CARNA BIOSCIENCES

News Release

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Carna Biosciences, Inc.

Carna announces a poster presentation on design of ongoing Phase 1b study for 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 on Phase 1b study design of AS-1763 was presented at the 65th American Society of Hematology (ASH) Annual Meeting & Exposition on December 10, 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, “Trial in Progress: A Phase 1b Study of AS-1763, an Oral, Potent and Selective Noncovalent BTK Inhibitor, in Patients with Previously Treated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma or Non-Hodgkin Lymphoma”, presented by Nitin Jain, MD, Department of Leukemia, The University of Texas MD Anderson Cancer Center, includes:

- An open-label, multi-center, Phase 1b study of oral AS-1763 in patients with chronic lymphocytic leukemia (CLL)/ small lymphocytic lymphoma (SLL) and other B-cell non-Hodgkin lymphoma (NHLs) who have failed or are intolerant to at least two prior lines of systemic therapy (NCT05602363).
- Key inclusion criteria: *age ≥18 years; B-cell malignancy including CLL/SLL, WM, MCL, MZL, or FL; failed or intolerant to ≥2 prior lines of systemic therapy; prior therapy with a covalent BTKi is permitted; ECOG performance status 0 to 2.*
- Key exclusion criteria: *transformed disease (e.g., Richter’s transformation); refractory to transfusion support; requiring therapeutic anticoagulation with warfarin; known CNS involvement by systemic lymphoma; active uncontrolled autoimmune cytopenia; prior treatment with noncovalent BTKi.*
- The study consists of two parts, dose escalation (3+3 design, 6 dose levels starting from 100 mg BID, up to 27 patients) and expansion (2 cohorts, 3 dose levels, up to 83 patients) parts.
- Dose escalation part: *the primary objective is to determine the maximum tolerated dose/dose-limiting toxicity. Key secondary endpoints include the evaluation of safety profile and tolerability,*

pharmacokinetics properties, and preliminary anti-tumor activity based on overall response rate (ORR).

- Dose expansion part: *the primary objective is to assess ORR. Key secondary objectives are to investigate safety, tolerability, and pharmacokinetic profiles and to evaluate best overall response, duration of response, progression-free survival and overall survival.*
- The recommended phase 2 dose (RP2D) will be determined based on all the data generated in the study.

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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