

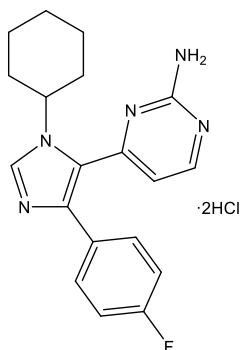
**Catalog # 10-4692**

**PF-670462 dihydrochloride**

CAS# 950912-80-8

4-[3-Cyclohexyl-5-(4-fluorophenyl)imidazol-4-yl]pyrimidin-2-amine 2HCl

Lot # FBS3035



PF-670462 is a potent inhibitor of casein kinase 1 $\epsilon/\delta$  (CK1 $\epsilon$ , IC<sub>50</sub> = 7.7 nM; CK1 $\delta$ , IC<sub>50</sub> = 14 nM).<sup>1</sup> It is a circadian clock modifier that caused robust phase delays in rats<sup>1</sup> and Cynomolgus monkeys<sup>2</sup>. PF-670462 caused nuclear retention of the clock protein PER resulting in period lengthening in a phase-specific manner that was dependent on CK1 $\delta$  inhibition and not CK1 $\epsilon$ .<sup>3</sup> It improved cognitive performance and reduced amyloid load in various mouse models of Alzheimer's disease.<sup>4-6</sup> PF-670462 slowed the progression of and increased survival of chronic lymphocytic leukemia in mice alone and in combination with Ibrutinib.<sup>7</sup>

- 1) Badura *et al.* (2007), *An Inhibitor of Casein Kinase  $\epsilon$  Induces Phase Delays in Circadian Rhythms under Free-Running and Entrained Conditions*; J. Pharmacol. Exp. Ther. **322** 730
- 2) Sprouse *et al.* (2009), *Inhibition of casein kinase I  $\epsilon$ /delta produces phase shifts in the circadian rhythms of Cynomolgus monkeys*; Psychopharmacology (Berl) **204** 735
- 3) Meng *et al.* (2010), *Entrainment of disrupted circadian behavior through inhibition of casein kinase 1 (CK1) enzymes*; Proc. Natl. Acad. Sci. USA **107** 15240
- 4) Adler *et al.* (2019), *Therapeutic Targeting of Casein Kinase 1 $\delta/\epsilon$  in an Alzheimer's Disease Mouse Model*; J. Proteome Res. **18** 3383
- 5) Sundaram *et al.* (2019), *Inhibition of casein kinase 1 $\delta$  improves cognitive-affective behavior and reduces amyloid load in the APP-PS1 mouse model of Alzheimer's Disease*; Sci. Rep **9** 13743
- 6) Mahoney *et al.* (2021), *Inhibition of casein kinase 1 $\delta/\epsilon$  improves cognitive performance in adult C57BL/6J mice*; Sci. Rep. **11** 4746
- 7) Janovska *et al.* (2018), *Casein kinase 1 is a therapeutic target on chronic lymphocytic leukemia*; Blood **131** 1206

**PHYSICAL DATA**

Molecular Weight:	337.40
Molecular Formula:	C <sub>19</sub> H <sub>22</sub> Cl <sub>2</sub> FN <sub>5</sub>
Purity:	>98% by HPLC
	NMR: (Conforms)
Solubility:	DMSO (25 mg/mL)
Physical Description:	Off-white solid
Storage and Stability:	Store as supplied at -20°C for up to 2 years from the date of purchase. Solutions in DMSO may be stored at -20°C for up to 3 months.

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