CARNA BIOSCIENCES

News Release

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Carna Biosciences, Inc.

Carna announces a poster presentation featuring preclinical characterization of its non-covalent BTK inhibitor 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 characterization of AS-1763 was presented at the 65th American Society of Hematology (ASH) Annual Meeting & Exposition on December 9, 2023.

AS-1763, 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 a covalent BTK inhibitor.

Key presentation highlights:

Poster presentation, titled, “Characterization and Preclinical Evaluation of AS-1763, an oral, Potent and Selective Noncovalent BTK inhibitor, in Chronic Lymphocytic Leukemia”, presented by Shady I. Tantawy, MD, Department of Experimental Therapeutics, The University of Texas MD Anderson Cancer Center, includes:

- AS-1763 is a non-covalent, highly selective, wildtype and pan-mutant BTK inhibitor.
- AS-1763 showed potent inhibitory activities against covalent/non-covalent BTKi-resistant mutations (C481x, T474x, T316A, L528x) in enzymatic and cellular assays.
- AS-1763 induces cell death, a characteristic commonly observed in BTK inhibitors, in both untreated and relapsed/refractory CLL samples.
- AS-1763 inhibits B-cell activation and calcium release in CLL cells similar to ibrutinib and pirtobrutinib.
- AS-1763 treatment leads to an elevation in mitochondrial superoxide production in CLL lymphocytes.
- In CLL samples that had Bcl-2 mutations, AS-1763 enhanced cytotoxicity elicited by venetoclax or AZD5991.
- In CLL harboring WT BTK, combination of AS-1763 with ibrutinib was highly effective.
- Phase 1b clinical trial has been initiated with AS-1763.

About AS-1763

AS-1763 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 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 inhibitors including pirtobrutinib have been reported. AS-1763 potently inhibited both wild type and those mutant BTKs, strongly suggesting that AS-1763 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 AS-1763 as a next-generation BTK inhibitor.

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