CARNA BIOSCIENCES

News Release

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Carna Biosciences, Inc.

Carna Initiates Dosing in Dose Expansion Part of Phase 1b Study of AS-1763, a Next Generation, Pan-Mutant Inhibitor of BTK

Carna Biosciences, a clinical-stage biopharmaceutical company focusing on the discovery and development of innovative therapies to treat serious unmet medical needs, announces that it has initiated dosing in patients in the dose expansion part of the Phase 1b study of AS-1763.

AS-1763, a small molecule drug designed to non-covalently inhibit both the wild type and mutant Bruton's tyrosine kinase (BTK) in a highly selective manner, is being investigated in patients with B-cell malignancies in the Phase 1b study in the U.S. led by Prof. Nitin Jain, MD, Department of Leukemia, The University of Texas MD Anderson Cancer Center. This study consists of two parts: dose escalation part and dose expansion part. The dose escalation part of the study has been conducted since August 2023 as a multi-center clinical study. While the maximum tolerated dose has not been reached yet in the ongoing dose escalation part, Carna decided to start the dose expansion part ahead of its original schedule in parallel with the dose escalation part with the approval by the principal investigators of the study. This decision comes based on the encouraging preliminary data from the ongoing dose escalation part including favorable safety, tolerability and high overall response rate as well as favorable plasma concentrations that suggest therapeutic effects.

The dose expansion part consists of three Cohorts: Patients with CLL/SLL will be assigned to Cohort 1, patients with B-cell NHL to Cohort 2 and pirtobrutinib-pretreated patients to Cohort 3. Three dose levels were chosen for Cohort 1 and Cohort 2 and two dose levels were chosen for Cohort 3. Carna plans to swiftly enroll patients in each cohort to evaluate safety, efficacy and pharmacokinetic (PK) of AS-1763 and determine the recommended phase 2 dose (RP2D).

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 inhibitor, recently approved pirtobrutinib, has 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.

The Phase 1b study of AS-1763 is being conducted in the U.S. and preliminary data from the study was

presented at the European Hematology Association (EHA) 2024 Hybrid Congress in June 2024 by Prof. Nitin Jain, MD, Department of Leukemia, The University of Texas MD Anderson Cancer Center, who leads the study. Preliminary data 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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