

	Vol	Page No.
[11] Guba M, von Breitenbuch P, Steinbauer M, Koehl G, Fiegel S, Hornung M, Bruns CJ, Zuelke C, Farkas S, Anthuber M, Jauch KW, Geissler EK. Rapamycin inhibits primary and metastatic tumor growth by antiangiogenesis: involvement of vascular endothelial growth factor. <i>Nat Med</i> 2002;8:128-135.	2	8-220
[12] Vivanco I, Sawyers CL. The phosphatidylinositol 3-kinase-Akt pathway in human cancer. <i>Nature Cancer</i> 2002;2:489-501.	2	8-228
[13] Inoki K, Li Y, Zhu T, Wu J, Guan K-L. TSC2 is phosphorylated and inhibited by Akt and suppresses mTOR signalling. <i>Nat Cell Biol</i> 2002; published online: 12 August 2002; DOI: 10.1038/ncb839.	2	8-241
[14] Nave BT, Ouwens M, Withers DJ, Alessi DR, Shepherd PR. Mammalian target of rapamycin is a direct target for protein kinase B: identification of a convergence point for opposing effects of insulin and amino-acid deficiency on protein translation. <i>Biochem J</i> 1999;344:427-431.	2	8-251
[15] Neshat MS, Mellinger IK, Tran C, Stiles B, Thomas G, Petersen R, Frost P, Gibbons JJ, Wu H, Sawyers CL. Enhanced sensitivity of PTEN-deficient tumors to inhibition of FRAP/mTOR. <i>Proc Natl Acad Sci</i> 2001;98:10314-10319.	2	8-256
[16] Podsypanina K, Lee RT, Politis C, Hennessy I, Crane A, Puc J, Neshat M, Wang H, Yang L, Gibbons J, Frost P, Dreisbach V, Blenis J, Giaciong Z, Fisher P, Sawyers C, Hedrick-Ellenson L, Parsons R. An inhibitor of mTOR reduces neoplasia and normalizes p70/S6 kinase activity in Pten <sup>+/-</sup> mice. <i>Proc Natl Acad Sci</i> 2001;98:10320-10325	2	8-262
[17] Meyer T, Becker M, Centeleghe M, Köppler J, Liebetanz J, Manfrina D, Martin N, Muller L, Fabbro D, Lane H, O'Reilly T. Enzymatic profile of RAD001: In vitro inhibition of protein kinases. <i>Novartis Release Ready Report</i> 2001;RD-2001-01088	2	8-268
[18] Hattenberger M, Muller M, Vaxelaire J, Sedrani R, Lane H, O'Reilly T. RAD001 potentiates the activity of conventional anticancer cytotoxics in vitro. <i>Novartis Release Ready Report</i> 2000;RD-2000-02546.	2	8-282
[19] Hattenberger M, Boulay A, Lane HA, Maira M, O'Reilly T. In vitro antiproliferative activity of RAD001 against a broad panel of tumor cell lines. <i>Novartis Release Ready Study Report</i> 2002;RD-2002-03223.	2	8-295
[20] Beuvink I, Zilbermann F, Zumstein-Mecker S, Sedrani R, Thomas G, O'Reilly T, Lane H. Downregulation of mTOR targets in tumor cell lines in vitro (comparison with CCI-779). <i>Novartis Release Ready Report</i> 2000;RD-2000-02544.	2	8-313
[21] Hungerford V, Thomas G, Schuler W. RAD inhibits the growth factor-stimulated activation of p70 S6 kinase. <i>Novartis Release Ready Report</i> 2000;RD-2000-02151.	2	8-331

