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| **0-1** | **Form PCT/RO/134 (SAFE) Indications Relating to Deposited Microorganism(s) or Other Biological Material (PCT Rule 13bis)** | |
| 0-1-1 | Prepared Using | PCT Online Filing Version 3.5.000.221 MT/FOP 20020701/0.20.5.9 |
| **0-2** | **International Application No.** | |
| **0-3** | **Applicant's or agent's file reference** | 148122aa/ans |

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| **1** | **The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:** | |
| **1-1** | **Paragraph number** | 14 |
| **1-3** | **Identification of deposit** | |
| 1-3-1 | Name of depositary institution | DSMZ DSMZ-Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH |
| 1-3-2 | Address of depositary institution | Inhoffenstr. 7B, D-38124 Braunschweig, Germany |
| 1-3-3 | Date of deposit | 01 April 2010 (01.04.2010) |
| 1-3-4 | Accession Number | DSMZ ACC3054 |
| **1-5** | **Designated States for Which Indications are Made** | All designations |

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| **0-4** | **This form was received with the international application:** (yes or no) | yes |
| 0-4-1 | Authorized officer | T. Bröcker-Tazelaar |

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| **0-5** | **This form was received by the international Bureau on:** | |
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International Application PCT/EP2011/055253
Fundacio Privada Institut d'Investigacio
Oncologica Vall D'Hebron (VHIO)

Our Ref.: 148 122 n17/ehf
June 2012

**CLAIMS**

1. A monoclonal antibody or a fragment thereof, which recognizes full length human LIF, but does not recognize a LIF fragment corresponding to amino acids 1 to 160.
2. The monoclonal antibody of claim 1 wherein said antibody recognizes an epitope of human LIF comprised in the region corresponding to amino acids 160 to 202 of human LIF.
3. The monoclonal antibody of claim 1 wherein said antibody recognizes an epitope comprised in the regions selected from the following: a region corresponding to amino acids 160 to 180, a region corresponding to amino acids 170 to 190, a region corresponding to amino acids 180 to 200, a region corresponding to amino acids 182 to 202 of human LIF.
4. The monoclonal antibody according to any one of the preceding claims wherein the antibody is competitively inhibited in its binding to human LIF by the monoclonal antibody produced by a hybridoma deposited on April 1st 2010 by Vall d'Hebron Institute of Oncology at the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM ACC3054).
5. The monoclonal antibody according to any one of the preceding claims of the IgG1 isotype.
6. The antibody of any one of the preceding claims, wherein the antibody is a humanized antibody.
7. The monoclonal antibody according to any of claims 1 to 5, which is produced by the hybridoma cell line DSM ACC3054, deposited on April 1st 2010 by Vall d'Hebron Institute of Oncology at the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH.
8. The hybridoma cell line DSM ACC3054, deposited on April 1st 2010 by Vall d'Hebron Institute of Oncology at the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH.
9. The antibody or fragment thereof according to any of claims 1 to 7 for treatment of a cancer, wherein the cancer is characterized by
   (a) high LIF levels; or
   (b) a cell population expressing high levels of CD44 and

Id1.

10. The monoclonal antibody or fragment thereof for the use according to claim 9, wherein said antibody or fragment thereof acts through the inhibition of the self-regeneration of tumor stem cells.

11. The antibody or fragment thereof for the use according to claim 9, wherein said antibody or fragment thereof is capable of reducing the cell population characterized by high levels of CD 44 and Id1.

12. A pharmaceutical composition comprising a therapeutically effective amount of an antibody or fragment thereof according to any one of the claims 1 to 7 together with a pharmaceutically acceptable carrier.

13. The pharmaceutical composition of claim 12 for use in a method of treating cancer, wherein the cancer is characterized by

(a) high LIF levels; or

(b) a cell population expressing high levels of CD44 and Id1.

14. A kit comprising reagents for the quantification of the expression levels of LIF for the diagnosis of a cancer in a subject or for determining the predisposition of a subject to suffer from said cancer, or for determining the stage or severity of said cancer in a subject, or for monitoring the effect of the therapy administered to a subject with said cancer, wherein, if the reagents detect an increase in the expression of the gene encoding LIF or of LIF with respect to a control sample, then said subject can suffer from said disease, or present a greater predisposition to suffer from said disease, or present a greater severity of said disease, or the administered therapy is not being effective.

15. Use of the kit of claim 14.

16. An *in vitro* method for designing a customized therapy for a patient suffering from a disease associated with increased LIF levels comprising:

(a) quantifying the expression levels of LIF in said patient, and

(b) comparing said expression levels with control levels, wherein if the expression levels of LIF in said patient are greater than the control values, then the antibody or fragment of any one of claims 1 to 7 is administered to said patient.

