314 Hypoxia Inducible Factor 1 (HIF-1) Inhibitors

Asset Overview

Product Type	Small Molecule
Indication	Oncology
Current Stage	Target Identification
Target(MoA)	Hypoxia Inducible Factor 1 (HIF-1) Inhibitors
Brief Description	• Developed compounds inhibiting the activity of HIF-1 • The HIF-1 inhibitor compounds are designed around the scaffold of naturally occurring metabolite eudistidine • Compounds eudistidine A (IC_{50} 75uM) and C have been shown to disrupt the HIF-1/p300 interaction in vitro. Eudistidine C has also inhibited growth of malaria at low micromolar concentrations
Organization	National Institutes of Health

Differentiation

□ **HIF-1 as a therapeutic target**

- Hypoxia is a characteristic of many solid tumors resulting from accelerated cellular proliferation and inadequate vascularization
- HIF-1 is a transcription factor critical for maintaining cellular homeostasis in, and adaptively responding to, low oxygen environments
- HIF-1 becomes activated through binding to the transcriptional co-activator protein p300
- Disruption of the HIF-1/p300 interaction could potentially modulate HIF-1 activity
- In the past two decades, efforts have been devoted to seek or develop HIF inhibitors. A few inhibitors interfere directly with mRNA or protein of HIF-1 and/or HIF-2, the dimerization of α and β subunits, or the interaction of HIF with its co-activators; but most of them are indirect inhibitors or have multiple activities. Thus, developing more specific HIF inhibitors is still a major challenge
- Some HIF inhibitors have been clinically trialled for treating solid tumors. Unfortunately, up to now, no drugs directly inhibiting HIFs have been approved for treating cancer patients due to safety or limited therapeutic efficacy
- IDF-11774 (Ildong): Phase I for solid tumors, HIF-1alpha inhibitor, HSP70 identified as a target protein

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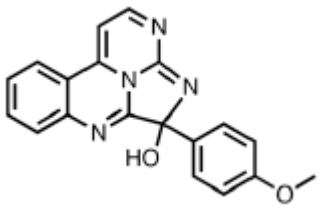
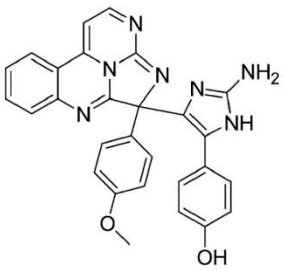
Key Data

Chemical Structure



eudistidine A



eudistidine C

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Intellectual Property

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Country	US

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