

New Generation Bitopic Bcr-Abl Inhibitors

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INVENTION NOVELTY

Scientists at UCSF have developed a novel class of BCR-ABL inhibitors that engages two binding sites in BCR-ABL simultaneously. This two-site binding (bitopic) mechanism of action is unprecedented against BCR-ABL, one of the most well-validated targets in oncology.

VALUE PROPOSITION

Classically, inhibitors bind to their targets through singular, well-formed pockets. In the case of chronic myeloid leukemia (CML), a disease characterized by its nearly absolute association with BCR-ABL dependency, the approved drugs directed against BCR-ABL only target a single binding site and cause a mixture of off-target toxicity issues. In addition to the off-target effects, commonly observed resistance mutations preclude the recognition of any single ‘optimal’ therapeutic regiment for CML that is able to universally enable patients to live normal lifespans or achieve a cure.

This novel invention provides the following advantages:

- ▶ Increased potency (especially against resistance mutations such as the T315I mutant in CML)
- ▶ Higher target specificity due to avidity (active site AND allosteric site recognition needed for binding)
- ▶ Potentially reduced cardio-toxicity
- ▶ Deeper target inhibition at BCR-ABL, potentially increasing the proportion of responsove patients

TECHNOLOGY DESCRIPTION

UCSF researchers have synthesized two classes bitopic inhibitors of BCR-ABL that have been verified for their biochemical activity against ABL1 kinase domain and validated for their ability to specifically inhibit BCR-ABL signaling in cells. Further optimization can be done in both the ligand and linker components and additional biological validation will be needed prior to clinical trial.

LOOKING FOR PARTNERS

To develop and commercialize this technology.

STAGE OF DEVELOPMENT

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OTHER INFORMATION

CATEGORIZED AS

- ▶ [Biotechnology](#)
- ▶ [Health](#)

RELATED CASES

2022-024-0

Pre-clinical

RELATED MATERIALS

► [IFITM proteins assist cellular uptake of diverse linked chemotypes](#)

DATA AVAILABILITY

Available upon request

PATENT STATUS

Patent Pending

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