Development of a selective CDK2-E inhibitor in CCNE-aberrant cancers

Yuan J. Choi, Steve Wang, Andrew V., Victoria Brown, Neil Bluford, Yeon S. Choh, Jun Guo, Megan Hatton, Joseph Kim, Tim LaBranche, Riahd Lobbard, Emanuela Penilla, Emily Roszalnaghy, Michelle Maynard, Phil Ramsden, Grace Sha, Faith Stephens, Richard Vargas, Raduan Halaby, Doug Wilson, Rob Weissman

1Blueprint Medicines Corporation, Cambridge, Massachusetts, USA

Results

Table 1: BLU2298, BLU1564, and BLU2256 are selective, potent CDK2 inhibitors spanning CDK sub-targets including CDK7.

Conclusions and future directions

- Preclinical data indicate that aberrant CCNE is a predictor of response to CDK2 inhibition.
- Targeting CDK2 in CCNE-aberrant cancer cell lines induces markers of senescence and irreversible growth arrest at G1/S.
- BLU0298, BLU2256, and BLU1564 are selective, potent CDK2 compounds that lead to tumor growth inhibition.
- CDK2 inhibitors show promise as monotherapy and are under evaluation in combination with CDK4/6-targeted therapies or chemotherapy.
- Taken together these results provide scientific rationale for advancing this class of compounds toward clinical development in CCNE-aberrant cancers.

References


Acknowledgments

Acknowledgments for this work were provided by Blueprint Medicines Corporation. Blueprint Medicines Corporation reviewed and provided feedback on the poster. The authors are grateful to members of the Blueprint Medicines Development Organization for their hard work and dedication to this research.

Disclosures

The authors declare no conflicts of interest. Blueprint Medicines Corporation provided funding and support for this research. The authors are employees of Blueprint Medicines Corporation. The authors declare no competing interests.

Presented at AACR 2021, April 9–14, 2021, Virtual Format. Please contact medinfo@blueprintmedicines.com for permission to reprint and/or distribute.