Data published on ANG4043, anti-HER2 monoclonal antibody for treatment of brain metastases

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Angiochem, a clinical stage biotechnology company creating and developing drugs that cross the blood-brain barrier, today announced the publication in *Molecular Cancer Therapeutics* demonstrating that ANG4043, a peptide-monoclonal antibody (mAb) conjugate, entered the brain at therapeutic concentrations, resulting in significantly prolonged survival in mice. The antibody is directed against HER2, which is the protein targeted by Herceptin®. Because the mAb is conjugated to Angiopep-2, it is recognized by the LRP1 receptor and takes advantage of a receptor-mediated transcytosis mechanism to cross the BBB. This proprietary technology has been clinically validated with ANG1005, a peptide-paclitaxel conjugate currently in Phase II studies. The data published today shows that Angiochem's technology to cross the BBB is applicable to biologics such as mAbs.

In the publication entitled "ANG4043, a Novel Brain-penetrant Peptide-mAb Conjugate, is Efficacious against HER2-positive Intracranial Tumors in Mice," Angiochem researchers show that ANG4043 binds LRP1 receptors while retaining the pharmacological properties of the native anti-HER2 mAb, including high affinity HER2 binding and anti-proliferative activity in HER2-expressing cells. In vivo, ANG4043 achieves therapeutic brain concentrations in healthy mice and in mice bearing intracranial HER2+ tumors, which are targeted by ANG4043. In this HER2+ intracranial tumor model, treatment with ANG4043 (15 mg/kg IV, twice-weekly) increased median survival time by 78% (80

days compared to 45 days for control).

"To the best of our knowledge, the data reported in this publication represent the first known peptide-monoclonal antibody conjugate for oncology that has been shown to cross the BBB using a clinically-validated technology. For biologics and more specifically for mAbs, brain penetration is the major obstacle for the treatment of CNS diseases," said Jean Paul Castaigne, M.D., President and CEO of Angiochem. "These data build upon previously reported Phase 2 clinical data with ANG1005, our peptide-paclitaxel drug conjugate, demonstrating indication of efficacy in primary and secondary brain tumors."

Jean Lachowicz, Ph.D., CSO at Angiochem, continued, "LRP-1 receptor-mediated transcytosis, can be leveraged to create brain penetrant mAbs, as demonstrated in the study published today, as well as Angiopep antibody-drug conjugates, which have been successfully generated by Angiochem. While our current data has focused on demonstrating the potential of Angiochem's technology in oncology, its applicability extends beyond oncology to include neurodegenerative diseases as well."

More information: angiochem.com/sites/default/fi … es/publications/AACR%202013%20ANG4043.pdf

Provided by Angiochem