CARNA BIOSCIENCES

News Release

December 9, 2024
Carna Biosciences, Inc.

Carna announces a poster presentation on preliminary results from ongoing Phase 1b study for its non-covalent BTK inhibitor docirbrutinib (AS-1763) at American Society of Hematology Annual Meeting

Carna Biosciences, a clinical-stage biopharmaceutical company focusing on the discovery and development of innovative therapies to treat serious unmet medical needs, announces that a poster on preliminary results from Phase 1b study of docirbrutinib (AS-1763) was presented at the 66th American Society of Hematology (ASH) Annual Meeting & Exposition on December 7, 2024.

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) and other B-cell malignancies who have developed resistance or are intolerant to at least two prior lines of systemic therapy including existing covalent/non-covalent BTK inhibitors (NCT05602363). Phase 1b study consists of two parts, dose escalation and expansion parts. Dosing in the dose expansion part was initiated in October in parallel with the dose expansion part to accelerate the development timeline.

Key presentation highlights:

Poster presentation, titled, “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”, presented by Nitin Jain, MD, Department of Leukemia, The University of Texas MD Anderson Cancer Center, includes:

- Docirbrutinib is a wild-type and pan-mutant non-covalent inhibitor potently inhibiting both wild-type and various mutant BTKs including C481S, covalent BTK inhibitor resistant mutation and T474I and L528W, non-covalent inhibitor (pirtobrutinib) resistant mutations. Therefore, it is expected to be effective in patients who have developed resistance to covalent/non-covalent BTK inhibitors.
- The poster presented the preliminary safety, efficacy and pharmacokinetics (PK) data of 15 patients enrolled in this clinical study as of the data cut-off of Oct 18, 2024. 15 patients include 10 CLL, 3 follicular lymphoma, 1 mantle cell lymphoma (MCL) and 1 marginal zone lymphoma.
- In the dose-escalation part, no dose-limiting toxicities were observed at doses of 100-500 mg BID, and the maximum tolerated dose has not been reached yet.
- No treatment discontinuation due to AEs and no drug-related atrial fibrillation or hypertension were reported.

- 6 out of 9 efficacy evaluable patients (67%) with CLL who have been previously treated with covalent BTK inhibitor or BTK inhibitor plus venetoclax achieved Partial Response (PR) or PR-Lymphocytosis (PR-L).
- The exposures at ≥300 mg BID exceeded the IC_{90} throughout the dosing interval, and all 4 CLL patients (100%) receiving ≥300 mg BID achieved PR or PR-L.
- One MCL patient was assigned to 400 mg BID dose level and achieved PR.
- These preliminary data indicate a favorable safety and PK profile and clinical responses in heavily pretreated patients with B-cell malignancies, including covalent BTK inhibitors and venetoclax.
- Based on preclinical and clinical data, a new cohort has been added to allow pirtobrutinib-pretreated patients in the dose-expansion part of the amended protocol.

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. and dosing in the dose expansion part was initiated in October 2024. Preliminary data from the study which was presented at the European Hematology Association (EHA) 2024 Hybrid Congress in June 2024 by Prof. Nitin Jain, MD, Department of Leukemia, MD Anderson, who leads the study showed a favorable safety and PK profile as well as promising efficacy in patients with CLL who have been heavily pretreated with systemic therapies including covalent BTK inhibitors and BCL2 inhibitor.

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