

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

|                                                           |                                                                                                  |                                                                                  |
|-----------------------------------------------------------|--------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Applicant's or agent's file reference<br>01277-0015-00PCT | <b>FOR FURTHER ACTION</b><br>see Form PCT/ISA/220<br>as well as, where applicable, item 5 below. |                                                                                  |
| International application No.<br>PCT/US2022/074589        | International filing date ( <i>day/month/year</i> )<br>5 August 2022 (05-08-2022)                | (Earliest) Priority Date ( <i>day/month/year</i> )<br>6 August 2021 (06-08-2021) |
| Applicant<br><br>CELGENE CORPORATION                      |                                                                                                  |                                                                                  |

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 8 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed  
☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☐ **Unity of invention is lacking** (see Box No III)

4. With regard to the **title**,

- ☒ the text is approved as submitted by the applicant  
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☐ the text is approved as submitted by the applicant  
☒ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. 2  
☐ as suggested by the applicant  
☒ as selected by this Authority, because the applicant failed to suggest a figure  
☐ as selected by this Authority, because this figure better characterizes the invention  
b. ☐ none of the figures is to be published with the abstract

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### Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
  - a. ☒ forming part of the international application as filed.
  - b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13*ter*.1(a)).

☐ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.
2. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.
3. Additional comments:

## Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

The present disclosure relates to engineered polypeptides comprising degradation domains, compounds, compositions, and methods for their preparation and use as for degrading engineered proteins in cells. The degradation domain comprises the sequence FCX1X2CGX3X4, preferably FCNQCGAS. The polypeptide is preferably a CAR comprising such degradation domain or degron, and is degraded by a degradation agent. The degradation agent is a small molecule binding the degradation domain and also binding cereblon.

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|                                                                                                                                                                         |                                                                                                                                      |            |                                                                                                                                                                                                                                                   |            |                                                              |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|--------------------------------------------------------------|
| A. CLASSIFICATION OF SUBJECT MATTER                                                                                                                                     |                                                                                                                                      |            |                                                                                                                                                                                                                                                   |            |                                                              |
| INV.                                                                                                                                                                    | A61K35/17                                                                                                                            | A61P35/00  | C07D401/14                                                                                                                                                                                                                                        | C07D417/14 | C07D471/04                                                   |
|                                                                                                                                                                         | C07K14/47                                                                                                                            | C07K14/725 | C12N5/0783                                                                                                                                                                                                                                        |            |                                                              |
| ADD.                                                                                                                                                                    |                                                                                                                                      |            |                                                                                                                                                                                                                                                   |            |                                                              |
| According to International Patent Classification (IPC) or to both national classification and IPC                                                                       |                                                                                                                                      |            |                                                                                                                                                                                                                                                   |            |                                                              |
| B. FIELDS SEARCHED                                                                                                                                                      |                                                                                                                                      |            |                                                                                                                                                                                                                                                   |            |                                                              |
| Minimum documentation searched (classification system followed by classification symbols)                                                                               |                                                                                                                                      |            |                                                                                                                                                                                                                                                   |            |                                                              |
| A61K A61P C07D C07K C12N                                                                                                                                                |                                                                                                                                      |            |                                                                                                                                                                                                                                                   |            |                                                              |
| Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched                                           |                                                                                                                                      |            |                                                                                                                                                                                                                                                   |            |                                                              |
| Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)                                            |                                                                                                                                      |            |                                                                                                                                                                                                                                                   |            |                                                              |
| EPO-Internal, BIOSIS, COMPENDEX, Sequence Search, EMBASE, FSTA, INSPEC, WPI Data                                                                                        |                                                                                                                                      |            |                                                                                                                                                                                                                                                   |            |                                                              |
| C. DOCUMENTS CONSIDERED TO BE RELEVANT                                                                                                                                  |                                                                                                                                      |            |                                                                                                                                                                                                                                                   |            |                                                              |
| Category*                                                                                                                                                               | Citation of document, with indication, where appropriate, of the relevant passages                                                   |            |                                                                                                                                                                                                                                                   |            | Relevant to claim No.                                        |
| X                                                                                                                                                                       | CN 1 352 301 A (BODE GENE DEV CO LTD<br>SHANGHAI [CN]) 5 June 2002 (2002-06-05)<br><br>page 26; sequence 2<br>-----                  |            |                                                                                                                                                                                                                                                   |            | 1, 2, 7,<br>11,<br>24-32,<br>34, 35,<br>37, 59,<br>62-65, 71 |
| X                                                                                                                                                                       | CN 110 438 112 A (SUZHOU KENING POLYOL CO<br>LTD) 12 November 2019 (2019-11-12)<br>pages 13-14; claims; sequence 2<br>-----<br>--/-- |            |                                                                                                                                                                                                                                                   |            | 1, 3-5, 8,<br>24-31                                          |
| <input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.                                                                          |                                                                                                                                      |            |                                                                                                                                                                                                                                                   |            |                                                              |
| <input checked="" type="checkbox"/> See patent family annex.                                                                                                            |                                                                                                                                      |            |                                                                                                                                                                                                                                                   |            |                                                              |
| * Special categories of cited documents :                                                                                                                               |                                                                                                                                      |            |                                                                                                                                                                                                                                                   |            |                                                              |
| "A" document defining the general state of the art which is not considered to be of particular relevance                                                                |                                                                                                                                      |            | "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention                                               |            |                                                              |
| "E" earlier application or patent but published on or after the international filing date                                                                               |                                                                                                                                      |            | "X" document of particular relevance;; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone                                                                     |            |                                                              |
| "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) |                                                                                                                                      |            | "Y" document of particular relevance;; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |            |                                                              |
| "O" document referring to an oral disclosure, use, exhibition or other means                                                                                            |                                                                                                                                      |            |                                                                                                                                                                                                                                                   |            |                                                              |
| "P" document published prior to the international filing date but later than the priority date claimed                                                                  |                                                                                                                                      |            | "&" document member of the same patent family                                                                                                                                                                                                     |            |                                                              |
| Date of the actual completion of the international search                                                                                                               |                                                                                                                                      |            | Date of mailing of the international search report                                                                                                                                                                                                |            |                                                              |
| 18 November 2022                                                                                                                                                        |                                                                                                                                      |            | 07/12/2022                                                                                                                                                                                                                                        |            |                                                              |
| Name and mailing address of the ISA/<br>European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040,<br>Fax: (+31-70) 340-3016    |                                                                                                                                      |            | Authorized officer<br><br>Madruga, Jaime                                                                                                                                                                                                          |            |                                                              |

