

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
31 May 2019 (31.05.2019)



(10) International Publication Number
WO 2019/102494 A1

(51) International Patent Classification:

<i>C07D 471/04</i> (2006.01)	<i>A61K 31/519</i> (2006.01)
<i>C07D 487/04</i> (2006.01)	<i>A61K 31/5025</i> (2006.01)
<i>C07D 498/04</i> (2006.01)	<i>A61K 31/4985</i> (2006.01)
<i>C07D 519/00</i> (2006.01)	<i>A61K 31/5377</i> (2006.01)
<i>A61P 35/00</i> (2006.01)	<i>A61K 31/437</i> (2006.01)
<i>A61K 31/506</i> (2006.01)	<i>A61K 31/5383</i> (2006.01)
<i>A61K 31/4725</i> (2006.01)	<i>A61K 31/496</i> (2006.01)
<i>A61K 31/501</i> (2006.01)	

(21) International Application Number:

PCT/IN2018/050778

(22) International Filing Date:

23 November 2018 (23.11.2018)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

201741042307	24 November 2017 (24.11.2017)	IN
201841001334	11 January 2018 (11.01.2018)	IN

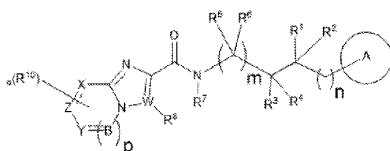
(71) Applicant: JUBILANT BIOSYS LIMITED [IN/IN];

#96, Industrial Suburb, 2nd Stage, Industrial Area, Yeshwanthpur, Karnataka, Bangalore 560022 (IN).

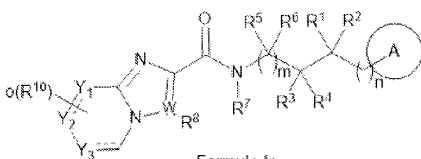
(72) Inventors: VADIVELU, Saravanan; #96, Industrial Suburb, 2nd Stage, Yeshwanthpur, Bangalore 560022 (IN).

RAJAGOPAL, Sridharan; #96, Industrial Suburb, 2nd Stage, Yeshwanthpur, Bangalore 560 022 (IN). BURRI, Raghunadha Reddy; #96, Industrial Suburb, 2nd Stage, Yeshwanthpur, Bangalore 560 022 (IN). GARAPATY, Shivani; #96, Industrial Suburb, 2nd Stage, Yeshwanthpur, Bangalore 560 022 (IN). SIVANANDHAN, Dhanalakshmi; #96, Industrial Suburb, 2nd Stage, Yeshwanthpur, Bangalore 560 022 (IN). THAKUR, Manish Kumar; #96, Industrial Suburb, 2nd Stage, Yeshwanthpur, Bangalore 560 022 (IN). NATARAJAN, Tamizharasan; #96, Industrial Suburb, 2nd Stage, Yeshwanthpur, Bangalore 560 022 (IN). SWAMY, Indu N; #96, Industrial Suburb, 2nd Stage, Yeshwanthpur, Bangalore 560 022 (IN). NAGARAJU, Nagendra; #96, Industrial Suburb, 2nd Stage, Yeshwanthpur, Bangalore 560 022 (IN). KANAGARAJ, Subramaniam; #96, Industrial Suburb, 2nd Stage, Yeshwanthpur, Bangalore 560 022 (IN). MOHD, Zainuddin; #96, Industrial Suburb, 2nd Stage, Yeshwanthpur, Bangalore 560 022 (IN). SARKAR, Sayantani; #96, Industrial Suburb, 2nd Stage, Yeshwanthpur, Bangalore 560 022 (IN). SAMANTA, Swapan Kumar; #96, Industrial Suburb, 2nd Stage, Yeshwanthpur, Bangalore 560 022 (IN). , Hariprakash; B 34, Sector 58, Noida, Uttar Pradesh 201301 (IN).

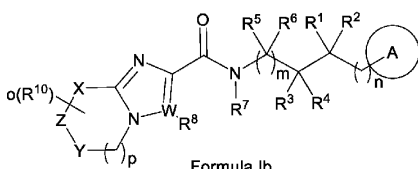
(54) Title: HETEROCYCLIC COMPOUNDS AS PRMT5 INHIBITORS



Formula I



Formula Ia



Formula Ib

(57) Abstract: The compounds of Formula I, Formula Ia, and Formula Ib are described herein along with their analogs, tautomeric forms, stereoisomers, polymorphs, hydrates, solvates, pharmaceutically acceptable salts, pharmaceutical compositions, metabolites, and prodrugs thereof. These compounds inhibit PRMT5 and are useful as therapeutic or ameliorating agent for diseases that are involved in cellular growth such as malignant tumors, schizophrenia, Alzheimer's disease, Parkinson's disease and the like.

WO 2019/102494 A1

[Continued on next page]

(74) **Agent:** LAKSHMIKUMARAN, Malathi et al.; B6/10,
Safdarjung Enclave, New Delhi 110029 (IN).

(81) **Designated States** (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *of inventorship (Rule 4.17(iv))*

Published:

— *with international search report (Art. 21(3))*