CARNA BIOSCIENCES

News Release

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Carna Biosciences, Inc.

Carna Announces Positive Results for AS-0871 Phase 1 Single Ascending Dose Clinical Trial

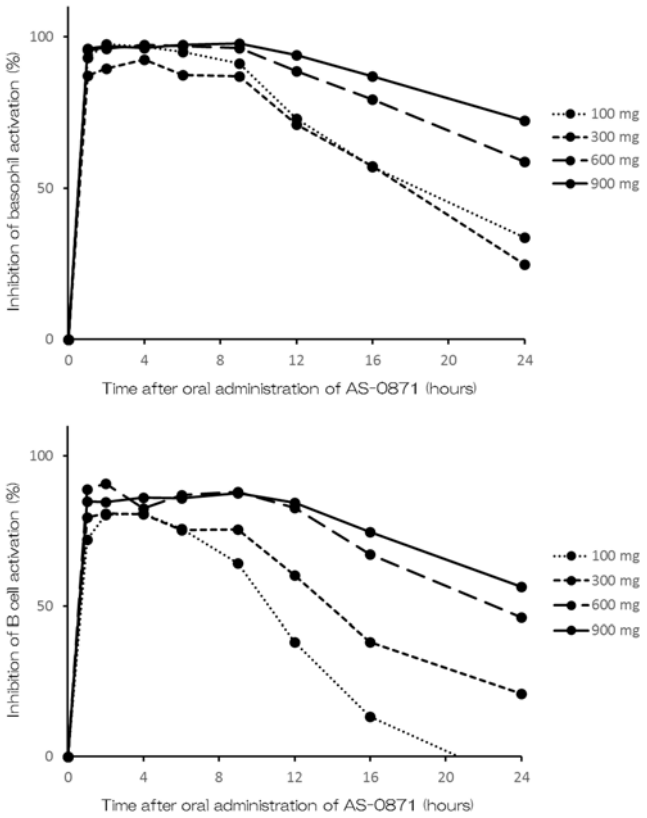
Carna Biosciences, a clinical-stage biopharmaceutical company focusing on the discovery and development of innovative therapies to treat serious unmet medical needs, announces positive results from its Phase 1 oral Single Ascending Dose ("SAD") study of AS-0871, an investigational small molecule drug designed to non-covalently inhibit Bruton's tyrosine kinase (BTK) with high selective profile targeting inflammatory and immune disorders.

The SAD study of the randomized, double-blind, placebo controlled phase 1 trial evaluated the safety, tolerability and pharmacokinetics of AS-0871 in a total of 53 healthy volunteers. The study measured its pharmacodynamics as well. AS-0871 was shown to be safe and well-tolerated at all dose levels tested from 5 mg to 900 mg. There were no serious adverse events reported at all dose levels. The adverse events reported were all mild and transient. AS-0871 demonstrated a favorable pharmacokinetic profile with dose-dependent exposures (Cmax and AUC) and elimination half-life ranging 7-9 hours after administration at 100 mg or above. Pharmacodynamic effects following administration of AS-0871 were investigated as the study's secondary objective. The results demonstrated that subjects who received AS-0871 showed dose proportional inhibitions in basophil and B-cell activations, and significant and sustained inhibitory effects were observed at 100 mg and above. Basophils play crucial roles in allergic inflammation, through secretion of proinflammatory chemical mediators including histamine and leukotrienes. Aberrant BCR signaling in B cells is considered to promote autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus, through production of autoantibodies. In the phase 1 SAD study, oral administration of AS-0871 achieved therapeutic plasma levels needed to inhibit B cells and basophils activation, suggesting that AS-0871 has a potential to become a new treatment option for inflammatory diseases.

Based on the favorable results of the phase 1 SAD study, Carna is preparing to initiate the phase 1 Multiple Ascending Dose (MAD) study in the second half of 2021 with a new drug formulation.

<Summary of results>

- Safety and tolerability: Well-tolerated at all doses (5 mg to 900 mg) with no serious adverse events reported.
- Pharmacokinetic parameters (100 – 900 mg): Cmax 980 - 5746 ng/mL, AUC_{last} 7086 - 64105 ng・h/mL, half-life 7.3 - 9.0 h
- Pharmacodynamic effects (100 – 900 mg): Inhibitory effects of AS-0871 on basophils and B-cell activation are shown below.



About BTK

BTK is a Tec family tyrosine kinase expressed in B cells and myeloid cell populations including monocytes, macrophages, neutrophils, basophils and mast cells. BTK has a crucial role in B cell antigen receptor (BCR) signaling during B cell development and activation. In autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus, aberrant BCR signaling is considered to promote diseases through production of autoantibodies. In addition to BCR signaling, BTK mediates downstream signaling of the Fcγ receptors in myeloid cells to produce inflammatory cytokines such as IL-6 and TNF-α, which would aggravate RA symptoms. In allergic diseases, BTK is a critical enzyme for Fcε receptor (FcεR) signaling in mast cells and basophils to regulate release of chemical mediators such as histamine and leukotrienes. Therefore, BTK is being paid attention as an attractive therapeutic target for the treatment of autoimmune diseases and allergic diseases.

About AS-0871

AS-0871 is an investigational small molecule drug designed to bind non-covalently to Bruton's tyrosine kinase (BTK) with high selectivity, currently in development for inflammatory and immune disorders. In in vitro experiments, AS-0871 strongly inhibited B cell and basophil activation and suppressed production of inflammatory cytokines such as TNF-α, IL-17, MCP-1 and IL-6 in human blood. Oral administration of AS-0871 demonstrated the excellent therapeutic effects in a mouse model of collagen-induced arthritis. In addition, AS-0871 prevented IgE-mediated skin inflammation in mice and rats.

AS-0871 is a highly selective and non-covalent BTK inhibitor discovered by Carna, being developed for the treatment of inflammatory and immune disorders.

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