BGB-16673 (BTK-targeted Protein Degrader)

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BGB-16673 is an investigational drug for which safety and efficacy have not been established.

WHAT IS BGB-16673?

BGB-16673 is an orally available Bruton's tyrosine kinase (BTK) targeting chimeric degradation activation compound (CDAC) designed to promote the degradation, or breakdown, of both wildtype and mutant forms of BTK, including those that commonly result in resistance to BTK inhibitors in patients who experience progressive disease.

THE TARGET: BTK

BTK is a protein that plays an important role in the development and maturation of immune system B-cells.[1]	**Several types of blood cancer cells exhibit too much BTK activity, contributing to the cancer cells' survival and growth.[2]**	**BTK inhibitors, which reduce BTK activity, were first introduced in 2013 and play a critical role in the treatment of certain B-cell malignancies.[2]**	**BTK mutations can lead to resistance to current inhibitor treatments making them less effective. There is a need for therapies that overcome BTK inhibitor resistance.[3-5]**

HOW BGB-16674 WORKS

BGB-16673 is designed to trigger elimination of the BTK protein, which can prevent BTK activity and interrupt its functions as a binding partner.[6] BGB-16673 is intended to be active against both unmutated and mutated forms of BTK.[6-7]

DEVELOPMENT HIGHLIGHTS

BGB-16673 is being evaluated in the **ongoing phase 2 CaDAnCe study (NCT05006716) of patients with B-cell malignancies**, including relapsed or refractory chronic lymphocytic leukemia (CLL) and R/R mantle cell lymphoma (MCL), indications for which the U.S. Food and Drug Administration has granted BGB-16673 Fast Track Designations.

BGB-16673 is the most advanced BTK degrader in the clinic, **with more than 500 patients enrolled across the global clinical development program.**

BGB-16673 DIFFERENTIATION

- In both preclinical and early clinical studies, BGB-16673 appears to work as designed, leading to reduced levels of BTK protein in target tissues and anti-cancer effects.[6-9]
- Promising clinical responses have been seen in extensively pretreated patients with a range of B-cell malignancies, including in patients with covalent and non-covalent BTK inhibitor-resistant disease.[8,9]
- Based on its profile, BGB-16673 has the potential to be a treatment for CLL patients progressing after BTK inhibitor emergent resistance and may also have the potential to move to earlier lines of therapy and additional disease indications.

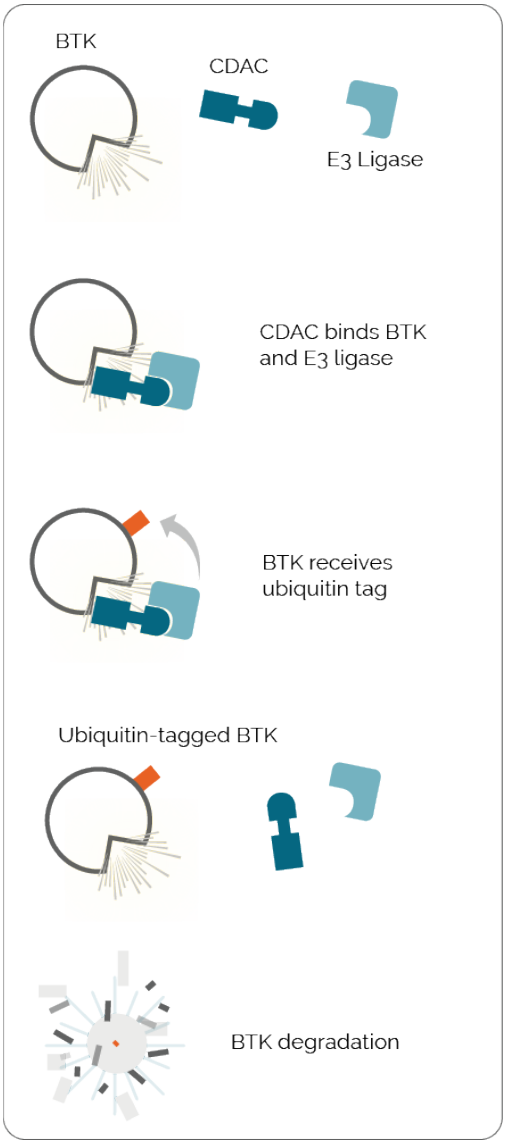
WHAT IS THE CDAC PLATFORM?

CDAC stands for Chimeric Degradation Activation Compound. BeOne's proprietary CDAC platform **leverages unique chemistry and expertise to develop investigational protein degraders** that work on a variety of targets.

Protein degraders function as molecular matchmakers, recruiting components of the cellular recycling machinery to act on target proteins that they would otherwise ignore. **One end of each degrader is designed to bind the disease-target protein. The other end binds to a cellular factor called E3 ligase,** which engages the cellular recycling process (the proteasome pathway) to eliminate the target.

Through the CDAC platform, **BeOne is designing degraders with selectivity for E3 ligases that are absent in tissues commonly associated with toxicity of cancer therapies.** This has the potential to preferentially eliminate the target protein in the tumor tissue and not in the normal tissues, where it may be serving a desired function.

BeOne's protein degraders **are engineered to minimize unwanted immunomodulatory drug (IMiD) activity** typical of some other degrader drugs that engage a more common E3 ligase.



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