7 years.	—	—	J Bone Miner Res. 2012;27(12):2429-2437.
5.4-25-070	—	Cipriani C, Irani D, Bilezikian JP.	Safety of osteoanabolic therapy: a decade of experience.	—	—	J Bone Miner Res. 2012;27(12):2419-2428.
5.4-25-071	—	Nishikawa A, Yoshiki F, Taketsuna M, et al.	Safety and effectiveness of daily teriparatide for osteoporosis in patients with severe stages of chronic kidney disease: post hoc analysis of a postmarketing observational study.	—	—	Clin Interv Aging. 2016;11:1653-1659.

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5.4-25-072	—	Gilsenan A, Harding A, Kellier-Steele N, et al.	The Forteo Patient Registry linkage to multiple state cancer registries: study design and results from the first 8 years.	—	—	Osteoporos Int. 2018;29(10):2335-2343.
5.4-25-073	—	Gilsenan A, Harris D, Reynolds M, et al.	Long-Term Cancer Surveillance: Results from the Forteo Patient Registry Surveillance Study.	—	—	Osteoporos Int. 2021a;32:645-651.
5.4-25-074	—	Gilsenan A, Midkiff K, Harris D, et al.	Teriparatide did not Increase Adult Osteosarcoma Incidence in a 15-Year US Postmarketing Surveillance Study.	—	—	J Bone Miner Res. 2021b;36(2):244-251.
5.4-25-075	—	-	Forteo Patient Registry. Accessed 30 Aug 2024.	—	—	https://www.rtihs.org/publications/long-termcancer-surveillance-five-year-update-forteo-patient-registry-surveillance
5.4-25-076	—	Gafni RI, Langman CB, Guthrie LC, et al.	Hypocitraturia Is an Untoward Side Effect of Synthetic Human Parathyroid Hormone (hPTH) 1-34 Therapy in Hypoparathyroidism That May Increase Renal Morbidity.	—	—	J Bone Miner Res. 2018;33(10):1741-1747.
5.4-25-077	—	Zuckerman JM, Assimos DG.	Hypocitraturia: pathophysiology and medical management.	—	—	Rev Urol. 2009;11(3):134-144.

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5.4-25-078	－	BPAC Briefing Document.	BLA 125611 Coagulation Factor IX (Recombinant), GlycoPEGylated N9-GP.	－	－	FDA Blood Products Advisory Committee. 04 April 2017.
5.4-25-079	－	Baumann A.	PEGylated biologics in haemophilia treatment: Current understanding of their long-term safety.	－	－	Haemophilia. 2020;26(1):e11-e13.
5.4-25-080	－	難病医学研究財団/難病情報センター.	235 副甲状腺機能低下症.	－	－	https://www.nanbyou.or.jp/wp-content/uploads/upload_files/File/235-202404-kijyun.pdf.
5.4-25-081	－	Hadker N, Egan J, Sanders J, et al.	Understanding the burden of illness associated with hypoparathyroidism reported among patients in the PARADOX study.	－	－	Endocr Pract. 2014;20(7):671-679.
5.4-25-082	－	Karpf DB, Pihl S, Mourya S, et al.	A Randomized Double-Blind Placebo-Controlled First-In-Human Phase 1 Trial of TransCon PTH in Healthy Adults.	－	－	J Bone Miner Res. 2020 Aug;35(8):1430-1440.
5.4-271-001	－	Food and Drug Administration	Guidance for Industry: Bioanalytical method validation – General Considerations. 2001.	－	－	－
5.4-271-002	－	Food and Drug Administration	Guidance for Industry: Bioanalytical method validation – General Considerations. 2018.	－	－	－
5.4-271-003	－	European Medicines Agency	Guideline on bioanalytical method validation. 21 July 2011.	－	－	－