	Vol	Page No.
[22] Boulay A, Zumstein-Mecker S, Stephan C, Solf R, Ruetz S, O'Reilly T, Lane HA. RAD001 potentiates the loss of A549 cell viability induced by gemcitabine treatment in vitro. Novartis Release Ready Study Report 2002;RD-2002-03250.	2	8-341
[23] Boulay A, Hattenberger M, Zumstein-Mecker S, Solf R, Ruetz S, O'Reilly T, Lane H. Effect of scheduling on the in vitro antiproliferative activity of RAD001/gemcitabine combinations in A549 cells. Novartis Release Ready Report 2001;RD-2001-01087.	26	8-9732
[24] Wood JM, Theuer A. RAD001: effects on endothelial and fibroblast cell proliferation. Novartis Release Ready Report 2001;RD-2001-00852.	2	8-357
[25] Boulay A, Hattenberger M, O'Reilly T, Maira M, Lane HA. Comparison of the antiproliferative activity of RAD001 with activation of the PTEN/PI3 kinase/Akt/mTOR pathway in tumor cell lines. Novartis Release Ready Study Report 2002;RD-2002-03252.	2	8-369
[26] Muller M, Vaxelaire J, Hattenberger M, Sedrani R, Lane H, O'Reilly T. RAD001 is an effective antitumor agent in experimental KB-31 xenograft tumor models of epidermoid cancer. Novartis Release Ready Report 2000;RD-2000-02549.	2	8-388
[27] Zumstein-Mecker S, Beuvink I, Zilbermann F, Muller M, Vaxelaire, Sedrani R, Thomas G, O'Reilly T, Lane H. Downregulation of mTOR targets in tumors and skin derived from KB-31 human epidermoid carcinoma xenograft studies. Novartis Release Ready Report 2000;RD-2000-02541.	2	8-404
[28] Marti A, Stolz B, Haller R, Tobler S, O'Reilly T, Lane H. Effect of the rapamycin derivative RAD001 in the syngeneic CA20948 rat pancreatic tumor model. Novartis Release Ready Report 2002;RD-2002-03707	26	8-9744
[29] Zumstein-Mecker S, Beuvink I, Zilbermann F, Stephan C, Haller R, Tobler S, Thomas G, Stolz B, O'Reilly T, Lane H. Prolonged inactivation of p70 <sup>s6k</sup> in tumors and skin derived from CA20948 pancreatic tumor-bearing rats. Novartis Release Ready Report 2001;RD-2001-00450.	2	8-422
[30] Zumstein-Mecker S, Beuvink I, Zilbermann F, Sedrani R, Hattenberger M, Thomas G, O'Reilly T, Lane H. Inhibition of the mTOR target p70s6k in rat peripheral lymphocytes. Novartis Release Ready Report 2000;RD-2000-02545.	2	8-437
[31] Zumstein-Mecker S, Boulay A, Beuvink I, Zilbermann F, Haller R, Tobler S, Thomas G, Stolz B, O'Reilly T, Lane H. Prolonged inactivation of p70 <sup>s6k</sup> in peripheral blood mononucleocytes derived from CA20948 pancreatic tumor-bearing rats and non-tumor-bearing rats. Novartis Release Ready Report 2002;RD-2002-03817.	3	8-451
[32] Gingras AC, Raught B, Sonenberg N. Regulation of translation initiation by FRAP/mTOR. Genes Dev 2001;15:807-826.	3	8-471

