

# PFI-E3H1: A chemical handle for GID4

Version 3.0 (24<sup>th</sup> April 2025)

Web link for more details: <https://www.thesgc.org/chemical-handles/pfi-e3h1>

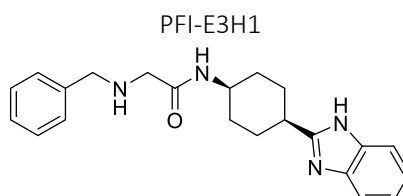
## Overview

Pfizer in collaboration with the SGC have developed PFI-E3H1 which is a chemical handle for the E3 ligase GID4. PFI-E3H1 binds potently to GID4 with  $K_D = 0.65 \mu\text{M}$  (SPR). Further characterization identifies C26 as a suitable site to attach an exit vector.

## Summary

Chemical handle name	PFI-E3H1
Negative control compound	NA
Target(s) (synonyms)	GID4 (glucose-induced degradation protein 4 homolog)
Recommended <i>in vitro</i> assay concentration	N/A
Suitability for <i>in vivo</i> use and recommended dose	Handles are not for <i>in vivo</i> use
Publications	<a href="https://pubmed.ncbi.nlm.nih.gov/38773330/">https://pubmed.ncbi.nlm.nih.gov/38773330/</a> <a href="https://pubmed.ncbi.nlm.nih.gov/38516600/">https://pubmed.ncbi.nlm.nih.gov/38516600/</a>
Related chemical probe	PFI-7
<i>In vitro</i> assay(s) used to characterise	SPR
Cellular assay(s) for target-engagement	nanoBRET
ChemicalProbes.org	

## Chemical Handle Structure and Use



SMILES: C1C[C@@H](CC[C@@H]1c1nc2ccccc2[nH]1)NC(CNCc1ccccc1)=O

InChiKey: NJJOKGWZQVSMR-HDICACEKSA-N

Molecular weight: 362.2

Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C.

DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use

Dissolution: Soluble in DMSO up to 50 mM; use only 1 freeze/thaw cycle per aliquot

## Chemical Handle Profile

*In vitro* Potency & Selectivity: PFI-E3H1 binds GID4 with a  $K_D$  of 650 nM (by SPR).

*Potency in Cells and Cellular Target Engagement:* Cell treatment with PFI-E3H1 resulted in a dose-dependent decrease in Gid4 binding to MPGLWKS peptide with  $IC_{50}$  of 2.5  $\mu\text{M}$ .