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5.4-271-004	−	Viswanathan CT, Bansal S, Booth B, et al.	Quantitative bioanalytical methods validation and implementation: best practices for chromatographic and ligand binding assays.	−	−	Pharm Res. 2007;24(10):1962-1973.
5.4-271-005	−	Knutsson M, Schmidt R, Timmerman P.	LC-MS/MS of large molecules in a regulated bioanalytical environment - which acceptance criteria to apply?	−	−	Bioanalysis. 2013;5(18):2211-2214.
5.4-271-006	−	Mire-Sluis AR, Barrett YC, Devanarayan V, et al.	Recommendations for the design and optimization of immunoassays used in the detection of host antibodies against biotechnology products.	−	−	Journal of Immunological Methods. 2004;289:1-16.
5.4-271-007	−	Shankar G, Devanarayan V, Amaravadi L, et al.	Recommendations for the validation of immunoassays used for detection of host antibodies against biotechnology products.	−	−	Journal of Pharmaceutical and Biomedical Analysis. 2008;48:1267-1281.
5.4-271-008	−	Gupta S, Indelicato SR, Jethwa V, et al.	Recommendations for the design, optimization, and qualification of cell-based assays used for the detection of neutralizing antibody responses elicited to biological therapeutics.	−	−	Journal of Immunological Methods. 2007;321:1-18.
5.4-271-009	−	Gupta S, Devanarayan V, Finco D, et al.	Recommendations for the validation of cell-based assays used for the detection of neutralizing antibody immune responses elicited against biological therapeutics.	−	−	Journal of Pharmaceutical and Biomedical Analysis. 2011;55:878-888.

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5.4-272-001	－	Goltzman D.	Physiology of Parathyroid Hormone.	－	－	Endocrinol Metab Clin North Am. 2018;47(4):743-758.
5.4-272-002	－	Rubin MR, Cusano NE, Fan WW, et al.	Therapy of hypoparathyroidism with PTH(1-84): a prospective six year investigation of efficacy and safety.	－	－	J Clin Endocrinol Metab. 2016;101(7):2742-2750.
5.4-272-003	－	National Kidney Foundation, Inc.	NKF KDOQI Guidelines	－	－	－
5.4-272-004	－	European Medicines Agency	CHMP Safety Working Party’s response to the PDCO regarding the use of PEGylated drug products in the paediatric population. 2012. 16 November 2012.	－	－	－
5.4-272-005	－	Food and Drug Administration	BPAC Briefing Document. BLA 125611 Coagulation Factor IX (Recombinant), GlycoPEGylated N9-GPN9-GP.	－	－	April 4, 2017.
5.4-272-006	－	Baumann A.	PEGylated biologics in haemophilia treatment: Current understanding of their longterm safety.	－	－	Haemophilia. 2020;26(1):e11-e13.
5.4-272-007	－	Takasu H, Bringhurst FR.	Type-1 parathyroid hormone (PTH)/PTH-related peptide (PTHrP) receptors activate phospholipase C in response to carboxyl-truncated analogs of PTH(1-34).	－	－	Endocrinology. 1998;139(10):4293-4299.

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5.4-272-008	−	Morley P, Whitfield JF, Willick GE.	Design and applications of parathyroid hormone analogues.	−	−	Curr Med Chem. 1999;6(11):1095-1106.
5.4-272-009	−	Horwitz MJ, Tedesco MB, Sereika SM, et al.	A 7-day continuous infusion of PTH or PTHrP suppresses bone formation and uncouples bone turnover.	−	−	J Bone Miner Res. 2011;26(9):2287-2297.
5.4-272-010	−	Syed MA, Horwitz MJ, Tedesco MB, et al.	Parathyroid hormone-related protein-(1-36) stimulates renal tubular calcium reabsorption in normal human volunteers: implications for the pathogenesis of humoral hypercalcemia of malignancy.	−	−	J Clin Endocrinol Metab. 2001;86(4):1525-1531.
5.4-272-011	−	Winer KK, Fulton KA, Albert PS, et al.	Effects of pump versus twice-daily injection delivery of synthetic parathyroid hormone 1-34 in children with severe congenital hypoparathyroidism.	−	−	J Pediatr. 2014;165(3):556-563.
5.4-272-012	−	Winer KK, Zhang B, Shrader JA, et al.	Synthetic human parathyroid hormone 1-34 replacement therapy: a randomized crossover trial comparing pump versus injections in the treatment of chronic hypoparathyroidism.	−	−	J. Clin. Endocrinol. Metab. 2012;97(2):391-399.
5.4-272-013	−	日本イーライリリー株式会社	フォルテオ®皮下注キット添付文書	−	−	2022 年 10 月改訂（第 3 版）

