



(51) International Patent Classification:

A61K 31/519 (2006.01) C07F 9/02 (2006.01)
A61K 31/4523 (2006.01) A61P 35/00 (2006.01)

(21) International Application Number:

PCT/US2019/059542

(22) International Filing Date:

01 November 2019 (01.11.2019)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/754,398 01 November 2018 (01.11.2018) US
62/877,189 22 July 2019 (22.07.2019) US
62/915,983 16 October 2019 (16.10.2019) US
62/927,469 29 October 2019 (29.10.2019) US

(71) Applicant: **SYROS PHARMACEUTICALS, INC.**
[US/US]; 35 CambridgePark Drive, Cambridge, MA 02140 (US).

(72) Inventors; and

(71) Applicants: **BRADLEY, Michael** [US/US]; 338 W. 21st Street, Houston, TX 77008 (US). **CIBLAT, Stephane** [CA/CA]; 607-408 Rue Saint Jacques, Montreal, Quebec, H2Y 1S2 (CA). **KABRO, Anzhelika** [CA/CA]; 815, 49e Avenue, Lachine, Quebec, H8T 2T3 (CA).

(72) Inventors: **MARINEAU, Jason, J.**; 2 MacKintosh Street, Franklin, MA 02038 (US). **CHUAQUI, Claudio**; 83 Menotomy Rd., Arlington, MA 02476 (US).

(74) Agent: **DENHART, Derek** et al.; Goodwin Procter LLP, 100 Northern Avenue, Boston, MA 02210 (US).

(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,

(54) Title: INHIBITORS OF CYCLIN-DEPENDENT KINASE 7 (CDK7)

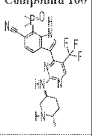
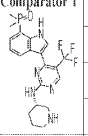
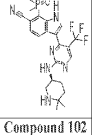
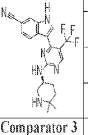
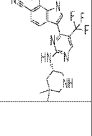
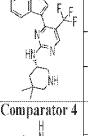
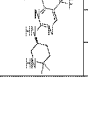
	CDK7 K _D (nM) = 0.057			CDK7 K _D (nM) = 0.18	
	CDK12 K _i (nM)	(K _i /K _D CDK7)		CDK12 K _i (nM)	(K _i /K _D CDK7)
	230	4100		51	280
	CDK7 K _D (nM) = 0.065			CDK7 K _D (nM) = 0.45	
	CDK12 K _i (nM)	(K _i /K _D CDK7)		CDK12 K _i (nM)	(K _i /K _D CDK7)
	870	13000		140	320
	CDK7 K _D (nM) = 0.059			CDK7 K _D (nM) = 0.21	
	CDK12 K _i (nM)	(K _i /K _D CDK7)		CDK12 K _i (nM)	(K _i /K _D CDK7)
	78	1300		18	89
				CDK7 K _D (nM) = 0.34	
	CDK2 K _i (nM)	(K _i /K _D CDK7)		CDK2 K _i (nM)	(K _i /K _D CDK7)
	390	6900		26	130
	CDK9 K _i (nM)	(K _i /K _D CDK7)		CDK9 K _i (nM)	(K _i /K _D CDK7)
	290	4900		20	99
	CDK12 K _i (nM)	(K _i /K _D CDK7)		CDK12 K _i (nM)	(K _i /K _D CDK7)
	48	140		48	140
	CDK2 K _i (nM)	(K _i /K _D CDK7)		CDK2 K _i (nM)	(K _i /K _D CDK7)
	64	190		64	190
	CDK9 K _i (nM)	(K _i /K _D CDK7)		CDK9 K _i (nM)	(K _i /K _D CDK7)
	36	100		36	100

FIG. 1

(57) **Abstract:** The present invention provides various compositions, including compounds of Formula (I) or (Ia), or a species thereof, and pharmaceutically acceptable salts, solvates (e.g., hydrates), stereoisomer, tautomers, isotopic and other specified forms thereof. Also provided are methods (or uses) and kits involving the compounds or pharmaceutically acceptable compositions containing them for treating or preventing a disease (e.g., a proliferative disease such as cancer) in a subject. Administration of a compound or pharmaceutical composition described herein is expected to inhibit cyclin-dependent kinase 7 (CDK7), and thereby, induce apoptosis in tumor cells in the subject.

[Continued on next page]

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).

Published:

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