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(54) Title **ALPHA-V BETA-6 INTEGRIN LIGANDS AND USES THEREOF**

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Patentkrav

1. $\alpha\beta 6$ -integrinligand omfattende:

5 $RG^1DLXaa^1Xaa^2L-Xaa^3Xaa^4L-R^1$ (SEQ ID NO: 96) (formel VIII)

hvor

R er L-arginin;

10 G^1 er L-glysin eller N-metylglysin;

D er L-asparaginsyre (L-aspartat);

L er L-leucin;

Xaa^1 er L-alanin;

Xaa^2 er L- α -aminosmørsyre (Abu);

15 Xaa^3 er citrullin (Cit);

Xaa^4 er aminoisosmørsyre (Aib); og

R^1 er valgfri og inkluderer PEG og/eller en koblingsgruppe hvis den er til stede.

20 2. $\alpha\beta 6$ -integrinliganden ifølge krav 1, hvor R^1 omfatter et polyetylenglykol som har 2–20 etylenoksidenheter.

3. $\alpha\beta 6$ -integrinliganden ifølge krav 1 eller krav 2, hvor $\alpha\beta 6$ -integrinliganden omfatter en aminendehette.

25 4. $\alpha\beta 6$ -integrinliganden ifølge et hvilket som helst av kravene 1 til 3, hvor aminendehetten er valgt fra gruppen som består av: CH_3CO , CH_3CH_2CO , $CH_3(CH_2)_2CO$, $(CH_3)_2CHCO$, $CH_3(CH_2)_3CO$, $(CH_3)_2CHCH_2CO$, $CH_3CH_2CH(CH_3)CO$, $(CH_3)_3CCO$, $CH_3(CH_2)_4CO$, CH_3SO_2 , $CH_3CH_2SO_2$, $CH_3(CH_2)_2SO_2$, $(CH_3)_2CHSO_2$, $CH_3(CH_2)_3SO_2$, $(CH_3)_2CHCH_2SO_2$, $CH_3CH_2CH(CH_3)SO_2$, $(CH_3)_3CSO_2$, $PhCO$, $PhSO_2$,
30 alkylgruppe som har 1, 2, 3, 4, 5, 6, 7, 8, 9 eller 10 karbonatomer, metyl, etyl, propyl, butyl, pentyl, NH_2NH , PEG, guanidinyll, $CH_3OCH_2CH_2OCH_2CH_2CO$, $CH_3O(CH_2CH_2O)_2CH_2CH_2CO$, $CH_3O(CH_2CH_2O)_3CH_2CH_2CO$,