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| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                       |
|------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Category*                                            | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Relevant to claim No. |
| X                                                    | <p>DATABASE GenBank [Online]<br/> NCBI;<br/> 17 August 2008 (2008-08-17),<br/> Shoo, L.P., Rose, R., Doughty, P.,<br/> Austin, J.J. and Melville, J.:<br/> "Recombination activating protein 1,<br/> partial [Amphibolurus muricatus]",<br/> XP002808018, accession no. ACG63874.1<br/> Database accession no. ACG63874<br/> <a href="https://www.ncbi.nlm.nih.gov/protein/195984593">https://www.ncbi.nlm.nih.gov/protein/195984593</a>;<br/> sequence<br/> &amp; SHOO L P ET AL: "Diversification<br/> patterns of pebble-mimic dragons are<br/> consistent with historical disruption of<br/> important habitat corridors in arid<br/> Australia",<br/> MOLECULAR PHYLOGENETICS AND EVOLUTION,<br/> ORLANDO, FL, US,<br/> vol. 48, no. 2, 1 August 2008 (2008-08-01)<br/> , pages 528-542, XP023518614,<br/> ISSN: 1055-7903, DOI:<br/> 10.1016/J.YMPEV.2008.03.022<br/> [retrieved on 2008-03-21]<br/> -----</p> | 1-6, 11,<br>24-31     |
| X                                                    | <p>DATABASE EBI [Online]<br/> EMBL;<br/> 17 March 2020 (2020-03-17),<br/> Ra Kim S J ET AL: "Solimonas terrae AAA<br/> family ATPase",<br/> XP055982896,<br/> retrieved from EMBL accession no. NGY06094<br/> Database accession no. NGY06094<br/> abstract; sequence<br/> &amp; KIM SOO-JIN ET AL: "Solimonas terrae<br/> sp. nov., isolated from soil",<br/> INTERNATIONAL JOURNAL OF SYSTEMATIC AND<br/> EVOLUTIONARY MICROBIOLOGY,<br/> vol. 64, no. Pt_4,<br/> 1 April 2014 (2014-04-01), pages<br/> 1218-1222, XP055982886,<br/> GB<br/> ISSN: 1466-5026, DOI:<br/> 10.1099/ijs.0.055574-0<br/> -----</p>                                                                                                                                                                                                                                                                                                      | 1-5, 7-12             |
| X                                                    | <p>WO 2019/038717 A1 (NOVARTIS AG [CH];<br/> BECKWITH ROHAN ERIC JOHN [US] ET AL.)<br/> 28 February 2019 (2019-02-28)<br/> cited in the application<br/> the whole document<br/> claims;<br/> Examples;<br/> Example 8;<br/> Compound I-130, page 186<br/> -----</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 95, 96                |
|                                                      | -/--                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                       |

