CARNA BIOSCIENCES

# News Release

December 9, 2025

Carna Biosciences, Inc.

## Updates from the ongoing Phase 1b study and new preclinical findings of the next-generation BTK inhibitor, docirbrutinib (AS-1763), presented at the 67th American Society of Hematology Annual Meeting

Carna Biosciences, a clinical-stage biopharmaceutical company focused on discovering and developing innovative therapies to address serious unmet medical needs, announced that two posters on docirbrutinib (AS-1763) were presented at the 67th American Society of Hematology (ASH) Annual Meeting & Exposition.

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 chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) and B-cell non-Hodgkin lymphomas (B-cell NHL) who have developed resistance or are intolerant to at least two prior lines of systemic therapy, including existing covalent/non-covalent BTK inhibitors.

**[Presentation Details]**

Publication Number: 3892

Poster Title: Docirbrutinib (AS-1763), a novel non-COVALENT pan-mutant BTK inhibitor, demonstrates durable clinical responses in patients with previously treated B-cell malignancies: Data from an ongoing Phase 1b study

**Key presentation highlights:**

- Prof. Nitin Jain, MD, Department of Leukemia, The University of Texas MD Anderson Cancer Center, who leads the clinical study, presented the poster on the updated results from the ongoing Phase 1b study.
- As of the data cut-off of October 17, 2025, 38 patients who received at least two prior lines of systematic therapy were enrolled: 23 CLL/SLL, 5 mantle cell lymphoma (MCL), 3 Waldenström macroglobulinemia (WM), and 7 other NHL patients.
- In the dose escalation part, docirbrutinib was well tolerated with no dose-limiting toxicities observed at doses ranging from 100 to 500 mg BID (twice daily), and the maximum tolerated dose was not reached. The dose expansion part consists of Cohort 1 for patients with CLL/SLL, Cohort 2 for patients with NHL, and Cohort 3 for patients previously treated with pirtobrutinib. Each cohort

includes 2 or 3 dose levels, with Cohort 1 and 2 starting at 300 mg BID, and Cohort 3 starting at 400 mg BID.

- Docirbrutinib demonstrated a favorable safety profile with no drug-related atrial fibrillation or hypertension reported. Grade ≥3 treatment-related adverse events (TEAEs) were reported in 13% of patients.
- Promising and durable responses were observed in heavily pretreated CLL/SLL, MCL and WM patients.
  - CLL/SLL: All patients experienced reduction in tumor size. Among 20 efficacy-evaluable CLL/SLL patients, 8 patients achieved partial response (PR) or partial response with lymphocytosis (PR-L) (overall response rate (ORR) 40%). Of those, 5 patients achieved >12-months duration of response (DoR). Stable disease (SD) was observed in 11 patients, 8 of whom remain on treatment with responses continuing to deepen. Among the 8 patients remaining on treatment, 5 patients showed more than 40% (40.1-49.9%) reduction in tumor size (response: ≥50% reduction in tumor size). Enrollment at 400 mg BID is ongoing.
  - MCL in Cohort 2: The ORR was 2 out of 2 patients (100%), with 1 patient achieving a complete response (CR). All patients remain on treatment.
  - WM: The ORR was 3 out of 3 patients (100%), and all patients remain on treatment.
- Phase 1b dose expansion part is underway to determine recommended phase 2 dose (RP2D).

Publication Number: 5077

Poster Title: Docirbrutinib (AS-1763), a novel non-COVALENT BTK inhibitor, demonstrates efficacy in BTK inhibitor-resistant mutant cells

**Key presentation highlights:**

- The in vitro studies indicated that docirbrutinib preferentially binds to an inactive conformation of BTK. Similar to other inhibitors targeting inactive states, docirbrutinib has been confirmed as a BTK inhibitor characterized by slow off-rate* profile.
- Previously, we demonstrated that docirbrutinib is effective against both wild-type and multiple resistant BTK mutants in in-vitro enzymatic assays. In the present study, we generated human diffuse large B-cell lymphoma (DLBCL) cell lines harboring these BTK mutations and demonstrated that docirbrutinib is effective in the cellular level as well.
- Furthermore, in combination with venetoclax**, docirbrutinib induced marked cell death in BTK-mutant OCI-Ly10 cells as well as primary CLL samples.

*Slow off-rate: Indicator used in pharmacology and biochemistry to describe the slow dissociation (prolonged binding) of a drug from its target after binding. Drugs with a slow off-rate are generally expected to exhibit higher efficacy.

**Venetoclax: B-cell/CLL lymphoma 2 (BCL-2) inhibitor widely used to treat hematologic malignancies including CLL and Acute Myeloid Leukemia (AML).

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.

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