

## THE DISTILLERY

## This week in therapeutics

receptor (IGF1R; CD221); arrestin $\beta1$ (ARRB1); MAPK (ERK)ERK could help increase the efficacy of IGF1R- targeting molecules. Therapeutic antibodies that exert their effect through IGF1R also can downregulate expression of the receptor, which could impede therapeutic efficacy over time. In Ewing's sarcoma cell lines treated with Pfizer Inc.'s IGF1R antibody figitumumab, IGF1R downregulation was mediated by ERK activation caused by ARRB1 recruitment. In the same cell lines, figitumumab and an ERK inhibitor decreased cell viability compared with figitumumab alone. Next steps include extending the studies to animal models of other cancers. Pfizer discontinued a Phase III trial of figitumumab in non-small cell lung cancer (NSCLC) in 2010. At least 14 companies have IGF1R antagonists	ndication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
receptor (IGF1R; CD221); arrestin β1 (ARRB1); MAPK (ERK)ERK could help increase the efficacy of IGF1R- targeting molecules. Therapeutic antibodies 	Cancer				
from preclinical to marketed to treat various indications.	Sarcoma	receptor (IGF1R; CD221); arrestin β1 (ARRB1);	ERK could help increase the efficacy of IGF1R- targeting molecules. Therapeutic antibodies that exert their effect through IGF1R also can downregulate expression of the receptor, which could impede therapeutic efficacy over time. In Ewing's sarcoma cell lines treated with Pfizer Inc's IGF1R antibody figitumumab, IGF1R downregulation was mediated by ERK activation caused by ARRB1 recruitment. In the same cell lines, figitumumab and an ERK inhibitor decreased cell viability compared with figitumumab alone. Next steps include extending the studies to animal models of other cancers. Pfizer discontinued a Phase III trial of figitumumab in non-small cell lung cancer (NSCLC) in 2010. At least 14 companies have IGF1R antagonists or antibodies in development stages ranging from preclinical to marketed to treat various	Patent and licensing status undisclosed	Zheng, H. <i>et al. Proc. Natl. Acad. Sci.</i> <i>USA</i> ; published online Nov. 27, 2012; doi:10.1073/pnas.1216348110 <b>Contact:</b> Leonard Girnita, Karolinska Institute and Karolinska University Hospital, Stockholm, Sweden e-mail: leonard.girnita@ki.se

Published online Dec. 20, 2012