CARNA BIOSCIENCES

News Release

June 16, 2025
Carna Biosciences, Inc.

Docirbrutinib, a next generation BTK inhibitor, demonstrates promising and durable responses in patients with B-cell malignancies in Phase 1b study

- *In a poster presentation at EHA 2025, preliminary data from the ongoing Phase 1b study of docirbrutinib showed a favorable safety profile with encouraging clinical tumor responses in heavily pretreated patients with B-cell malignancies*
- *Promising and durable responses were observed in heavily pretreated chronic lymphocytic leukemia (CLL) patients*
- *Phase 1b dose expansion is underway to determine recommended phase 2 dose (RP2D)*

Carna Biosciences, a clinical-stage biopharmaceutical company focusing on the discovery and development of innovative therapies to treat serious unmet medical needs, announces that preliminary safety and efficacy results from the ongoing Phase 1b study of docirbrutinib (AS-1763) was presented at the European Hematology Association (EHA) 2025 Congress on June 13, 2025.

Docirbrutinib, an investigational small molecule drug designed to non-covalently inhibit Bruton's tyrosine kinase (BTK) in a highly selective manner, is currently under development for the treatment of patients with CLL and other B-cell malignancies who have developed resistance or are intolerant to at least two prior lines of systemic therapy including a covalent BTK inhibitor (cBTKi) (NCT05602363).

The poster was presented by Nitin Jain, MD, Professor of Leukemia, The University of Texas MD Anderson Cancer Center and all the other principal investigators at the participating clinical sites.

Key presentation highlights:

Poster title: Preliminary Results from a Phase 1b Study of Non-covalent Pan-mutant BTK Inhibitor Docirbrutinib (AS-1763) in Patients with Previously Treated B-cell Malignancies

- Docirbrutinib is a highly selective, pan-mutant non-covalent BTK inhibitor (ncBTKi) which inhibits both wild-type (WT) and various c/ncBTKi-resistant mutations including C481x, T474x and L528x.
- Docirbrutinib demonstrated strong anti-tumor activities in B-cell lymphoma cell lines harboring resistant BTK mutations including a kinase-dead BTK L528W.

- The poster presented preliminary results of docirbrutinib from the ongoing Phase 1b study in B-cell malignancies.
- As of the data cut-off of May 7, 2025, 25 patients (17 CLL, 3 follicular lymphoma, 2 mantle cell lymphoma (MCL), 2 Waldenström macroglobulinemia (WM), and 1 marginal zone lymphoma) were enrolled to 5 dose levels.
- The dose escalation part was completed with no dose-limiting toxicities, and the maximum tolerated dose was not reached.
- The dose expansion was opened with three dose levels (300, 400 and 500 mg BID) and is currently ongoing.
- Docirbrutinib demonstrated a favorable safety profile with no discontinuation due to drug-related adverse events.
- Promising and durable responses were observed in heavily pretreated CLL patients.
    - ORR: 54% (7/13) for CLL, 100% (2/2) for MCL and 50% (1/2) for WM, with responses continuing to deepen.
    - Durable responses achieved: 3 CLL and 1 MCL patients with >12 months and 1 WM with >6 months.

About docirbrutinib (AS-1763)

Docirbrutinib is a highly selective, orally bioavailable, non-covalent inhibitor of both the wild type and mutant BTKs for the treatment of CLL and other B-cell malignancies. Covalent BTK inhibitors including ibrutinib are key therapeutic options for patients with B-cell malignancies. However, patients are reported to develop resistance during the treatment due to substitution of cysteine residue at 481 position with serine (C481S - 2 -mutation) in BTK, which reduces the efficacy of the covalent BTK inhibitors. In addition, the emergence of other types of resistance mutations to non-covalent BTK inhibitor, recently approved pirtobrutinib, has been reported. Docirbrutinib potently inhibited both wild type and those mutant BTKs, strongly suggesting that docirbrutinib will be a new therapeutic option for treating patients with B-cell malignancies both having wild type and resistance mutations in BTK. Carna is advancing development of docirbrutinib as a next-generation BTK inhibitor. The Phase 1b study of docirbrutinib is being conducted in the U.S.(NCT05602363).

Contact:
Corporate Planning
Carna Biosciences, Inc.
TEL: +81-78-302-7075
https://www.carnabio.com/english/