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5.4-272-014	－	Shire-NPS Pharmaceuticals, Inc.	NATPARA® (parathyroid hormone) for injection, for subcutaneous use. US prescribing information.	－	－	Revised: 04/2022
5.4-272-015	－	帝人ファーマ株式会社	オスタバロ®皮下注カートリッジ添付文書	－	－	2023 年 12 月改訂（第 3 版）
5.4-273-001	－	Brown EM, Jüppner H.	Parathyroid hormone: synthesis, secretion, and action.	－	－	Primer on the metabolic bone diseases and disorders of mineral metabolism. 2006:90-99.
5.4-273-002	－	Goltzman D, Mannstadt M, Marcocci C.	Physiology of the calcium-parathyroid hormone-vitamin D axis.	－	－	Front Horm Res. 2018;50:1-13.
5.4-273-003	－	DeLuca HF.	The kidney as an endocrine organ for the production of 1,25-dihydroxyvitamin D 3 , a calcium-mobilizing hormone.	－	－	N Engl J Med. 1973;289(7):359-365.
5.4-273-004	－	Haussler MR, McCain TA.	Basic and clinical concepts related to vitamin D metabolism and action (First of two parts).	－	－	N Engl J Med. 1977;297(18):974-983.
5.4-273-005	－	Haussler MR, McCain TA.	Basic and clinical concepts related to vitamin D metabolism and action (Second of two parts).	－	－	N Engl J Med. 1977;297(19):1041-1050.
5.4-273-006	－	Reichel H, Koeffler HP, Norman AW.	The role of the vitamin D endocrine system in health and disease.	－	－	N Engl J Med. 1989;320(15):980-991.

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5.4-273-007	－	Clemens TL, Cormier S, Eichinger A, et al.	Parathyroid hormone-related protein and its receptors: nuclear functions and roles in the renal and cardiovascular systems, the placental trophoblasts and the pancreatic islets.	－	－	Br J Pharmacol. 2001;134(6):1113-1136.
5.4-273-008	－	Reppe S, Stilgren L, Abrahamsen B, et al.	Abnormal muscle and hematopoietic gene expression may be important for clinical morbidity in primary hyperparathyroidism.	－	－	Am J Physiol Endocrinol Metab. 2007;292(5):E1465-1473.
5.4-273-009	－	Lupp A, Klenk C, Röcken C, et al.	Immunohistochemical identification of the PTHR1 parathyroid hormone receptor in normal and neoplastic human tissues.	－	－	Eur J Endocrinol. 2010;162(5):979-986.
5.4-273-010	－	Cheloha RW, Gellman SH, Vilardaga JP, et al.	PTH receptor-1 signalling-mechanistic insights and therapeutic prospects.	－	－	Nat Rev Endocrinol. 2015;11(12):712-724.
5.4-273-011	－	Brandi ML, Bilezikian JP, Shoback D, et al.	Management of Hypoparathyroidism: Summary Statement and Guidelines.	－	－	J Clin Endocrinol Metab. 2016;101(6):2273-2283.
5.4-273-012	－	Clarke BL, Brown EM, Collins MT, et al.	Epidemiology and Diagnosis of Hypoparathyroidism.	－	－	J Clin Endocrinol Metab. 2016;101(6):2284-2299.

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5.4-273-013	－	Mannstadt M, Clarke BL, Vokes T, et al.	Efficacy and safety of recombinant human parathyroid hormone (1-84) in hypoparathyroidism (Replace): a double-blind, placebo-controlled, randomised, phase 3 study.	－	－	Lancet Diabetes Endocrinol. 2013;1(4):275-283.
5.4-273-014	－	Shoback DM, Bilezikian JP, Costa AG, et al.	Presentation of Hypoparathyroidism: Etiologies and Clinical Features.	－	－	J Clin Endocrinol Metab. 2016;101(6):2300-2312.
5.4-273-015	－	Astor MC, Løvås K, Debowska A, et al.	Epidemiology and Health-Related Quality of Life in Hypoparathyroidism in Norway.	－	－	J Clin Endocrinol Metab. 2016;101(8):3045-3053.
5.4-273-016	－	Cianferotti L, Parri S, Gronchi G, et al.	Prevalence of Chronic Hypoparathyroidism in a Mediterranean Region as Estimated by the Analysis of Anonymous Healthcare Database.	－	－	Calcif Tissue Int. 2018;103(2):144-150.
5.4-273-017	－	Clarke BL, Leibson C, Emerson J, et al.	Co-morbid-medical conditions associated with prevalent hypoparathyroidism: a population-based study.	－	－	Journal of Bone and Mineral Research. 2011;S182:26 (Abstract SA1070).
5.4-273-018	－	Powers J, Joy K, Ruscio A, et al.	Prevalence and incidence of hypoparathyroidism in the United States using a large claims database.	－	－	J Bone Miner Res. 2013;28(12):2570-2576.
5.4-273-019	－	Underbjerg L, Sikjaer T,	Cardiovascular and renal complications to postsurgical hypoparathyroidism: a Danish nationwide controlled historic follow-up study.	－	－	J Bone Miner Res. 2013;28(11):2277-2285.