17. An *in vitro* method for selecting patients suffering from a cancer, to be treated with the antibody or fragment of any one of claims 1 to 7, comprising

(a) quantifying the expression levels of LIF in said patient, and

(b) comparing said expression levels with control levels, wherein if the expression levels of LIF in said patient are greater than the control values, then said patient is selected to receive treatment with said antibody or fragment thereof.

18. An *in vitro* method for the prognosis of life expectancy or of the probability of survival of subjects suffering from cancer, comprising quantification of the expression levels of LIF in a biological sample from said subject, wherein an increase of LIF expression with respect to LIF expression in a control sample, is indicative of a reduced life expectancy.

19. *In vitro* method for the diagnosis of cancer in a subject or for determining the predisposition of a subject to suffer from said cancer, or for determining the stage or severity of said cancer in a subject, or for monitoring the effect of the therapy administered to a subject suffering from said cancer, which comprises quantifying the expression levels of LIF in a biological sample from said subject, wherein an increase of the expression of the gene encoding LIF with respect to the expression of the gene encoding LIF in a control sample, is indicative of a cancer, or of greater predisposition of said subject to suffer from a cancer or of the non-response to the therapy administered to said subject.

20. The antibody or fragment thereof for the use of claim 9 or the pharmaceutical composition for use of claim 13, wherein the cancer is characterized by presenting high levels of LIF.

21. The antibody or fragment thereof for the use of claim 9 or the pharmaceutical composition for the use of claim 13, wherein the

cancer is characterized by a cell population expressing high levels of CD44 and Id1.

22. The antibody or fragment thereof for the use of claim 9 or the pharmaceutical composition for the use of claim 12, wherein the cancer is one of the following: glioma, pre-B cell acute lymphoblastic leukemia, acute myeloid leukemia, lung adenocarcinoma, prostate adenocarcinoma, colorectal carcinoma, bladder cancer, breast ductal cancer or breast carcinoma.

23. The antibody or fragment thereof or the pharmaceutical composition according to claim 22, wherein said glioma is grade IV glioma.

24. The method or kit according to any of claims 14 or 16 to 19, wherein the quantification of the levels of LIF is performed by means of Western blot, immunohistochemistry or ELISA.

25. The method or kit according to any of the claims 14 or 16 to 19 wherein the method or kit for measuring the expression levels of LIF comprises the monoclonal antibody according to claims 1 to 7 or fragment thereof.

26. The method or kit according to any of claims 14 or 17 to 19, wherein the cancer is characterized by a cell population expressing high levels of CD44 and Id1.

27. The method or kit according to any of claims 14 or 17 to 19, wherein the cancer is one of the following: glioma, pre-B cell acute lymphoblastic leukemia, acute myeloid leukemia, lung adenocarcinoma, prostate adenocarcinoma, colorectal carcinoma, bladder cancer, breast ductal cancer or breast carcinoma.

28. The method or kit of claim 27, wherein said glioma is grade IV glioma.

29. An immunoanalytical reagent used in the measurement of human LIF, which comprises the monoclonal antibody or fragment thereof according to any one of claims 1 to 7.

## CLAIMS

1. A monoclonal antibody or a fragment thereof, which binds full length human Leukemia inhibitory factor (LIF), but does not bind a LIF fragment corresponding to amino acids 1 to 160, wherein the full length human LIF is the precursor to human LIF isoform 1.

2. The monoclonal antibody of claim 1, wherein said antibody binds an epitope of human LIF comprised in the region corresponding to amino acids 160 to 202 of human LIF.

3. The monoclonal antibody of claim 1, wherein said antibody binds an epitope comprised in the regions selected from the following: a region corresponding to amino acids 160 to 180, a region corresponding to amino acids 170 to 190, a region corresponding to amino acids 180 to 200, a region corresponding to amino acids 182 to 202 of human LIF.

4. The monoclonal antibody according to claim 1, wherein the antibody is competitively inhibited in its binding to human LIF by the monoclonal antibody produced by a hybridoma deposited on Apr. 1, 2010 by Vall d'Hebron Institute of Oncology at the Deutsche Sammlung von Mikroorganismen and Zellkulturen GmbH (deposit number DSM ACC3054).

5. The monoclonal antibody according to claim 1 of the IgG 1 isotype.

6. The antibody of claim 1, wherein the antibody is a humanized antibody.

7. The monoclonal antibody according to claim 1, which is produced by the hybridoma cell line deposit number DSM ACC3054, deposited on Apr. 1, 2010 by Vall d'Hebron Institute of Oncology at the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH.

8. A pharmaceutical composition comprising a therapeutically effective amount of an antibody or fragment thereof according to claim 1 together with a pharmaceutically acceptable carrier.

9. An immunoanalytical reagent comprising the monoclonal antibody or fragment thereof according to claim 1, for the measurement of human LIF.

10. The hybridoma cell line deposit number DSM ACC3054, deposited on Apr. 1, 2010 by Vall d'Hebron Institute of Oncology at the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH.