Innovations
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Wee1 Kinase Inhibitors for the Treatment of Medulloblastoma and Acute Myeloid Leukemia (AML)

Product

WEE1 Inhibitors

Indication

Medulloblastoma and AML

Value Propositions

- Reduced cytotoxicity compared to AZD1775
- Improved potency and WEE1 selectivity

Market

- $400 Million—US AML Therapeutic Market in 2020 (15% CAGR through 2026)

Intellectual Property

- Patent pending*
- Available for licensing

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Ref# CU4399H

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Background on CU4399H

Cell cycle checkpoints monitor for defects in the division program of a cell and halt cell cycle progression, inducing apoptosis, in the setting of DNA damage. Cancer cells possessing a deficient G1 checkpoint allows these cells to accumulate mutations and propagate irregularities that are favorable to cancer formation. These cells are reliant on the G2 checkpoint to prevent excessive DNA damage that leads to apoptosis via mitotic catastrophe. Wee1 is a tyrosine kinase that is a critical component of the G2 checkpoint. The small molecule Wee1 inhibitor AZD1775 has demonstrated synergistic activity with DNA-damaging agents against several cancer types but has found to be a potent cytotoxicity as a single agent. There is also concern that AZD1775 has off-target effects that may exacerbate therapy-related adverse effects in cancer patients.

Technical Innovation

Dr. Philip Reigan and his team at the University of Colorado have developed Wee1 kinase inhibitors (substituted pyrazolopyrimidines) for the treatment of brain tumors such as medulloblastoma and blood cancers such as AML that uncouple WEE1 inhibition from the potent cytotoxicity observed with AZD1775. In addition, their compounds have shown improved WEE1 inhibitory potency and increased WEE1 selectivity compared with AZD1775. Their team has developed these compounds using structure-activity relationships that have elucidated the structural features required for WEE1 inhibition. The inventors have found that their compounds are effective in combination with cisplatin at reducing tumor growth *in vivo,* which they have demonstrated in xenograft mouse models.

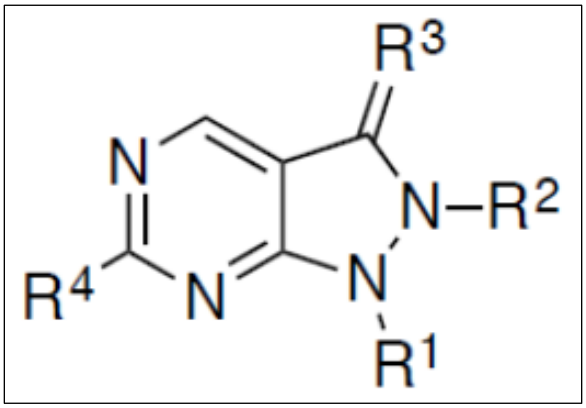

Figure: The substituted pyrazolopyrimidines have the general structure as shown.

Resources & Documents:

***US, EU, CA, AUS, JP patents pending:** "1,2,3,6-Subsituted Pyrazolopyrimidine Inhibitors of WEE1 Kinase"—Filed 2020.*