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		Mosekilde L, et al.				
5.4-273-020	－	Underbjerg L, Sikjaer T, Mosekilde L, et al.	The Epidemiology of Nonsurgical Hypoparathyroidism in Denmark: A Nationwide Case Finding Study.	－	－	J Bone Miner Res. 2015;30(9):1738-1744.
5.4-273-021	－	Vadiveloo T, Donnan PT, Leese GP.	A Population-Based Study of the Epidemiology of Chronic Hypoparathyroidism.	－	－	J Bone Miner Res. 2018;33(3):478-485.
5.4-273-022	－	Yoshimasa S, Tsuneo I, Makato K, et al.	Prevalence of postsurgical hypoparathyroidism in Japan: Estimated from the data of multiple institutes.	－	－	J JAES JSTS. 2017;34(1):51-56.
5.4-273-023	－	Takatani R, Kubota T, Minagawa M, et al.	Prevalence of Pseudohypoparathyroidism and Nonsurgical Hypoparathyroidism in Japan in 2017: A Nationwide Survey.	－	－	J Epidemiol. 2023;33(11):569-573.
5.4-273-024	－	Dolores Shoback DM.	Clinical practice. Hypoparathyroidism.	－	－	N Engl J Med. 2008;359(4):391-403.
5.4-273-025	－	Almquist M, Ivarsson K, Nordenström E, et al.	Mortality in patients with permanent hypoparathyroidism after total thyroidectomy.	－	－	Br J Surg. 2018;105(10):1313-1318.

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5.4-273-026	－	Mannstadt M, Bilezikian JP, Thakker RV, et al.	Hypoparathyroidism.	－	－	Nat Rev Dis Primers. 2017;3:17080.
5.4-273-027	－	Büttner M, Musholt TJ, Singer S.	Quality of life in patients with hypoparathyroidism receiving standard treatment: a systematic review.	－	－	Endocrine. 2017;58(1):14-20.
5.4-273-028	－	Mitchell DM, Regan S, Cooley MR, et al.	Long-Term Follow-Up of Patients with Hypoparathyroidism.	－	－	J Clin Endocrinol Metab. 2012;97(12):4507-4514.
5.4-273-029	－	Bilezikian JP, Cusano NE, Khan AA, et al.	Primary hyperparathyroidism.	－	－	Nat Rev Dis Primers. 2016;2:16033.
5.4-273-030	－	Abate EG, Clarke BL.	Review of Hypoparathyroidism.	－	－	Front Endocrinol (Lausanne). 2017;7:172.
5.4-273-031	－	Takeda Statement, 04 October 2022.	Takeda to Discontinue Manufacturing of NATPAR® / NATPARA® for Patients with Hypoparathyroidism at the End of 2024	－	－	https://www.takeda.com/en-us/newsroom/statements/2022/takeda-to-discontinue-manufacturing-of-natpar-natpara/

