NEWS RELEASE

British Journal of Cancer: Zurletrectinib is a next-generation TRK inhibitor with strong intracranial activity against NTRK fusion-positive tumors with on-target resistance to first-generation agents

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BEIJING--(BUSINESS WIRE)-- InnoCare announced British Journal of Cancer, part of leading science journal Nature, recently published a paper entitled "Zurletrectinib is a next-generation TRK inhibitor with strong intracranial activity against NTRK fusion-positive tumors with on-target resistance to first-generation agents" . The journal concluded that zurletrectinib is a novel, highly potent next-generation TRK inhibitor with higher in vivo brain penetration and stronger intracranial activity than other next-generation agents.

The paper pointed out that zurletrectinib displayed strong potency against TRKA, TRKB, and TRKC WT kinases, as well as acquired resistance mutations TRKA G595R and TRKA G667C. Zurletrectinib was more active than other FDA approved or clinically tested first generation (larotrectinib) and next-generation (selitrectinib and repotrectinib) TRK inhibitors against most TRK inhibitor resistance mutations. Similarly, zurletrectinib (1 mg/kg BID) inhibited tumor growth in xenograft models derived from NTRK fusion-positive cells at a dose 30 times lower when compared to selitrectinib.

The paper further demonstrated that, in a central nervous system (CNS) penetrant pharmacokinetic study in SD rats, zurletrectinib showed improved ability to penetrate the blood-brain barrier, reaching the brain more effectively than selitrectinib and repotrectinib. Zurletrectinib's increased brain penetration was also translated into improved antitumor activity. In an orthotopic mouse glioma xenograft model carrying the TRKA G598R/G670A resistance mutation, zurletrectinib (15 mg/kg) significantly improved the survival of mice harboring orthotopic NTRK fusion-positive, TRK-mutant gliomas (median survival = 41.5, 66.5, and 104 days for selitrectinib, repotrectinib, and

zurletrectinib respectively; P < 0.05), showing superior efficacy compared to repotrectinib (15 mg/kg) and selitrectinib (30 mg/kg) (P=0.0384 and 0.0022, respectively), with an excellent safety profile.

The corresponding authors of the paper are Dr. Alexander Drilon, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA, and Dr. Emiliano Cocco, Department of Biochemistry and Molecular Biology, University of Miami, Miller School of Medicine, FL, USA. The first author is Paolo Roa, Department of Biochemistry and Molecular Biology, University of Miami, Miller School of Medicine, FL, USA. Full text can be found in **https://www.nature.com/articles/s41416-024-02760-1** .

InnoCare is accelerating the registrational trial of zurletrectinib in China. The clinical study with zurletrectinib has covered NTRK fusion adult patients, adolescent patients and pediatric patients. Zurletrectinib has demonstrated good efficacy and safety profile, and overcome acquired resistance to the first generation TRK inhibitors, bringing benefit to patients who failed prior TRKi therapy.

About InnoCare

InnoCare (HKEX: 09969; SSE: 688428) is a commercial stage biopharmaceutical company committed to discovering, developing, and commercializing first-in-class and/or best-in-class drugs for the treatment of cancer and autoimmune diseases with unmet medical needs in China and worldwide. InnoCare has branches in Beijing, Nanjing, Shanghai, Guangzhou, Hong Kong, and United States.

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