BGB-16673
BTK-targeted Chimeric Degradation Activation Compound (CDAC)

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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, an investigational drug, is an orally available Bruton's tyrosine kinase (BTK)-targeted protein degrader and is the first candidate from our Chimeric Degradation Activation Compound (CDAC) platform.

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]

BGB-16673: HOW IT WORKS

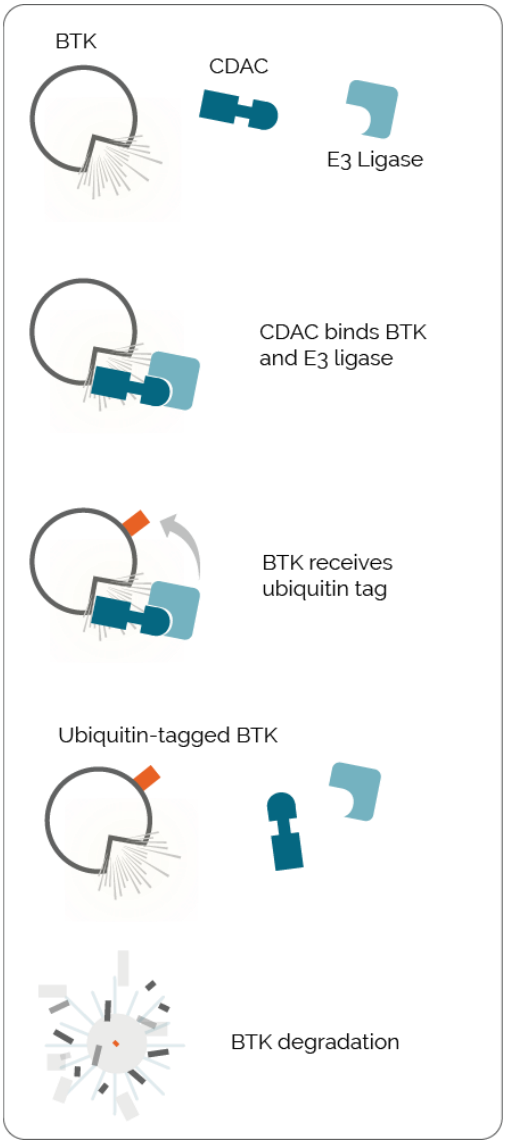
- BGB-16673 triggers elimination of the BTK protein, which can prevent BTK activity and interrupt its functions as a binding partner.[6]
- BGB-16673 is active against both unmutated and mutated forms of BTK.[6-7]

BGB-16673 DIFFERENTIATION and DEVELOPMENT HIGHLIGHTS

- 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]
- We have seen promising clinical responses 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]
- BGB-16673 **CaDAnCe** program clinical trials are ongoing, including a phase 2 trial of patients with relapsed or refractory chronic lymphocytic leukemia (CLL), an indication for which BGB-16673 has been granted U.S. FDA Fast Track Designation.[10,11]
- Emerging data from ongoing and future CaDAnCe trials will provide further insights regarding the efficacy and tolerability of this investigational drug.
- Based on its profile, we believe BGB-16673 has potential as a treatment for CLL patients progressing after BTK inhibitor emergent resistance and that it may also have the potential to move to earlier lines of therapy and additional disease indications.

WHAT ARE CDACs?

- CDAC stands for Chimeric Degradation Activation Compound
- CDACs 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 CDAC molecule is designed to bind the disease-target protein -- BTK in the case of BGB-16673. The other end binds to a cellular factor called E3 ligase, which engages the cellular recycling process (the proteasome pathway) to eliminate the target.



CDAC PLATFORM ADVANTAGES

- We have developed platform chemistry and expertise to generate investigational CDACs that work on a variety of targets. Our CDACs are engineered to minimize unwanted immunomodulatory drug (IMiD) activity typical of some other degrader drugs that engage a more common E3 ligase.
- We are designing CDACs 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.

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