CARNA BIOSCIENCES

News Release

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Carna Biosciences, Inc.

Carna announces a poster presentation featuring preclinical findings of 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 featuring preclinical findings of docirbrutinib (AS-1763) using blood samples obtained from chronic lymphocytic leukemia (CLL) patients treated with docirbrutinib 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 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.

Key presentation highlights:

Poster presentation, titled, “Impact of Docirbrutinib (AS-1763) Treatment in CLL: Preclinical Data and Early Clinical Biomarkers”, presented by Natalia Timofeeva, MD, Department of Experimental Therapeutics, The University of Texas MD Anderson Cancer Center, includes:

- Docirbrutinib, a pan-mutant non-covalent BTK inhibitor, showed equipotent activity against wild-type and multiple BTK mutants in biochemical and cellular assays.
- Docirbrutinib potently inhibited proliferation of BTK mutant cell lines.
- Demonstrated robust inhibition of B-cell antigen receptor (BCR) pathway signaling in both treatment-naïve (TN) and relapsed/refractory (R/R) primary CLL cells.
- Increased sensitivity to B cell lymphoma-2 (BCL-2) and Myeloid cell leukemia 1 (MCL-1) inhibitors, even in diverse BTK-mutant and BCL-2 mutant backgrounds.
- In a dose-escalation trial, docirbrutinib treatment reduced BCR pathway biomarkers, including chemokines CCL3/CCL4, autophosphorylation of BTK and phosphorylation of phospholipase C-γ2 (PLCγ2).

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.

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