	Vol	Page No.
[33] Zumstein-Mecker S, Stephan C, Boulay A, Lane HA. Detection of p70S6 activity in human peripheral mononucleocytes (PBMCs) using the 40S ribosomal protein kinase assay. Novartis Release Ready Study Report 2002;RD-2002-02974.	3	8-491
[34] Vaxelaire J, Muller M, Hattenberger, Lane H, O'Reilly T. RAD001 is an effective antitumor agent in experimental A549 xenograft tumor model of lung cancer. Novartis Release Ready Report 2001;RD-2001-00848.	3	8-507
[35] Wenger F, O'Reilly T, Martinuzzi-Duboc L, Tinetto W, Lane H, Brandt R, Cozens R. RAD001 is an effective antitumor agent in experimental NCI H-596 lung xenograft tumor model of lung cancer. Novartis Release Ready Report; 2001;RD-2001-00860.	3	8-523
[36] Hattenberger M, Weckbecker G, Muller M, Vaxelaire J, Sedrani R, Lane H, O'Reilly T. Evaluation of the antitumor activity of RAD001 in experimental xenograft tumor models of pancreatic cancer. Novartis Release Ready Report 2000;RD-2000-02548.	3	8-538
[37] Vaxelaire J, Muller M, Hattenberger M, Sedrani R, Lane H, O'Reilly T. RAD001 is active in vivo against xenograft tumors of HCT116 human colon carcinoma, a cell line resistant to RAD001 in vitro. Novartis Release Ready Report 2000;RD-2000-02550.	3	8-565
[38] Muller M, Vaxelaire J, Hattenberger M, Maira SM, Lane H, O'Reilly T. RAD001 is an effective antitumor agent in the experimental NCI H-520 xenograft tumor model of lung cancer. Novartis Release Ready Study Report 2002;RD-2002-00002.	3	8-594
[39] Fiebig HH, Dengler WA, Roth T. Human tumor xenografts: predictivity, characterization and discovery of new anticancer agents. In: Fiebig HH, Burger AM, editors. Relevance of tumor models for anticancer drug development. Contrib Oncol Basel: Karger, 1999;54:29-50.	3	8-612
[40] Fiebig HH, Cozens R, O'Reilly T. Activity of RAD001 against low passage human tumor xenografts. Novartis Release Ready Report 2000;RD-2000-02552.	3	8-634
[41] Arceci RJ, Stieglitz K, Bierer BE. Immunosuppressants FK506 and rapamycin function as reversal agents of the multidrug resistance phenotype. Blood 1992;80:1528-1536.	3	8-654
[42] Muller M, Vaxelaire J, Hattenberger M, Lane H, O'Reilly T. RAD001 is an effective antitumor agent against experimental epidermoid multi-drug resistant KB-8511 tumors. Novartis Release Ready Study Report 2002;RD-2002-03237.	3	8-663
[43] Akiyam S, Fojo A, Hanover JA, Pastan I, Gottesman MM. Isolation and genetic characterization of human KB cell lines resistant to multiple drugs. Somatic Cell Molec Genetics 1985;11:117-126.	3	8-682

	Vol	Page No.
[44] Fojo A, Akiyama S, Gottesman MM, Pastan I. Reduced drug accumulation in multiply drug-resistant human KB carcinoma cell lines. <i>Cancer Res</i> 1997;45:3002-3007.	3	8-692
[45] Wenger F, O'Reilly T, Martinuzzi-Duboc L, Tinetto W, Lane H, Brandt R, Cozens R. Evaluation of RAD001 in combination with conventional anticancer agents against experimental NCI H-596 lung xenograft tumor models of cancer. <i>Novartis Release Ready Report</i> 2001;RD-2001-00861.	3	8-698
[46] Muller M, Hattenberger M, Vaxelaire J, Lane H, O'Reilly T. Evaluation of RAD001 in combination with conventional anticancer agents against experimental KB-31 epidermoid xenograft tumors. <i>Novartis Release Ready Report</i> 2001;RD-2001-00849.	3	8-727
[47] Vaxelaire J, Hattenberger M, Muller M, Lane HA, O'Reilly T. Effect of administration schedule on the antitumor activity of RAD001 in combination with Taxol®. <i>Novartis Release Ready Study Report</i> 2002;RD-2002-03251.		To be submitted in 12/2002
[48] Muller M, Vaxelaire J, Hattenberger M, Lane HA, O'Reilly T. Administration schedule has little effect on the antitumor activity of RAD001 in combination with cisplatin. <i>Novartis Release Ready Study Report</i> 2002;RD-2002-03253.		To be submitted in 12/2002
[49] Hattenberger M, Muller M, Vaxelaire J, Lane HA, O'Reilly T. Administration schedule has little effect on the antitumor activity of RAD001 in combination with low dose gemcitabine against NCI H-596 lung tumor xenografts. <i>Novartis Release Ready Study Report</i> 2002;RD-2002-02354.		To be submitted in 12/2002
[50] Wood JM, Schnell CR. RAD001: effects on angiogenesis-induced by growth factor-impregnated, subcutaneous implants in mice. <i>Novartis Release Ready Report</i> 2001; RD-2001-00853.	3	8-768
[51] Wood JM, Schnell CR. RAD001: effects in orthotopic B16/BL6 melanoma model in C57BL/6 mice. <i>Novartis Release Ready Report</i> 2001; RD-2001-00854.	3	8-783
[52] Saunders RN, Metcalfe MS, Nicholson ML. Rapamycin in transplantation: A review of the evidence. <i>Kidney Int.</i> 2000; 59:3-16.	3	8-809
[53] Schuler W, Sedrani R, Cottens S, Haberlin B, Schulz M, Schuurman HJ, Zenke G, Zerwes HG, Schreier MH. A new rapamycin derivative: pharmacological properties in vitro and in vivo. <i>Transplantation</i> 1997;64: 36-42.	3	8-823
[54] Kovarik JM, Kaplan B, Tedesco Silva H, Kahan BD, Dantal J, Vitko S, Boger R, Rordorf C. Exposure-response relationships for everolimus in de novo kidney transplantation: defining a therapeutic range. <i>Transplantation</i> 2000;73:920-925.	3	8-830

