Interim Phase 2 Data for Hexavalent OX40 Agonist Combination Therapy in First-Line HNSCC Demonstrate Potential Benefit Over PD-1 Monotherapy

Elpiscience's partner Inhibrx recently announced positive interim Phase 2 results for INBRX-106, a hexavalent OX40 agonist, in combination with pembrolizumab as a first-line treatment for head and neck squamous cell carcinoma (HNSCC).

Data showed that in first-line HNSCC patients with high PD-L1 expression, the combination treatment group achieved a confirmed objective response rate (cORR) of 44.0%, approximately double that observed with PD-1 monotherapy (21.4%). Three complete responses (CRs) were observed in the combination arm. Peripheral blood analyses of combination-treated subjects also demonstrated enhanced T-cell expansion and immune activation, while the overall safety profile remained manageable. These results further support the mechanistic potential of INBRX-106 to enhance the activity of immune checkpoint inhibitors and reinforce the clinical relevance of the OX40 costimulatory pathway in cancer immunotherapy.

The Phase 2 portion of the HexAgon study is designed to evaluate the safety and efficacy of INBRX-106 in combination with pembrolizumab versus pembrolizumab monotherapy in first-line patients with treatment-naïve, PD-L1 positive (CPS $\geqslant$ 20) metastatic or unresectable recurrent Head and Neck Squamous Cell Carcinoma (HNSCC). A total of 68 patients were enrolled and the study is being conducted at over 80 sites in the United States, Europe and Asia. The interim analysis was based on data from 53 patients representing the evaluable population for confirmed response, including 25 patients in the combination arm and 28 patients in the monotherapy arm.

Interim Phase 2 findings included:

- **Approximately doubled cORR:** In the preliminary confirmed response-evaluable population, the combination arm achieved a cORR of 44.0% (11/25), compared with 21.4% (6/28) in the pembrolizumab monotherapy arm, representing a 22.6% absolute increase in cORR.
- **Superior depth of response:** Responding patients in the combination arm demonstrated deeper tumor reductions overall, with the majority achieving target lesion shrinkage exceeding 50%; notably, three patients in the combination arm achieved a complete response (CR), while no complete responses were observed with pembrolizumab alone.

- **Significant enhancement of systemic T-cell expansion and immune activation:** Peripheral blood analysis showed robust CD8+ and CD4+ T-cell proliferation in the combination arm, with up to a 15-fold increase in peripheral CD8+ and CD4+ T-cell proliferation and up to a four-fold increase in activation in INBRX-106 combination-treated patients compared with up to 2.5-fold and 1.5-fold increases, respectively, in those receiving pembrolizumab alone. This further validates the clinical activity of INBRX-106, consistent with the expected mechanism of action of INBRX-106 as a potent T-cell costimulator.
- **Manageable safety profile:** The combination demonstrated a manageable preliminary safety profile consistent with that expected from an immunotherapy combination. The most common treatment-related adverse events were rash, diarrhea, fatigue, and infusion-related reactions, which were predominantly low-grade. No treatment-related deaths were reported in either arm.

Based on these positive results, Inhibrx plans to begin the Phase 3 clinical trials and aims to evaluate INBRX-106 across broader indications to potentially improve the efficacy of checkpoint inhibitors. In addition, Inhibrx is beginning to plan for expansion into the front-line metastatic NSCLC setting, with studies expected to begin in 2027. Inhibrx will also explore combinations with agents that could benefit from T-cell costimulation, such as vaccines, T-cell engagers, and CAR-Ts.

As the Greater China rights holder of INBRX-106 (ES102), Elpiscience has completed two Phase 1 clinical studies of ES102 in patients with advanced solid tumors in China. Data showed that ES102 in combination with Toripalimab demonstrated promising anti-tumor activity and synergistic effects in advanced solid tumors. The company is currently conducting a Phase 2 clinical trial of this combination therapy in advanced NSCLC and plans to further advance the development and commercialization of the product in Greater China based on the clinical data announced in this update.

About INBRX-106 (ES102)

INBRX-106 is a hexavalent agonist targeting OX40 (CD134), a costimulatory receptor on T-cells. The activation of OX40 enhances T cell expansion, differentiation, and memory T-cell generation, and strengthens antitumor immune responses. INBRX-106 (ES102) consists of six OX40 single-domain antibody structures. Its differentiated design facilitates OX40 receptor clustering and enhances the activation of OX40 signaling, enabling immune activation capabilities beyond traditional bivalent antibody approaches.

About Head and Neck Squamous Cell Carcinoma (HNSCC)

HNSCC is a group of cancers arising from mucosal surfaces of the mouth, nose and throat and accounts for approximately 90% of head and neck cancers (HNC). HNC is the seventh most common cancer worldwide. In China, the incidence of HNC continues to rise, with approximately 146,000 new cases and nearly 81,000 deaths annually[1]. Approximately 60% of HNSCC patients present with locally advanced disease, representing a significant therapeutic challenge.

Reference:
[1] Head and Neck Oncology Committee of China Anti-Cancer Association, *China Oncology Discipline Development Report (2023) – Advances in Head and Neck Malignancies Research*.

About Elpiscience

Elpiscience is a clinical-stage biopharmaceutical company dedicated to the development of innovative immunotherapies for oncology and autoimmune diseases. By advancing breakthrough biologics and leveraging global strategic partnerships, Elpiscience has built a differentiated pipeline to deliver transformative treatment solutions for patients worldwide.

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BD inquiries:
BD@elpiscience.com

Media inquiries:
PR@elpiscience.com