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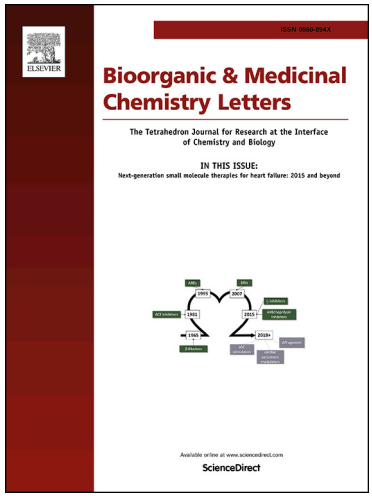

Discovery and lead identification of quinazoline-based BRD4 inhibitors

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Graphical Abstract

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Discovery and lead identification of quinazoline-based BRD4 inhibitors

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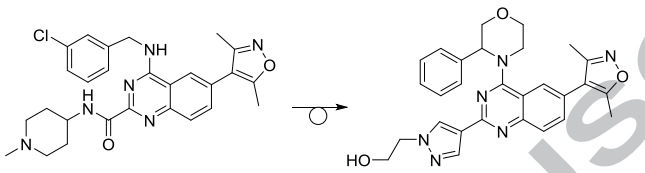
Shyh-Ming Yang[a,*], Daniel J. Urban[a], Makoto Yoshioka[b], Jeffrey W. Strovel[b], Steven Fletcher[c], Amy Q. Wang[a], Xin Xu[a], Pranav Shah[a], Xin Hu[a], Matthew D. Hall[a], Ajit Jadhav[a], David J. Maloney[a,*]



34 (early lead)
BRD4 K_d= 80 nM
MV4-11 viability IC_{50}= 1.02 μM
mouse PK, $AUC_{(0\text{-}inf)}$= 54 (h•ng/mL)

65 (new lead)
BRD4 K_d= 66 nM
MV4-11 viability IC_{50}= 1.10 μM
mouse PK, $AUC_{(0\text{-}inf)}$= 4494 (h•ng/mL)
oral bioavailability (*F*%)= 51%