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5.4-273-032	－	Winer KK, Yanovski JA, Sarani B, et al.	A randomized, cross-over trial of once-daily versus twice-daily parathyroid hormone 1-34 in treatment of hypoparathyroidism.	－	－	J Clin Endocrinol Metab. 1998;83(10):3480-3486.
5.4-273-033	－	Winer KK, Sinaii N, Peterson D, et al.	Effects of once versus twice-daily parathyroid hormone 1-34 therapy in children with hypoparathyroidism.	－	－	J Clin Endocrinol Metab. 2008;93(9):3389-3395.
5.4-273-034	－	Winer KK, Zhang B, Shrader JA, et al.	Synthetic human parathyroid hormone 1-34 replacement therapy: a randomized crossover trial comparing pump versus injections in the treatment of chronic hypoparathyroidism.	－	－	J Clin Endocrinol Metab. 2012;97(2):391-399.
5.4-273-035	－	Winer KK, Kelly A, Johns A, et al.	Long-Term Parathyroid Hormone 1-34 Replacement Therapy in Children with Hypoparathyroidism.	－	－	J Pediatr. 2018;203:391-399.
5.4-273-036	－	A Iida-Klein, S Shou Lu, R Kapadia, et al.	Short-term continuous infusion of human parathyroid hormone 1-34 fragment is catabolic with decreased trabecular connectivity density accompanied by hypercalcemia in C57BL/J6 mice.	－	－	J Endocrinol. 2005;186(3):549-557.
5.4-273-037	－	Takasu H, Bringhurst FR.	Type-1 parathyroid hormone (PTH)/PTH-related peptide (PTHrP) receptors activate phospholipase C in response to carboxyl-truncated analogs of PTH(1-34).	－	－	Endocrinology. 1998;139(10):4293-4299.

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5.4-273-038	－	Morley P, Whitfield JF, Willick GE.	Design and applications of parathyroid hormone analogues.	－	－	Curr Med Chem. 1999;6(11):1095-1106.
5.4-273-039	－	Habener JF, Rosenblatt M, Potts JT Jr.	Parathyroid hormone: biochemical aspects of biosynthesis, secretion, action, and metabolism.	－	－	Physiol Rev. 1984;64(3):985-1053.
5.4-273-040	－	Lee C, Luck MD, Jüppner H, et al.	Homolog-scanning mutagenesis of the parathyroid hormone (PTH) receptor reveals PTH-(1-34) binding determinants in the third extracellular loop.	－	－	Mol Endocrinol. 1995;9(10):1269-1278.
5.4-273-041	－	Drechsler N, Fröbel J, Jahreis G, et al.	Binding specificity of the ectodomain of the parathyroid hormone receptor.	－	－	Biophys Chem. 2011;154(2-3):66-72.
5.4-273-042	－	Bilezikian JP, Khan A, Potts Jr. JT, et al.	Hypoparathyroidism in the adult: epidemiology, diagnosis, pathophysiology, target-organ involvement, treatment, and challenges for future research.	－	－	J Bone Miner Res. 2011;26(10):2317-2337.
5.4-273-043	－	[redacted]	Central Laboratory Services Manual (Reference Ranges).	－	－	V. 6.0.0.20[redacted].
5.4-273-044	－	[redacted]	Charter for Independent Imaging Assessment, Dual-energy X-ray Absorptiometry(DXA). 20[redacted].	－	－	
5.4-273-045	－	Gosmanova EO, Houillier P,	Renal complications in patients with chronic hypoparathyroidism on conventional therapy : a	－	－	Rev Endocr Metab Disord. 2021;22(2):297-316.

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		Rejnmark L, et al.	systematic literature review : renal disease in chronic hypoparathyroidism.			
5.4-273-046	－	Rejnmark L, Gosmanova EO, Khan AA, et al.	Palopegteriparatide treatment improves renal function in adults with chronic hypoparathyroidism: 1-year results from the Phase 3 PaTHway Trial.	－	－	Adv Ther. 2024 Jun;41(6):2500-2518.
5.4-273-047	－	Clarke J, Hurst C, Martin P, et al.	Duration of chronic toxicity studies for biotechnology-derived pharmaceuticals: is 6 months still appropriate?	－	－	Regul Toxicol Pharmacol. 2008;50(1):2-22.
5.4-273-048	－	Parfitt AM.	Misconceptions (2): turnover is always higher in cancellous than in cortical bone.	－	－	Bone. 2002;30(6):807-809.
5.4-273-049	－	McKiernan FE, Berg RL, Linneman JG.	The utility of BMD Z-score diagnostic thresholds for secondary causes of osteoporosis.	－	－	Osteoporos Int. 2011;22(4):1069-1077.
5.4-273-050	－	Shuhart CR, Yeap SS, Anderson PA, et al.	Executive Summary of the 2019 ISCD Position Development Conference on Monitoring Treatment, DXA Cross-calibration and Least Significant Change, Spinal Cord Injury, Peri-prosthetic and Orthopedic Bone Health, Transgender Medicine, and Pediatrics.	－	－	J Clin Densitom. 2019;22(4):453-471.
5.4-274-001	－	Clarke BL, Brown EM,	Epidemiology and diagnosis of hypoparathyroidism.	－	－	J Clin Endocrinol Metab. 2016;101(6):2284-2299.

