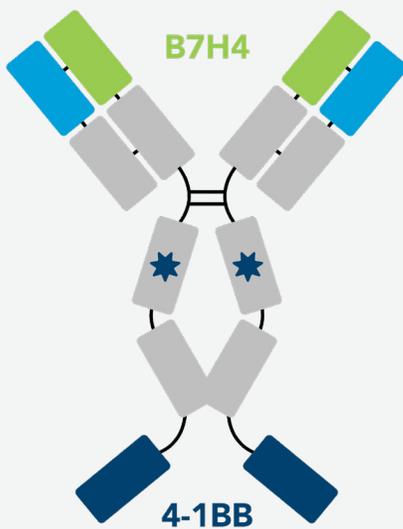


# About CLN-418

CLN-418 is a bispecific immune activator with contingent activation of the 4-1BB pathway upon binding to the tumor-associated antigen (TAA), B7H4. B7H4 is highly expressed on the surface of tumor cells with limited expression on normal cells. B7H4 is a member of the B7 family of immune regulatory proteins that includes many of the “master switches” of T cell activation, such as PD-L1. It binds to both T cells and natural killer (NK) cells and functions as an immune checkpoint. 4-1BB is a key costimulatory molecule for both T and NK cells. Activation of the 4-1BB pathway has the potential to induce a potent anti-tumor immune response.

## CLN - 418



### ABOUT THE MOLECULE

CLN-418 is a bispecific immune activator that stimulates the 4-1BB pathway only upon binding the tumor target B7H4.\*

- Dual B7H4 binding sites enable avidity for enhanced binding to tumor cells
- Silenced Fc domain avoids unwanted binding to immune cells expressing Fc-gamma receptors
- 4-1BB activation dependent on B7H4 crosslinking avoids non-specific immune agonism

### WHERE IT'S BEING STUDIED

CLN-418 is being studied in an ongoing Phase 1, open-label, multicenter trial evaluating safety, tolerability, pharmacokinetics and anti-tumor activity in patients with advanced solid tumors.

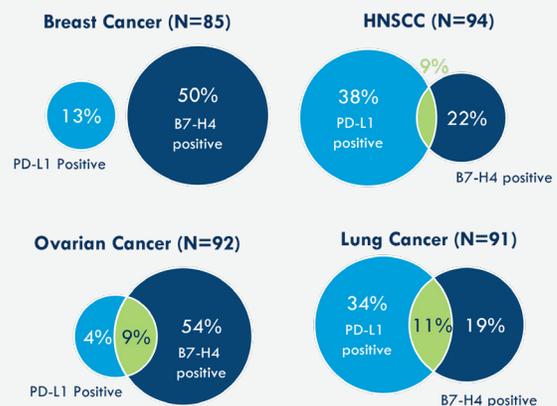
### WHAT IS 4-1BB?

4-1BB (also known as CD137) is a costimulatory molecule whose activation increases proliferation and cytotoxicity of T and NK-cells. Monoclonal antibodies targeting 4-1BB have shown the ability to powerfully stimulate T cells and mediate anti-tumor activity but have also demonstrated challenging toxicity issues.

### WHAT IS B7H4?

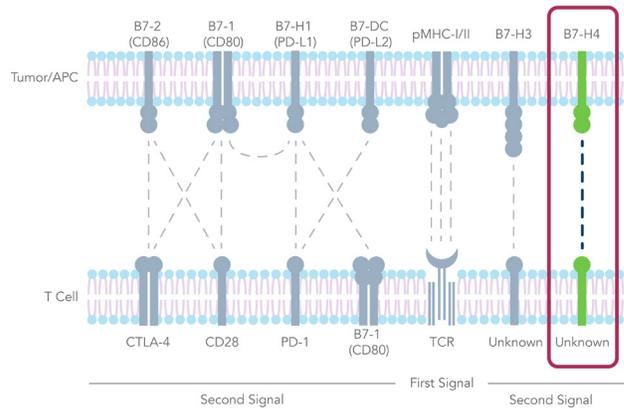
B7H4 is a TAA and immune checkpoint that inhibits T cell activation and correlates with poor prognosis in multiple tumor types. B7H4 is an attractive target for cancer immunotherapy due to high expression on multiple tumor types, with low expression on normal tissue. B7H4 expression demonstrates minimal overlap with PD-L1, potentially addressing tumor types for which immunotherapy exhibits limited efficacy, including cold tumors.

### Minimal overlap with PD-L1 expression<sup>1</sup>



## CLN-418'S TARGETS AND MECHANISM OF ACTION

B7H4, a TAA and a member of the B7 family of ligands, provides an ideal target to harness the potential of T and NK-cell activation through 4-1BB. CLN-418 activates 4-1BB signaling only when bound to both B7H4 and 4-1BB, limiting 4-1BB activation to the tumor and potentially reducing toxicities.\*



## CLN-418'S POTENTIAL

CLN-418 is the only B7H4 x 4-1BB bispecific in clinical development and is positioned favorably relative to alternate approaches due to its potential for single-agent activity, applicability to multiple indications, high tumor selectivity, predicted broad therapeutic index and potential in PD-L1 low tumors.

## PRECLINICAL EVIDENCE

In preclinical experiments, CLN-418 has robust anti-tumor activity in mouse syngeneic tumor models and the ability to trigger a memory response capable of inhibiting tumor growth upon rechallenge. These preclinical efficacy signals support the potential for CLN-418 to have single-agent activity.<sup>1</sup>

\*Based on preclinical data.

### REFERENCE

1. Bao M. Innovative B7H4 x CD3 & B7H4 x 4-1BB bispecifics for solid tumor therapies. Presented at: 13th Annual Summit World Multispecifics; September 20, 2022; Boston, MA. Accessed January 6, 2023. <https://www.harbourbiomed.com/upload/files/202210191155013408.pdf>

