Claims

1. Use of a long-acting growth hormone or a pharmaceutical formulation comprising such long-acting growth hormone in the preparation of a medicament for reducing the percentage of non-responders in a patient population suffering from growth hormone deficiency.

2. The use of claim 1, wherein the percentage of non-responders is reduced to less than 10%.

3. Use of a long-acting growth hormone or a pharmaceutical formulation comprising such long-acting growth hormone in the preparation of a medicament for the treatment of growth hormone deficiency, wherein said treatment increases IGF-1 levels in plasma by a standard deviation score of at least 0.2 more than the equivalent dose of daily hGH.

4. The use of claim 3, wherein the increase is at least 0.3 SDS.

5. Use of a long-acting growth hormone or a pharmaceutical formulation comprising such long-acting growth hormone in the preparation of a medicament for increasing the percentage of responders in a patient population suffering from growth hormone deficiency.

6. The use of claim 5, wherein the percentage of responders is increased to at least 90%.

7. Use of a long-acting growth hormone or a pharmaceutical formulation comprising the long-acting growth hormone in the preparation of a medicament for the treatment of growth hormone deficiency, wherein said long-acting growth hormone or the pharmaceutical formulation is to be administered in a dose of 0.24 mg/kg/week growth hormone or growth hormone equivalents and administration of said long-acting growth hormone pharmaceutical composition comprising said long-acting growth hormone leads to superior efficacy compared to administration of a dose of 0.24 mg/kg/week of a daily somatropin.

8. The use of claim 7, wherein the superior efficacy is measured as annualized height velocity.

9. The use of any one of claims 1 to 8, wherein the growth hormone deficiency is growth hormone deficiency in children.

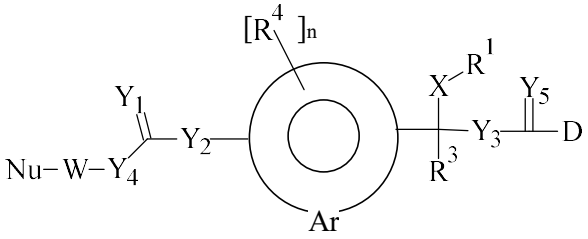
10. The use of any one of claims 1 to 9, wherein the long-acting growth hormone is to be administered no more than once per week.

11. The use of any one of claims 1 to 10, wherein the time between two consecutive administrations is 1 week.

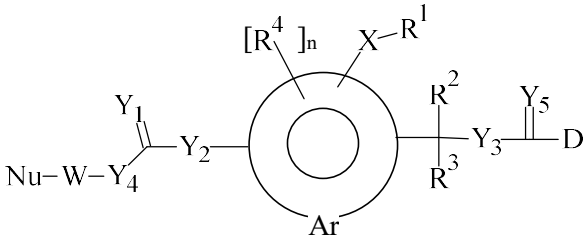
12. The use of any one of claims 1 to 11, wherein the pharmaceutical formulation is a dry formulation.

13. The use of any one of claims 1 to 11, wherein the pharmaceutical formulation is a liquid formulation.

14. The use of any one of claims 1 to 13, wherein the long-acting growth hormone is of formula (Ia) or (Ib)



(Ia),



(Ib),

wherein

-D is a hGH moiety connected to the rest of the molecule through an amine functional group;

n is 0, 1, 2, 3, or 4;

-X- is a chemical bond or a spacer;

$=Y_1$, $=Y_5$ are selected independently from the group consisting of =O and =S;

$-Y_2-$, $-Y_3-$ are selected from the group consisting of -O- and -S-;

$-Y_4-$ is selected from the group consisting of -O-, $-NR^5-$ and $-C(R^6R^{6a})-$;

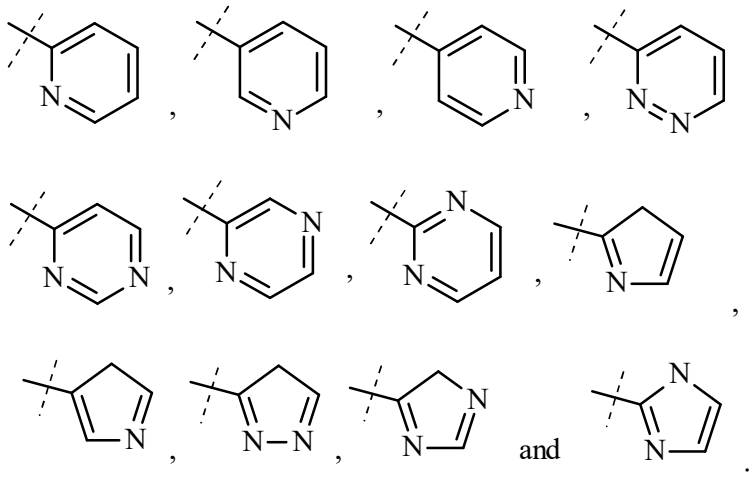
$-R^1$ is a carrier, preferably a water-soluble PEG-based moiety comprising at least 40% PEG;