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		Collins MT, et al.				
5.4-274-002	－	Powers J, Joy K, Ruscio A, et al.	Prevalence and incidence of hypoparathyroidism in the United States using a large claims database.	－	－	J Bone Miner Res. 2013;28(12):2570-2576.
5.4-274-003	－	Vadiveloo T, Donnan PT, Leese GP.	A population-based study of the epidemiology of chronic hypoparathyroidism.	－	－	J Bone Miner Res. 2018;33(3):478-485.
5.4-274-004	－	Mannstadt M, Clarke BL, Vokes T, et al.	Efficacy and safety of recombinant human parathyroid hormone (1-84) in hypoparathyroidism (REPLACE): a double-blind, placebo-controlled, randomised, phase 3 study.	－	－	Lancet Diabetes Endocrinol. 2013;1(4):275-283.
5.4-274-005	－	Bilezikian JP, Khan A, Potts JT Jr, et al.	Hypoparathyroidism in the adult: epidemiology, diagnosis, pathophysiology, target organ involvement, treatment, and challenges for future research.	－	－	J Bone Miner Res. 2011;26(10):2317-2337.
5.4-274-006	－	Shoback D.	Clinical practice. Hypoparathyroidism.	－	－	N Engl J Med. 2008;359(4):391-403.
5.4-274-007	－	Zuckerman JM, Assimos DG.	Hypocitraturia: pathophysiology and medical management.	－	－	Rev Urol. 2009;11(3):134-144.
5.4-274-008	－	Natpara USPI (recent major change 2018,		－	－	https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125511s020lbl.pdf

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		accessed 30 Aug 2024).				
5.4-274-009	―	Forteo USPI (recent major change 2020, accessed 30 Aug 2024).		―	―	https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/021318s054lbl.pdf
5.4-274-010	―	Forsteo EPAR	Scientific Discussion. 2005.	―	―	https://www.ema.europa.eu/en/documents/scientific-discussion/forsteo-epar-scientific-discussion_en.pdf
5.4-274-011	―	Natpar EPAR	Public Assessment Report, 2017. Accessed 30 Aug 2024.	―	―	https://www.ema.europa.eu/en/documents/assessment-report/natpar-epar-public-assessment-report_en.pdf
5.4-274-012	―	Jerome CP, Burr DB, Van Bibber T, et al.	Treatment with human parathyroid hormone (1-34) for 18 months increases cancellous bone volume and improves trabecular architecture in ovariectomized cynomolgus monkeys (Macaca fascicularis).	―	―	Bone. 2001;28(2):150-159.

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5.4-274-013	－	Jimenez C, Yang Y, Kim HW, et al.	Primary hyperparathyroidism and osteosarcoma: examination of a large cohort identifies three cases of fibroblastic osteosarcoma.	－	－	J Bone Miner Res. 2005;20(9):1562-1568.
5.4-274-014	－	Cinamon U, Turcotte RE.	Primary Hyperparathyroidism and malignancy: “Studies by nature”.	－	－	Bone. 2006;39(2):420-423.
5.4-274-015	－	Fox J, Miller MA, Newman MK, et al.	Treatment of skeletally mature ovariectomized rhesus monkeys with PTH(1-84) for 16 months increases bone formation and density and improves trabecular architecture and biomechanical properties at the lumbar spine.	－	－	J Bone Miner Res. 2007;22(2):260-273.
5.4-274-016	－	Vahle JL, Zuehlke U, Schmidt A, et al.	Lack of bone neoplasms and persistence of bone efficacy in cynomolgus macaques after long-term treatment with teriparatide [rhPTH(1-34)].	－	－	J Bone Miner Res. 2008;23(12): 2033-2039.
5.4-274-017	－	Andrews EB, Gilsenan AW, Midkiff K, et al.	The US postmarketing surveillance study of adult osteosarcoma and teriparatide: study design and findings from the first 7 years.	－	－	J Bone Miner Res. 2012;27(12):2429-2437.
5.4-274-018	－	Cipriani C, Irani D, Bilezikian JP.	Safety of osteoanabolic therapy: a decade of experience.	－	－	J Bone Miner Res. 2012;27(12):2419-2428.
5.4-274-019	－	Nishikawa A, Yoshiki F, Taketsuna M, et al.	Safety and effectiveness of daily teriparatide for osteoporosis in patients with severe stages of chronic kidney disease: post hoc analysis of a postmarketing observational study.	－	－	Clin Interv Aging. 2016;11:1653-1659.

