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Identification of 3-substituted-6-(1-(1*H*-[1,2,3]triazolo[4,5-*b*]pyrazin-1-yl)ethyl)quinoline derivatives as highly potent and selective mesenchymal-epithelial transition factor (c-Met) inhibitors via metabolite profiling-based structural optimization

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compound 1

 IC_{50} = 1.45 nM (enzyme) IC_{50} = 24.7 nM (H1993) IC_{50} = 11.8 nM (SNU-5)

Metabolite profiling-based structural optimization

Filtration by SAR studies

racemate 14

$$\begin{split} & IC_{50} = 0.6 \text{ nM (enzyme)} \\ & IC_{50} = 1.1 \text{ nM (H1993)} \\ & IC_{50} = 2.0 \text{ nM (SNU-5)} \\ & T_{1/2} = 3.7 \text{ h} \quad F = 12.1\% \end{split}$$

Xenograft models H1993 TGI (10mg/kg): 90.8% SNU-5 PTR (3mg/kg): 87.9%

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