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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

Published:

- with international search report (Art. 21(3))

(88) Date of publication of the international search report:

12 June 2025 (12.06.2025)

(54) Title: SYNTHESIS AND IN VITRO CHARACTERIZATION OF PROTEOLYSIS TARGETING CHIMERAS (PROTACS) FOR DEGRADATION OF DNA METHYLTRANSFERASE 1 (DNMT1)

(57) Abstract: Disclosed are bifunctional compounds (degraders) comprising a [Targeting ligand]-[Linker]-[Degron] adduct, the targeting ligand comprising a substituted pyridine compound, the bifunctional compounds targeting the epigenetic writer protein deoxyribonucleic acid methyltransferase 1, which is responsible for the maintenance of DNA methylation during cell proliferation, for degradation. Also disclosed are pharmaceutical compositions containing the compounds and methods of using the compounds to treat diseases and disorders characterized or mediated by aberrant DNMT1 activity.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2024/036042

A. CLASSIFICATION OF SUBJECT MATTER

IPC - INV. A61K 31/44; A61K 31/4427; A61K 47/18; A61K 47/54; A61P 35/00; C07D 213/73; C07D 213/74 (2024.01)

ADD.

CPC - INV. C07D 401/04; A61K 31/44; A61K 31/4427; A61K 47/18; A61K 47/545; A61P 35/00; C07D 213/73; C07D 213/74; C07D 401/02

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)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History document

Electronic database consulted during the international search (name of database and, where practicable, search terms used)

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2022/0017510 A1 (DANA-FARBER CANCER INSTITUTE, INC.) 20 January 2022; paragraphs [0009]-[0011], [0066]-[0067], [0620], [0658]	1-4, 7-10
Y	US 2019/0194166 A1 (GLAXOSMITHKLINE INTELLECTUAL PROPERTY DEVELOPMENT LIMITED, ET AL.) 27 June 2019; abstract; paragraphs [0023]-[0025], [9279], [9538], [9891]	1-10
Y	US 2023/0024096 A1 (HOFFMANN-LA ROCHE INC., ET AL.) 26 January 2023; paragraphs [0008]-[0009], [0016], [0516], [0558], [1011]	1-2, 5-6
Y	(National Center for Biotechnology Information) "2-(3,5-Dicyano-4-ethyl-6-piperidin-1-ylpyridin-2-yl)sulfanyl-2-phenylacetamide: PUBCHEM CID 132248944" Pubchem entry (online), pages 1-8, 29 January 2018; Retrieved on 21 August 2024 from the Internet: [URL: https://pubchem.ncbi.nlm.nih.gov/compound/132248944]; page 2, see 2D structure	1-2, 5-6

☐ Further documents are listed in the continuation of Box C.☐ 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

"D" document cited by the applicant in the international application

"E" earlier application or patent but published on or after the international filing date

"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)

"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

"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

"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

"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

"&" document member of the same patent family

Date of the actual completion of the international search

23 August 2024 (23.08.2024)

Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2024/036042

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 12-25
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Groups I+, claims 1-11, Formula TL-1 (DNMT1 targeting ligand), Formula D1 (degron).
Exemplary election: Formula TL-2 (DNMT1 targeting ligand), Formula D2 (degron).

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-10; Formula TL-1 (DNMT1 targeting ligand), Formula D1 (degron)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.