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5.4-274-020	－	Gilsenan A, Harding A, Kellier-Steele N, et al.	The Forteo Patient Registry linkage to multiple state cancer registries: study design and results from the first 8 years.	－	－	Osteoporos Int. 2018;29(10):2335-2343.
5.4-274-021	－	Gilsenan A, Harris D, Reynolds M, et al.	Long-Term Cancer Surveillance: Results from the Forteo Patient Registry Surveillance Study.	－	－	Osteoporos Int. 2021a;32:645-651.
5.4-274-022	－	Gilsenan A, Midkiff K, Harris D, et al.	Teriparatide did not Increase Adult Osteosarcoma Incidence in a 15-Year US Postmarketing Surveillance Study.	－	－	J Bone Miner Res. 2021b;36(2):244-251.
5.4-274-023	－		Forteo Patient Registry. Accessed 30 Aug 2024.	－	－	https://www.rtihs.org/publications/long-term-cancer-surveillance-five-year-update-forteo-patient-registry-surveillance
5.4-274-024	－	Stidl R, Denne M, Goldstine J, et al.	Polyethylene Glycol Exposure with Antihemophilic Factor (Recombinant), PEGylated (rurioctocog alfa pegol) and Other Therapies Indicated for the Pediatric Population: History and Safety.	－	－	Pharmaceuticals (Basel). 2018;11(3).

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5.4-274-025	－	Webster R, Didier E, Harris P, et al.	PEGylated proteins: evaluation of their safety in the absence of definitive metabolism studies.	－	－	Drug Metab Dispos. 2007;35(1):9-16.
5.4-274-026	－		CHMP Safety Working Party's response to the PDCO regarding the use of PEGylated drug products in the paediatric population. 2012. 16 November 2012.	－	－	EMA/CHMP/SWP/647258/2012.
5.4-274-027	－	Ivens IA, Achanzar W, Baumann A, et al.	PEGylated biopharmaceuticals: current experience and considerations for nonclinical development.	－	－	Toxicol Pathol. 2015;43(7):959-983.
5.4-274-028	－	Forsteo SmPC (latest renewal 2013, accessed 30 Aug 2024).		－	－	https://www.ema.europa.eu/en/documents/product-information/forsteo-epar-product-information_en.pdf
5.4-274-029	－	Natpar SmPC (latest renewal 2022, accessed 30 Aug 2024).		－	－	https://www.ema.europa.eu/en/documents/product-information/natpar-epar-product-information_en.pdf

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5.4-276-001	－	Winer KK, Yanovski JA, Cutler GB Jr.	Synthetic human parathyroid hormone 1-34 vs calcitriol and calcium in the treatment of hypoparathyroidism.	－	－	JAMA. 1996;276(8):631-636.
5.4-276-002	－	－	Briefing Document, BLA #125511 Natpara. 2014.	－	－	
5.4-276-003	－	－	BLA #125511, Natpara. Center for Drug Evaluation and Research, Food & Drug Administration. 2015.	－	－	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/125511Orig1s000AdminCorres.pdf.
5.4-276-004	－	Khurana M, Zadezensky I, Lowy N, et al.	Use of a systems pharmacology model based approach toward dose optimization of Parathyroid hormone therapy in hypoparathyroidism.	－	－	Clinical Pharmacology & Ther. 2018.
5.4-276-005	－	Shirado O, Doi T, Akai M, et al.	An outcome measure for Japanese people with chronic low back pain: an introduction and validation study of Japan Low Back Pain Evaluation Questionnaire.	－	－	Spine (Phila Pa 1976). 2007;32(26):3052-9.
5.4-276-006	－	Herdman M.	Using Patient Reported Outcome measures in a cross-cultural context: conceptual and linguistic issues.	－	－	ISPOR 2023.