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| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                      |
|------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|
| Category*                                            | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Relevant to claim No.                                                |
| X                                                    | <p>WO 2019/089592 A1 (MASSACHUSETTS GEN HOSPITAL [US]; BRIGHAM &amp; WOMENS HOSPITAL [US] ET AL.) 9 May 2019 (2019-05-09)</p> <p>the whole document</p> <p>Claims</p> <p>page 58, first formula: lenalidomide;</p> <p>page 2 last para., page 4, para. 2-5;</p> <p>Tables 1-3;</p> <p>page 28, para 2, Fig, 5</p> <p>-----</p>                                                                                                                                                                                                                                                                                                                             | <p>1-11,</p> <p>13-22,</p> <p>24-71,</p> <p>82-93,</p> <p>95, 96</p> |
| X                                                    | <p>MAX JAN ET AL: "Reversible ON-and OFF-switch chimeric antigen receptors controlled by lenalidomide",</p> <p>SCI. TRANSL. MED,</p> <p>vol. 13, no. 6295,</p> <p>6 January 2021 (2021-01-06), XP055982210,</p> <p>the whole document</p> <p>Fig. 3,</p> <p>Fig. S4A,</p> <p>Fig. S4B</p> <p>-&amp; JAN MAX ET AL: "Supplementary Data: Reversible ON- and OFF-switch chimeric antigen receptors controlled by lenalidomide",</p> <p>SCIENCE TRANSLATIONAL MEDICINE,</p> <p>vol. 13, no. 575,</p> <p>6 January 2021 (2021-01-06), XP055982578,</p> <p>ISSN: 1946-6234, DOI:</p> <p>10.1126/scitranslmed.abb6295</p> <p>the whole document</p> <p>-----</p> | <p>1-11,</p> <p>13-22,</p> <p>24-71,</p> <p>82-93,</p> <p>95, 96</p> |
| X                                                    | <p>QUINLAN L. SIEVERS ET AL: "Defining the human C2H2 zinc finger degrome targeted by thalidomide analogs through CRBN",</p> <p>SCIENCE,</p> <p>vol. 362, no. 6414,</p> <p>2 November 2018 (2018-11-02), page</p> <p>eaat0572, XP055708883,</p> <p>US</p> <p>ISSN: 0036-8075, DOI:</p> <p>10.1126/science.aat0572</p> <p>the whole document</p> <p>Abstract, Results, Fig. 1, 3</p> <p>-----</p>                                                                                                                                                                                                                                                           | <p>1-11,</p> <p>13-22,</p> <p>24-71,</p> <p>82-93,</p> <p>95, 96</p> |
| A                                                    | <p>WO 2019/079569 A1 (NOVARTIS AG [CH]; BRADNER JAMES E [US])</p> <p>25 April 2019 (2019-04-25)</p> <p>the whole document</p> <p>claims; examples</p> <p>-----</p> <p style="text-align: center;">-/--</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                 | <p>1-96</p>                                                          |

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| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT |                                                                                                                                                                                                                                                                                                                                                                                                  |                       |
|------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Category*                                            | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                                                                                                               | Relevant to claim No. |
| A                                                    | WO 2020/219742 A1 (NOVARTIS AG [CH];<br>CARBONNEAU SETH [US] ET AL.)<br>29 October 2020 (2020-10-29)<br>the whole document<br>claims;<br>claim 1, page 95,<br>-----                                                                                                                                                                                                                              | 1-96                  |
| A                                                    | JAN MAX ET AL: "Cancer therapies based on<br>targeted protein degradation - lessons<br>learned with lenalidomide",<br>NATURE REVIEWS CLINICAL ONCOLOGY, NATURE,<br>NY, US,<br>vol. 18, no. 7, 2 March 2021 (2021-03-02),<br>pages 401-417, XP037488719,<br>ISSN: 1759-4774, DOI:<br>10.1038/S41571-021-00479-Z<br>[retrieved on 2021-03-02]<br>the whole document<br>Box 3;<br>figure 1<br>----- | 1-96                  |

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Information on patent family members

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| Patent document<br>cited in search report |    | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
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|                                           |    |                     | US 2021040166 A1           | 11-02-2021          |
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