	Vol	Page No.
[55] O'Reilly T, Schmutz P, Hattenberger M, Vaxelaire J, Muller M, Lane H, Huesser C. Reduction of the immunosuppressive properties of RAD001 by intermittent administration. Novartis Release Ready Study Report 2002; RD-2002-01534.	26	8-9759
[56] Vaxelaire J, Muller M, Hattenberger M, O'Reilly, T. Studies on the tolerability of athymic BALB/c <i>nu/nu</i> (nude) mice to RAD001. Novartis Release Ready Report 2000;RD-2000-02547.	3	8-836
[57] Muller M, Hattenberger M, Vaxelaire J, O'Reilly, T. Tolerability of athymic BALB/c <i>nu/nu</i> (nude) mice to RAD001 in combination with conventional cytotoxic anti-cancer agents. Novartis Release Ready Report 2001;RD-2001-00401.	3	8-845
[58] Vaxelaire J, Muller M, Hattenberger M, Lane H, O'Reilly, T. Tolerability of athymic BALB/c <i>nu/nu</i> (nude) mice to RAD001 in combination with carboplatin. Novartis Release Ready Report 2001;RD-2001-00844.	3	8-864
[59] Muller M, Hattenberger M, Vaxelaire J, Lane H, O'Reilly, T. Effect of schedule on the tolerability of athymic BALB/c <i>nu/nu</i> (nude) mice to RAD001 in combination with gemcitabine. Novartis Release Ready Report 2001;RD-2001-00850.	3	8-879
[60] Capdeville R, Buchdunger E, Zimmermann J, Matter A. Glivec (STI571, imatinib), a rationally developed, targeted anticancer drug. <i>Nat Rev Drug Discov.</i> 2002;1:493-502	3	8-893
[61] Muller M, O'Reilly T, Vaxelaire J, Hattenberger M, Maira SM. Tolerability of concomitant STI571 (Glivec®) and RAD001 in athymic Harlan mice. Novartis Release Ready Study Report 2002;RD-2002-03186.	26	8-9777
• Cited DMPK & Toxicology Reports and Literature		
[1] Kretz O. Pharmacokinetics and excretion after single intravenous and peroral administration (0.9 mg/kg) of 3H-labeled RAD001 to mice. Novartis Pharma AG, 28-Aug-2000. Document DMPK(CH)R98-707	4	8-903
[2] Figueiredo J, Kretz O. RAD001: Pharmacokinetics in mice after intravenous bolus administration (0.9 mg/kg) with RAD001. Novartis Pharma AG, 16-Mar-2000. Document DMPK(CH)R00-874	4	8-920
[3] Lemaire M, Dannecker R. SDZ RAD: Absorption, distribution, metabolism and excretion in rats after single intravenous (1 mg/kg, 10 mg/kg) and oral (1.5 mg/kg, 15 mg/kg) administration of [ <sup>3</sup> H]SDZ RAD. Sandoz Pharma Ltd., 25-Jan-1996. Document 303-013 (159604.010)		**x- reference to IND 52,003 11/15/96
[4] Schuetz H. SDZ RAD: Distribution and excretion of total radioactivity in rats after peroral administration of 1.5 mg/kg <sup>14</sup> C-labelled SDZ RAD. Novartis Pharma AG, 10-Mar-1998. Document 303-092 (DMPK(CH)1997/515)	4	8-936

# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

## LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

## FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

## E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.