



(51) International Patent Classification:

C07D 487/04 (2006.01) A61K 31/5517 (2006.01)
C07D 519/00 (2006.01) A61P 35/00 (2006.01)

(21) International Application Number:

PCT/EP2012/070233

(22) International Filing Date:

12 October 2012 (12.10.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/547,198 14 October 2011 (14.10.2011) US

(71) Applicants: **SPIROGEN SÀRL** [CH/CH]; Chemin De La Pacottaz 1, c/o Michael Forer, CH-1806 St-Légier-La Chiésaz (CH). **SEATTLE GENETICS, INC.** [US/US]; 21823 30th Drive S.E., Bothell, Washington 98021 (US).

(72) Inventors: **HOWARD, Philip Wilson**; Spirogen Limited, The QMB Innovation Centre, 42 New Road, London Greater London E1 2AX (GB). **TIBERGHIE, Arnaud**; Spirogen Limited, The QMB Innovation Centre, 42 New Road, London Greater London E1 2AX (GB). **JEFFREY, Scott**; Seattle Genetics, Inc., 21823 30th Drive S.E., Bothell, Washington 98021 (US). **BURKE, Patrick**; Seattle Genetics, Inc., 21823 30th Drive S.E., Bothell, Washington 98021 (US).

(74) Agents: **WATSON, Robert** et al.; Mewburn Ellis LLP, 33 Gutter Lane, London Greater London EC2V 8AS (GB).

(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, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, 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, 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, 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, ML, MR, NE, SN, TD, TG).

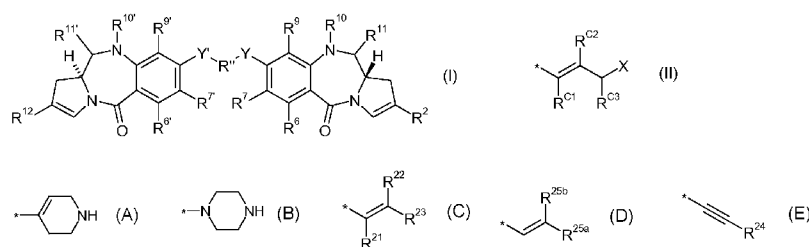
Declarations under Rule 4.17:

— of inventorship (Rule 4.17(iv))

Published:

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

(54) Title: PYRROLOBENZODIAZEPINES



(57) Abstract: A compound with the formula (I), wherein: R² is of formula (II), where X is selected from the group comprising: OH, SH, CO₂H, COH, N=C=O, NHNH₂, CONHNH₂, formula (A), formula (B), NHR^N, wherein R^N is selected from the group comprising H and C₁₋₄ alkyl; R^{C1}, R^{C2} and R^{C3} are independently selected from H and unsubstituted C₁₋₂ alkyl; and either: R¹² is selected from the group consisting of: (ia) C₅₋₁₀ aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, C₁₋₇ alkyl, C₃₋₇ heterocyclyl and bis-oxy-C₁₋₃ alkylene; (ib) C₁₋₅ saturated aliphatic alkyl; (ic) C₃₋₆ saturated cycloalkyl; (id) formula (C), wherein each of R²¹, R²² and R²³ are independently selected from H, C₁₋₃ saturated alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl and cyclopropyl, where the total number of carbon atoms in the R¹² group is no more than 5; (ie) formula (D), wherein one of R^{25a} and R^{25b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy, pyridyl; and thiophenyl; and (if) formula (E), where R²⁴ is selected from: H; C₁₋₃ saturated alkyl; C₂₋₃ alkenyl; C₂₋₃ alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy, pyridyl; and thiophenyl; R⁶ and R⁹ are independently selected from H, R, OH, OR, SH, SR, NH₂, NHR, NRR', nitro, Me₃Sn and halo; where R and R' are independently selected from optionally substituted C₁₋₁₂ alkyl, C₃₋₂₀ heterocyclyl and C₅₋₂₀ aryl groups; R⁷ is selected from H, R, OH, OR, SH, SR, NH₂, NHR, NHRR', nitro, Me₃Sn and halo; either: (a) R¹⁰ is H, and R¹¹ is OH, OR^A, where R^A is C₁₋₄ alkyl; (b) R¹⁰ and R¹¹ form a nitrogen-carbon double bond between the nitrogen and carbon atoms to which they are bound; or (c) R¹⁰ is H and R¹¹ is SO₂M, where z is 2 or 3 and M is a monovalent pharmaceutically acceptable cation; R¹² is a C₃₋₁₂ alkylene group, which chain may be interrupted by one or more heteroatoms, and/or aromatic rings; Y and Y' are selected from O, S, or NH; R⁶, R⁷, R⁹ are selected from the same groups as R⁶, R⁷ and R⁹ respectively and R¹⁰ and R¹¹ are the same as R¹⁰ and R¹¹, wherein if R¹¹ and R^{11'} are SO₂M, M may represent a divalent pharmaceutically acceptable cation.