

# Sonrotoclax (BGB-11417)

## BCL2 Inhibitor

Disclaimer: This asset is intended for U.S. media professionals only.  
Sonrotoclax is an investigational drug for which safety and efficacy have not been established.

### WHAT IS SONROTOCLAX?

Sonrotoclax is an investigational small molecule B-cell lymphoma 2 (BCL2) inhibitor with a differentiated profile

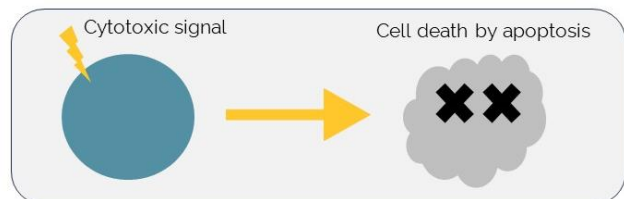
### THE TARGET: BCL2

- BCL2 is a member of a family of proteins that regulate a cellular death program called apoptosis. Certain family members activate the cell death program, while BCL2 opposes the initiation of apoptosis and promotes cellular survival.
- Many cancer cells make abnormally high amounts of BCL2, which effectively overrides the natural apoptosis protocol, allowing the cancer cells to survive despite signals such as DNA damage that would otherwise trigger cancer cell destruction.

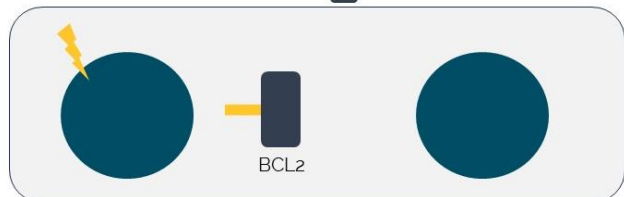
### SONROTOCLAX: HOW IT WORKS

- Sonrotoclax binds BCL2 and prevents it from blocking the apoptosis signals. Therefore, when sonrotoclax is present, the BCL2 blockade is removed, and the cellular self-destruction protocol proceeds to destroy cancer cells.
- Many cancer drugs act by triggering apoptosis, so blocking BCL2 with an inhibitor like sonrotoclax has the potential to work in concert with those cancer drugs to make them more effective.

Normal cell responds to toxic signal with programmed cell death



Cancer cell with excessive BCL2 ( ) avoids apoptosis and survives



Sonrotoclax ( ) inhibits BCL2 and restores cell death program



## DIFFERENTIATION: BEST-IN-CLASS POTENTIAL

- The first-generation BCL2 inhibitor was approved for the treatment of patients with certain types of leukemia, but its use can be limited due to drug-related toxicities, burdensome monitoring, and resistance mutations.<sup>1,2,3</sup>
- Sonrotoclax was designed to improve upon the first-generation BCL2 inhibitor in several ways. *In preclinical studies:*<sup>4</sup>
  - Sonrotoclax is more potent, meaning less of the drug is needed to achieve the same level of inhibition of BCL2, which may contribute to efficacy and tolerability.
  - Sonrotoclax is more selective, meaning it shows a higher degree of preference for BCL2 versus other family members, making it less likely to bind to the wrong target, which may lead to a favorable safety and side effect profile.
  - Sonrotoclax has a shorter half-life, meaning it does not last as long in the body, potentially reducing or avoiding toxic drug accumulation, which may allow improved dosing protocols.
  - Sonrotoclax inhibits both unaltered BCL2 as well as a commonly mutated version of BCL2 that is resistant to inhibition by the first-generation BCL2 inhibitor.
  - ***Disclaimer: The clinical significance of data based on non-clinical studies has not been established.***

## DEVELOPMENT HIGHLIGHTS

- Sonrotoclax is currently in clinical development in various hematologic cancers, both in combinations with other oncology medicines and on its own as a monotherapy.
- CELESTIAL-TNCLL, a Phase 3 trial of sonrotoclax in combination with zanubrutinib in patients with treatment naïve chronic lymphocytic leukemia, is underway.<sup>5</sup>

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<sup>1</sup> Montero J, Letai A. Cell Death Differ. 2018;25:56–64

<sup>2</sup> Opat et al. EHA Presentation. 2022. Abstract number: P687

<sup>3</sup> Tausch, Eugen et al. "Venetoclax resistance and acquired BCL2 mutations in chronic lymphocytic leukemia." Haematologica vol. 104,9 (2019): e434-e437.

<sup>4</sup> Hu N et al. Cancer Res. 2020;80(16 Suppl):Abstract 3077, AACR 2020

<sup>5</sup> <https://clinicaltrials.gov/study/NCT06073821>