This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Cancer				
Prostate cancer	Androgen receptor	<p>Cell culture and mouse studies identified androgen receptor antagonists that could help treat prostate cancers that acquire resistance to Xtandi enzalutamide. Structural modeling and <i>in vitro</i> mutagenesis assays identified F876L as a mutation in the androgen receptor that prevents antagonism by Xtandi and instead causes the drug to behave as a partial agonist. A series of compounds with D-ring substitutions to the enzalutamide scaffold were synthesized and shown to inhibit the F876L mutant androgen receptor. In mouse xenograft models for prostate cancer and in cell lines, the lead D-ring-substituted compound inhibited growth of F876L mutant prostate cancers, whereas enzalutamide did not. Next steps include evaluating the lead compound in additional mouse xenograft models for prostate cancer and determining the clinical relevance of the mutation.</p> <p>Medivation Inc. and Astellas Pharma Inc. market Xtandi, a triple-acting oral antiandrogen receptor, to treat castration-resistant prostate cancer. Aragon Pharmaceuticals Inc.'s ARN-509, a second-generation androgen receptor antagonist, is in Phase II testing to treat prostate cancer. Corresponding author Charles Sawyers is a cofounder of Aragon Pharmaceuticals and a co-inventor of both Xtandi and ARN-509.</p> <p>SciBX 6(18); doi:10.1038/scibx.2013.437 Published online May 9, 2013</p>	Two provisional patent applications filed; licensing status undisclosed	<p>Balbas, M.D. <i>et al.</i> <i>eLife</i>; published online April 9, 2013; doi:10.7554/eLife.00499</p> <p>Contact: Charles L. Sawyers, Memorial Sloan-Kettering Cancer Center, New York, N.Y. e-mail: sawyersc@mskcc.org</p> <p>Contact: Yang Shen, Toyota Technological Institute at Chicago, Chicago, Ill. e-mail: yangshen@ttic.edu</p>