CARNA BIOSCIENCES

News Release

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Carna Biosciences, Inc.

AS-1763, a next generation BTK inhibitor, demonstrates encouraging safety and efficacy in patients with B-cell malignancies in Phase 1b study

- *In a poster presentation at EHA 2024, preliminary data from the ongoing Phase 1b study of AS-1763 showed a favorable safety and pharmacokinetics (PK) profile with encouraging clinical tumor responses in heavily pretreated patients with B-cell malignancies*
- *The overall response rate (ORR) was 57% in 7 patients with chronic lymphocytic leukemia (CLL) who have been previously treated with covalent BTK inhibitor (cBTKi) or cBTKi plus venetoclax at the time of the data cut-off (April 19, 2024)*
- *2 of 3 patients with CLL (67%) for 100 mg BID and 2 of 2 patients with CLL (100%) for 300 mg BID achieved partial response (PR) or PR-lymphocytosis (PR-L)*
- *The dose escalation with higher doses is still ongoing*
- *Based on the promising results, Carna plans to initiate the dose expansion part later this year*

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 safety and efficacy results from ongoing Phase 1b study of AS-1763 was presented at the European Hematology Association (EHA) 2024 Hybrid Congress on June 14, 2024.

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 (BTKi). AS-1763 is a wild-type and pan-mutant BTK inhibitor exhibiting inhibitory activities against emerging resistance mutations (C481x, T474x and L528x) in BTK to both approved covalent and non-covalent BTK inhibitors in preclinical studies.

The poster titled “Preliminary safety and efficacy results from a Phase 1b study of oral non-covalent BTK inhibitor AS-1763 in patients with previously treated B-cell malignancies” was presented by Prof. Nitin Jain, MD, Department of Leukemia, The University of Texas MD Anderson Cancer Center. The first patient in this study was dosed in August 2023, and the preliminary data, until April 2024, of the first 4 dose cohorts (100 - 400 mg BID) including safety, pharmacokinetics (PK) profile and clinical responses in heavily pretreated patients with B-cell malignancies, including covalent BTK inhibitors and B-cell

lymphoma 2 protein (BCL2) inhibitor, was disclosed. Dose escalation part with higher doses is ongoing.

Poster Presentation Highlights:

Study Design

- Open-label, multi-center, Phase 1b study of oral AS-1763 in patients with CLL/small lymphocytic lymphoma (SLL) and other B-cell non-Hodgkin lymphomas who have failed or are intolerant to at least two prior lines of systemic therapy (NCT05602363).
- Two parts: dose escalation part (3+3 design) and dose expansion part.
- Twice daily (BID) oral administration.
- Key Inclusion Criteria: B-cell malignancy including CLL/SLL, Waldenström macroglobulinemia, mantle cell lymphoma (MCL), marginal zone lymphoma, or follicular lymphoma (FL). Prior therapy with a covalent BTKi is permitted.
- Key Exclusion Criteria: Prior treatment with non-covalent BTKi such as pirtobrutinib and nemtabrutinib.

Safety

- As of April 19, 2024, 12 patients (9 CLL, 2 FL, 1 MCL) were enrolled to 4 dose levels (100 - 400 mg BID).
- No dose-limiting toxicities were observed to date.
- There has been no treatment discontinuation due to adverse events (AEs).
- No drug-related atrial fibrillation or bleeding-related events were reported.
- The dose escalation with higher doses is ongoing.

PK

- The plasma concentrations of AS-1763 was increased in a dose dependent manner based on available PK data of 100 - 300 mg BID dose levels.
- The maximum plasma concentrations exceeded the calculated IC_{90} for BTK at all doses, and the exposures at 300 mg BID exceeded the IC_{90} throughout dosing interval.

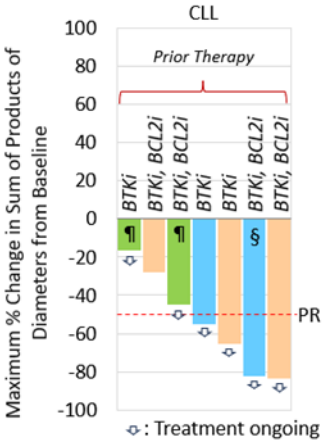
Efficacy

- At the time of the data cut-off (April 19, 2024), 9 patients at 100 - 300 mg BID dose levels were evaluable for tumor response (7 CLL, 2 FL).
- Notably, AS-1763 demonstrated an overall response rate (ORR)* of 57% among 7 patients with CLL who have been heavily pretreated with systemic therapies, including covalent BTKi and BCL2 inhibitor.
  - ✓ 2 of 3 patients with CLL (67%) for 100 mg BID and 2 of 2 patients with CLL (100%) for 300 mg BID achieved partial response (PR) or PR-lymphocytosis (PR-L).
  - ✓ 2 of 2 patients with CLL at 200 mg BID experienced stable diseases (SD) with 16 - 45% reduction in tumor size.

*ORR includes patients with the best response of PR and PR-L.

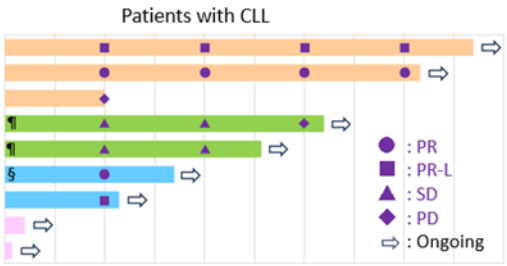
Efficacy of AS-1763 in CLL patients

a) Tumor response



b) Treatment duration and response

Prior cBTKi	Prior BCL2i	Pts	Doses
✔ Combo		CLL	100 mg BID
✔	-	CLL	100 mg BID
✔	✔	CLL	100 mg BID
✔	✔	CLL	200 mg BID
✔	-	CLL	200 mg BID
✔	✔	CLL	300 mg BID
✔	-	CLL	300 mg BID
✔ Combo		CLL	400 mg BID
✔	✔	CLL	400 mg BID



Data cutoff date of 19 April 2024.
Combo: Combination therapy

¶ BTK C481S detected centrally by next generation sequencing (CLL mutation panel).
§ BTK C481S detected locally by Sanger sequencing.

Conclusion

Overall, preliminary data from the ongoing study of AS-1763 indicate a favorable safety and PK profile and clinical responses in heavily pretreated patients with B-cell malignancies, including covalent BTKis and BCL2 inhibitor.

“These preliminary safety and efficacy data in the ongoing Phase 1b study are encouraging to further investigate the usefulness of AS-1763 in patients who have failed or are intolerant to covalent BTK inhibitors,” said Prof. Nitin Jain, MD, Department of Leukemia, MD Anderson, the lead investigator of the study.

Based on the promising results, the company plans to initiate the dose expansion part later this year.

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.

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