# Contents

## Highlights of This Issue 1689

### REVIEW

**BH3 Mimetics: Status of the Field and New Developments**  
Christian Billard

### SMALL MOLECULE THERAPEUTICS

**Pharmacologic Inhibition of MEK Signaling Prevents Growth of Canine Hemangiosarcoma**  
Nicholas J. Andersen, Brian J. Nickoloff, Karl J. Dykema, Elissa A. Boguslawski, Roman I. Krivochenits, Roe E. Froman, Michelle J. Dawes, Laurence H. Baker, Dafydd G. Thomas, Debra A. Kamstock, Barbara E. Kitchell, Kyle A. Furge, and Nicholas S. Duesbery

**AZD3514: A Small Molecule That Modulates Androgen Receptor Signaling and Function In Vitro and In Vivo**  

### LARGE MOLECULE THERAPEUTICS

**Targeted Cytolysins Synergistically Potentiate Cytoplasmic Delivery of Gelonin Immunotoxin**  
Christopher M. Pirie, David V. Liu, and K. Dane Wittrup

### CANCER THERAPEUTICS INSIGHTS

**Smac Mimetics in Combination with TRAIL Selectively Target Cancer Stem Cells in Nasopharyngeal Carcinoma**  
Man-si Wu, Guang-feng Wang, Zhi-qian Zhao, Yi Liang, Heng-bang Wang, Miao-ji Wu, Ping Min, Li-zhen Chen, Qi-sheng Feng, Jin-xin Bei, Yi-xin Zeng, and Dajun Yang

**Targeting Protein Tyrosine Phosphatase SHP2 for the Treatment of PTPN11-Associated Malignancies**  

**S49076 Is a Novel Kinase Inhibitor of MET, AXL, and FGFR with Strong Preclinical Activity Alone and in Association with Bevacizumab**  
Mike F. Burbridge, Céline J. Bossard, Carine Saunier, Imre Fejes, Alain Bruno, Stéphane Léonc, Gilles Ferry, Georges Da Violante, François Bouzom, Valérie Cattan, Anne Jacquet-Bescond, Paolo M. Comoglio, Brian P. Lockhart, Jean A. Boutin, Alex Cordi, Jean-Claude Ortuno, Alain Pierré, John A. Hickman, Francisco H. Cruzalegui, and Stéphane Depil

**Synergistic Induction of Apoptosis in Multiple Myeloma Cells by Bortezomib and Hypoxia-Activated Prodrug TH-302, In Vivo and In Vitro**  
Jinsong Hu, Els Van Valkenborgh, Dehui Xu, Eline Menu, Hendrik De Raeye, Elke De Bryune, Song Xu, Ben Van Camp, Damian HANDISIDES, Charles P. Hart, and Karin Vanderkerken

**Cyclin G1 Expands Liver Tumor-Initiating Cells by Sox2 Induction via Akt/mTOR Signaling**  
Wen Wen, Tao Han, Cheng Chen, Lei Huang, Wen Sun, Xue Wang, Shu-Zhen Chen, Dai-Min Xiang, Liang Tang, Dan Cao, Gen-Sheng Feng, Meng-Chao Wu, Jin Ding, and Hong-Yang Wang
An Autocrine Loop between TGF-β1 and the Transcription Factor Brachyury Controls the Transition of Human Carcinoma Cells into a Mesenchymal Phenotype

Cecilia Larocca, Joseph R. Cohen, Romaine I. Fernando, Bruce Huang, Duane H. Hamilton, and Claudia Palena

Impact of Tumor HER2/ERBB2 Expression Level on HER2-Targeted Liposomal Doxorubicin-Mediated Drug Delivery: Multiple Low-Affinity Interactions Lead to a Threshold Effect

Bart S. Hendriks, Stephan G. Klinz, Joseph G. Reynolds, Christopher W. Espelin, Daniel F. Gaddy, and Thomas J. Wickham

Inhibition of ABCB1 Expression Overcomes Acquired Docetaxel Resistance in Prostate Cancer

Yeqi Zhu, Chengfei Liu, Nagalakshmi Nadiminty, Wei Lou, Ramakumar Tummala, Christopher P. Evans, and Allen C. Gao

Ethacrynic Acid Oxadiazole Analogs Induce Apoptosis in Malignant Hematologic Cells through Downregulation of Mcl-1 and c-FLIP, Which Was Attenuated by GSTP1-1

Guyue Liu, Rui Wang, Yuetong Wang, Pengzhan Li, Guisen Zhao, Linxiang Zhao, and Yongkui Jing

Sulindac Selectively Inhibits Colon Tumor Cell Growth by Activating the cGMP/PKG Pathway to Suppress Wnt/β-Catenin Signaling


Chk1/2 Inhibition Overcomes the Cisplatin Resistance of Head and Neck Cancer Cells Secondary to the Loss of Functional p53

Mayur A. Gadhikar, Maria Rita Sciuto, Marcus Vinicius Ortega Alves, Curtis R. Pickering, Abdulllah A. Osman, David M. Neskey, Mei Zhao, Alison L. Fitzgerald, Jeffrey N. Myers, and Mitchell J. Frederick

BCL-2 Hypermethylation Is a Potential Biomarker of Sensitivity to Antimitotic Chemotherapy in Endocrine-Resistant Breast Cancer


Apoptotic Circulating Tumor Cells in Early and Metastatic Breast Cancer Patients

Galatea Kallergi, Georgios Konstantinidis, Harris Markomanolaki, Maria A. Papadaki, Dimitris Mavroudis, Christos Stournaras, Vassilis Georgoulis, and Sofia Agelaki

A c-Myc Activation Sensor-Based High-Throughput Drug Screening Identifies an Antineoplastic Effect of Nitazoxanide

Hua Fan-Minogue, Sandhya Bodapati, David Solow-Cordero, Alice Pan, Ramasamy Paulmurugan, Tarik F. Massoud, Dean W. Felsher, and Sanjiv S. Gambhir

NF1 Deletion Generates Multiple Subtypes of Soft-Tissue Sarcoma That Respond to MEK Inhibition

Rebecca D. Dodd, Jeffrey K. Mito, William C. Eward, Rhea Chitalia, Mohit Sachdeva, Yan Ma, Jordi Barretina, Leslie Dodd, and David G. Kirsch

O. Michael Colvin, MD: In Memoriam (1936–2013)

Correction: MPT0B098, a Novel Microtubule Inhibitor That Destabilizes the Hypoxia-Inducible Factor-1α mRNA through Decreasing Nuclear-Cytoplasmic Translocation of RNA-Binding Protein HuR

Correction: Dual Programmed Cell Death Pathways Induced by p53 Transactivation Overcome Resistance to Oncolytic Adenovirus in Human Osteosarcoma Cells

ABOUT THE COVER

Continued androgen receptor (AR) expression and signaling is a key driver in castration-resistant prostate cancer (CRPC). AZD3514 is an orally bioavailable drug that inhibits androgen-dependent and -independent AR signalling in vitro and in vivo. Using immunohistochemistry, R3327H prostate tumors were scored for intensity of nuclear AR to assess the impact of AZD3514 on AR. For more details, see article by Loddick and colleagues on page 1715.