$-R^2$, $-R^3$, $-R^5$, $-R^6$, $-R^{6a}$ are independently of each other selected from the group consisting of -H, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, 2-methylbutyl, 2,2-dimethylpropyl, n-hexyl, 2-methylpentyl, 3-methylpentyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl and 3,3-dimethylpropyl;

$-R^4$ is selected from the group consisting of methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, 2-methylbutyl, 2,2-dimethylpropyl, n-hexyl, 2-methylpentyl, 3-methylpentyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl and 3,3-dimethylpropyl;

-W- is selected from the group consisting of C_{1-20} alkyl optionally interrupted by one or more groups selected from the group consisting of C_{3-10} cycloalkyl, 8- to 30-membered carbopolycyclyl, 3- to 10-membered heterocyclyl, $-C(O)-$, $-C(O)N(R^7)-$, -O-, -S- and $-N(R^7)-$;

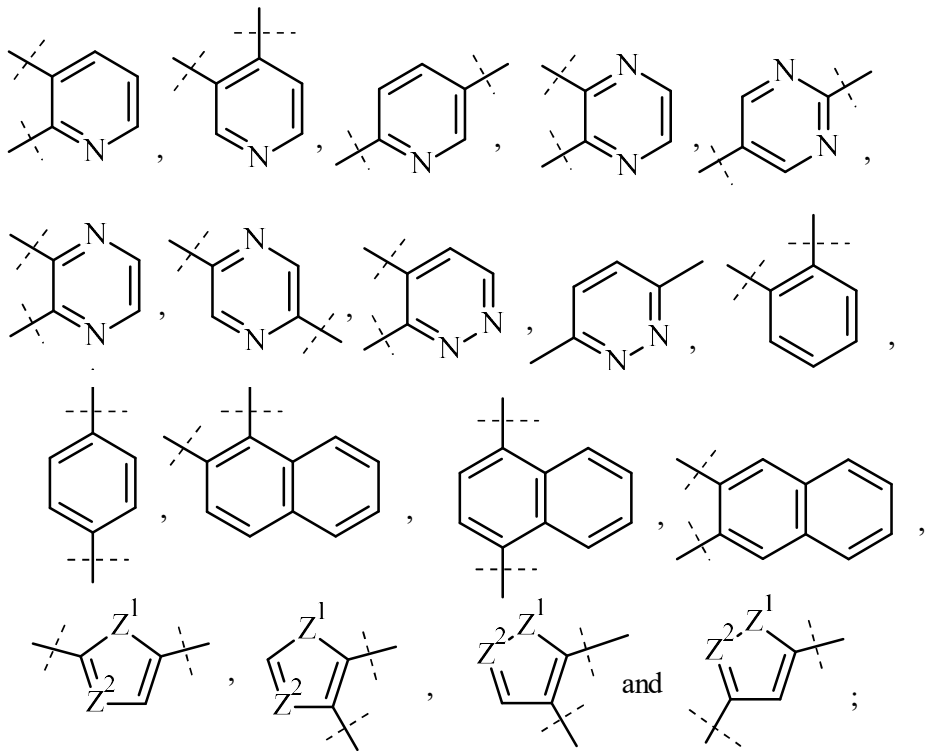
-Nu is a nucleophile selected from the group consisting of $-N(R^7R^{7a})$, $-N(R^7OH)$, $-N(R^7)-N(R^{7a}R^{7b})$, $-S(R^7)$, -COOH,



and

;

-Ar- is selected from the group consisting of



wherein

dashed lines indicate attachment to the rest of the prodrug,

$-Z^1-$ is selected from the group consisting of -O-, -S- and $-N(R^7)-$, and

$-Z^2-$ is $-N(R^7)-$; and

$-R^7$, $-R^{7a}$, $-R^{7b}$ are independently of each other selected from the group consisting of -H, C_{1-6} alkyl, C_{2-6} alkenyl and C_{2-6} alkynyl;

wherein the prodrug of formula (Ia) and (Ib) is optionally further substituted.

15. The use of any one of claims 1 to 14, wherein the long-acting growth hormone is ACP-011.

16. The use of any one of claims 1 to 14, wherein the long-acting growth hormone is somapacitan.