- $\text{CH}_3\text{O}(\text{CH}_2\text{CH}_2\text{O})_4\text{CH}_2\text{CH}_2\text{CO}$, $\text{CH}_3\text{O}(\text{CH}_2\text{CH}_2\text{O})_5\text{CH}_2\text{CH}_2\text{CO}$,
 $\text{CH}_3\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CO}$, $\text{CH}_3\text{O}(\text{CH}_2\text{CH}_2\text{O})_2\text{CH}_2\text{CO}$, $\text{CH}_3\text{O}(\text{CH}_2\text{CH}_2\text{O})_3\text{CH}_2\text{CO}$,
 $\text{CH}_3\text{O}(\text{CH}_2\text{CH}_2\text{O})_4\text{CH}_2\text{CO}$, $\text{CH}_3\text{O}(\text{CH}_2\text{CH}_2\text{O})_5\text{CH}_2\text{CO}$, $\text{CH}_3\text{OCH}_2\text{CH}_2\text{OCO}$,
 $\text{CH}_3\text{O}(\text{CH}_2\text{CH}_2\text{O})_2\text{CO}$, $\text{CH}_3\text{O}(\text{CH}_2\text{CH}_2\text{O})_3\text{CO}$, $\text{CH}_3\text{O}(\text{CH}_2\text{CH}_2\text{O})_4\text{CO}$,
5 $\text{CH}_3\text{O}(\text{CH}_2\text{CH}_2\text{O})_5\text{CO}$, $\text{HOCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{CO}$, $\text{HO}(\text{CH}_2\text{CH}_2\text{O})_2\text{CH}_2\text{CH}_2\text{CO}$,
 $\text{HO}(\text{CH}_2\text{CH}_2\text{O})_3\text{CH}_2\text{CH}_2\text{CO}$, $\text{HO}(\text{CH}_2\text{CH}_2\text{O})_4\text{CH}_2\text{CH}_2\text{CO}$,
 $\text{HO}(\text{CH}_2\text{CH}_2\text{O})_5\text{CH}_2\text{CH}_2\text{CO}$, $\text{HOCH}_2\text{CH}_2\text{OCH}_2\text{CO}$, $\text{HO}(\text{CH}_2\text{CH}_2\text{O})_2\text{CH}_2\text{CO}$,
 $\text{HO}(\text{CH}_2\text{CH}_2\text{O})_3\text{CH}_2\text{CO}$, $\text{HO}(\text{CH}_2\text{CH}_2\text{O})_4\text{CH}_2\text{CO}$, $\text{HO}(\text{CH}_2\text{CH}_2\text{O})_5\text{CH}_2\text{CO}$,
 $\text{HOCH}_2\text{CH}_2\text{OCO}$, $\text{HO}(\text{CH}_2\text{CH}_2\text{O})_2\text{CO}$, $\text{HO}(\text{CH}_2\text{CH}_2\text{O})_3\text{CO}$, $\text{HO}(\text{CH}_2\text{CH}_2\text{O})_4\text{CO}$,
10 $\text{HO}(\text{CH}_2\text{CH}_2\text{O})_5\text{CO}$, $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{CO}$,
 $\text{CH}_3\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_2\text{CH}_2\text{CH}_2\text{CO}$, $\text{CH}_3\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_3\text{CH}_2\text{CH}_2\text{CO}$,
 $\text{CH}_3\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_4\text{CH}_2\text{CH}_2\text{CO}$, $\text{CH}_3\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_5\text{CH}_2\text{CH}_2\text{CO}$,
 $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CO}$, $\text{CH}_3\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_2\text{CH}_2\text{CO}$,
 $\text{CH}_3\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_3\text{CH}_2\text{CO}$, $\text{CH}_3\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_4\text{CH}_2\text{CO}$,
15 $\text{CH}_3\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_5\text{CH}_2\text{CO}$, $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCO}$, $\text{CH}_3\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_2\text{CO}$,
 $\text{CH}_3\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_3\text{CO}$, $\text{CH}_3\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_4\text{CO}$, $\text{CH}_3\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_5\text{CO}$,
 $\text{CH}_3\text{OCH}_2\text{CH}_2\text{CO}$, $\text{HOCH}_2\text{CH}_2\text{CO}$ eller $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_2\text{CO}$.

5. $\alpha\beta 6$ -integrinliganden ifølge krav 4, hvori aminendehetten er CH_3CO .
 20
 6. $\alpha\beta 6$ -integrinliganden ifølge krav 1, hvori $\alpha\beta 6$ -integrinliganden omfatter sekvensen ifølge SEQ ID NO: 4 (Ac-RGDLAAbuLCitAibL).
 7. $\alpha\beta 6$ -integrinliganden ifølge et hvilket som helst av kravene 1 til 6, hvori $\alpha\beta 6$ -
 25 integrinliganden også konjugeres til et lastmolekyl.
 8. $\alpha\beta 6$ -integrinliganden ifølge et hvilket som helst av kravene 1 til 7, hvori $\alpha\beta 6$ -
 integrinliganden konjugeres til et lastmolekyl som omfatter et lite molekyl, et antistoff, et antistofffragment, et immunglobulin, et monoklonalt antistoff, en etikett eller markør,
 30 et lipid, en naturlig eller modifisert nukleinsyre eller polynukleotid, et peptid, en aptamer, en polymer, et polyamin, et protein, et toksin, et vitamin, et polyetylenglykol,

et haptent, et digoksin, et biotin, et radioaktivt atom eller molekyl, eller en fluorofor.

5 **9.** $\alpha\beta6$ -integrinliganden ifølge et hvilket som helst av kravene 1 til 8, hvori $\alpha\beta6$ -integrinliganden konjugeres til et lastmolekyl som omfatter en aktiv farmasøytisk ingrediens.

10. $\alpha\beta6$ -integrinliganden ifølge et hvilket som helst av kravene 1 til 9, hvori $\alpha\beta6$ -integrinliganden konjugeres til et lastmolekyl som omfatter en oligomerforbindelse.

10 **11.** $\alpha\beta6$ -integrinliganden ifølge krav 10, hvori oligomerforbindelsen er et RNAi-middel.

12. Sammensetning omfattende $\alpha\beta6$ -integrinliganden ifølge et hvilket som helst av kravene 1 til 11, og en farmasøytisk akseptabel eksipiens.

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