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**MMAE Delivery Using the Bicycle Toxin Conjugate**

**BT5528**

- Gavin Bennett, Amy Brown, Gemma Mudd, Philip Huxley, Katerine Van Rietschoten, Silvia Pavan, Liuhong Chen, Sophie Watcham, Johanna Lahdenranta, and Nicholas Keen

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**The Dysregulated Pharmacology of Clinically Relevant ESR1 Mutants is Normalized by Ligand-activated WT Receptor**


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#### 1415

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- Shiva Kant, Pravin Keswani, Anthony R. Guastella, Praveen Kumar, Stewart F. Graham, Katie L. Buelow, Ichiro Nakano, and Prakash Chinnaiyan

#### 1423

**A Genome-scale CRISPR Screen Identifies the ERBB and mTOR Signaling Networks as Key Determinants of Response to PI3K Inhibition in Pancreatic Cancer**


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**Targeting the PI3K/AKT Pathway Overcomes Enzalutamide Resistance by Inhibiting Induction of the Glucocorticoid Receptor**


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**Preclinical Testing of a Novel Niclosamide Stearate Prodrug Therapeutic (NSPT) Shows Efficacy Against Osteosarcoma**

- Gireesh B. Reddy, David L. Kerr, Ivan Spasojevic, Artak Tovmasyan, David Hsu, Brian E. Brigan, Jason A. Somarelli, David Needham, and William C. Eward

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**Rac Signaling Drives Clear Cell Renal Carcinoma Tumor Growth by Priming the Tumor Microenvironment for an Angiogenic Switch**

- Erik T. Goka, Pallavi Chaturvedi, Dayrelis T. Mesa Lopez, and Marc E. Lippman

## LARGE MOLECULE THERAPEUTICS

#### 1474

**Inhibition of Tumor Cell Growth and Cancer Stem Cell Expansion by a Bispecific Antibody Targeting EGFR and HER3**


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#### 1486

**Early Assessment of Molecular Progression and Response by Whole-genome Circulating Tumor DNA in Advanced Solid Tumors**

- Andrew A. Davis, Wade T. Iams, David Chan, Michael S. Oh, Robert W. Lentz, Neil Peterman, Alex Robertson, Abhik Shah, Rohith Srivas, Timothy J. Wilson, Nicole J. Lambert, Peter S. George, Becky Wong, Haleigh W. Wood, Jason C. Close, Ayse Tezcan, Ken Nesmith, Haluk Tezcan, and Young Kwang Chae
1497  A Qualitative Transcriptional Signature for Predicting Prognosis and Response to Bevacizumab in Metastatic Colorectal Cancer
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1506  Functional miRNA Screening Identifies Wide-ranging Antitumor Properties of miR-3622b-5p and Reveals a New Therapeutic Combination Strategy in Ovarian Tumor Organoids

1520  EWS-FLI1-regulated Serine Synthesis and Exogenous Serine are Necessary for Ewing Sarcoma Cellular Proliferation and Tumor Growth
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1530  A Novel Peptidylarginine Deiminase 4 (PAD4) Inhibitor BMS-PS Blocks Formation of Neutrophil Extracellular Traps and Delays Progression of Multiple Myeloma
Marina Li, Cindy Lin, Hui Deng, Joann Strnad, Luca Bernabei, Dan T. Vogl, James J. Burke, and Yulia Nefedova

1539  DCLK1- Isoform2 Alternative Splice Variant Promotes Pancreatic Tumor Immunosuppressive M2-Macrophage Polarization
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1550  Blockade of Cell Volume Regulatory Protein NKCC1 Increases TMZ-Induced Glioma Apoptosis and Reduces Astroglisis
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1562  Pathway-Specific Genome Editing of PI3K/mTOR Tumor Suppressor Genes Reveals that PTEN Loss Contributes to Cetuximab Resistance in Head and Neck Cancer
Hiroki Izumi, Zhiyong Wang, Yusuke Goto, Toshinori Ando, Xingyu Wu, Xuefeng Zhang, Hua Li, Daniel E. Johnson, Jennifer R. Grandis, and J. Silvio Gutkind

ABOUT THE COVER
In this month’s edition, Bennett and colleagues disclose BT5528, a Bicycle toxin-conjugate targeting EphA2. On the cover, BT5528 is shown bound to EphA2 on the surface of HT1080 fibrosarcoma cells in a High Content Screening assay. BT5528 provided persistent toxins to tumor cells while avoiding systemic exposure and has entered a Phase I clinical trial (NCT04180371). Read the First Disclosure on page 1385.