信達生物製藥

INNOVENT BIOLOGICS, INC.

(Incorporated in the Cayman Islands with Limited Liability)

(Stock Code: 1801)

VOLUNTARY ANNOUNCEMENT
THE NATIONAL MEDICAL PRODUCTS ADMINISTRATION ACCEPTS THE NEW DRUG APPLICATION AND GRANTS PRIORITY REVIEW DESIGNATION TO IPILIMUMAB INJECTION IN COMBINATION WITH SINTILIMAB AS NEOADJUVANT TREATMENT FOR COLON CANCER

This announcement is made by Innovent Biologics, Inc. (the "**Company**" or "**Innovent**", together with its subsidiaries, the "**Group**") on a voluntary basis to inform the shareholders and potential investors of the Company about the latest business updates of the Group.

The board of directors of the Company (the "**Board**") is pleased to announce that the new drug application ("**NDA**") of ipilimumab injection (anti-cytotoxic T lymphocyte antigen 4 ("**CTLA-4**") monoclonal antibody; R&D Code: IBI310) has been accepted by the Center for Drug Evaluation ("**CDE**") of National Medical Products Administration of China ("**NMPA**") and granted Priority Review designation in combination with sintilimab as neoadjuvant treatment for resectable microsatellite instability-high or mismatch repair deficient ("**MSI-H/dMMR**") colon cancer. This is China's first NDA for a domestic CTLA-4 inhibitor and another milestone strengthening sintilimab's leadership position in cancer immunotherapy.

The NDA acceptance and Priority Review designation are based on results from a randomized, controlled, multicenter, pivotal Phase 3 clinical trial (NeoShot, NCT05890742) which evaluated the safety and efficacy of ipilimumab combined with sintilimab as neoadjuvant therapy and as compared with direct radical surgery for MSI-H/dMMR colon cancer. The primary endpoints are pathologic complete response ("**pCR**") rate and event-free survival (EFS). Interim analysis by the Independent Data Monitoring Committee (IDMC) showed that the NeoShot trial has met its primary endpoint. Detailed results will be presented at future academic conferences or in academic journals.

Previously, the results of a randomized controlled Phase 1b trial evaluating ipilimumab in combination with sintilimab as neoadjuvant treatment for MSI-H/dMMR colon cancer were presented orally at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting[i]. Based on promising Phase 1b results, the CDE has granted Breakthrough Therapy Designation (BTD) for ipilimumab.

- As of February 4, 2024, 101 patients were enrolled and randomized to receive ipilimumab plus sintilimab (n=52) or sintilimab alone (n=49).

- **In the per-protocol population, the pCR rate in the ipilimumab-plus-sintilimab arm was significantly improved compared to the sintilimab-alone arm (80.0% vs 47.7%, p=0.0007).**

- All patients in both treatment arms had R0 resection. With median follow-up of 5.65 months, no patient had disease recurrence.

- At postoperative pathological evaluation, 3.9% of patients with ipilimumab plus sintilimab and 15.9% of patients with sintilimab alone were stage N+. The majority of patients could be relieved from adjuvant treatment according to guidelines.

- Ipilimumab-plus-sintilimab increased neither safety risk compared to sintilimab alone nor risk for subsequent surgery delay or cancellation.

The results of the FOxTROT study suggested that neoadjuvant chemotherapy is not effective in MSI-H/dMMR colon cancer, and the pCR rate is only around 5%[ii]. Immune checkpoint blockade (ICB) therapy targeting PD-1 and CTLA-4 has transformed oncology treatment, ipilimumab with sintilimab as neoadjuvant treatment could increase R0 resection rate, achieve pathological complete response, and relieve majority of patients from adjuvant chemotherapy burdens. This novel treatment is also expected to reduce recurrence rate and improve long-term prognosis, and it is anticipated to benefit MSI-H/dMMR colon cancer patients following the NDA approval. We remain steadfast in our commitment to reinforcing the leadership position in oncology and driving forward treatment solutions through innovation and cooperation.

About Ipilimumab

Ipilimumab (R&D code: 310) is a fully human monoclonal antibody injection independently developed by Innovent. Ipilimumab can specifically bind CTLA-4, thereby blocking CTLA-4 mediated T cell inhibition, promoting T cell activation and proliferation, improving tumor immune response, and achieving anti-tumor effects.[iii]

The NDA for ipilimumab in combination with sintilimab as neoadjuvant treatment for resectable MSI-H/dMMR colon cancer is under the NMPA review and has been granted Priority Review designation.

About Sintilimab

Sintilimab, marketed as TYVYT® (sintilimab injection) in China, is a PD-1 immunoglobulin G4 monoclonal antibody co-developed by Innovent and Eli Lilly and Company. Sintilimab is a type of immunoglobulin G4 monoclonal antibody, which binds to PD-1 molecules on the surface of T cells, blocks the PD-1/PD-Ligand 1 (PD-L1) pathway, and reactivates T cells to kill cancer cells[iv].

In China, sintilimab has been approved and included in the updated National Reimbursement Drug List ("**NRDL**") for seven indications. The updated NRDL reimbursement scope for TYVYT® (sintilimab injection) includes:

- For the treatment of relapsed or refractory classic Hodgkin's lymphoma after two lines or later of systemic chemotherapy;

- For the first-line treatment of unresectable locally advanced or metastatic non-squamous non-small cell lung cancer ("**NSCLC**") lacking epidermal growth factor receptor ("**EGFR**") or anaplastic lymphoma kinase (ALK) driver gene mutations;

- For the treatment of patients with EGFR-mutated locally advanced or metastatic non-squamous NSCLC who progressed after EGFR-tyrosine kinase inhibitor (TKI) therapy;

- For the first-line treatment of unresectable locally advanced or metastatic squamous NSCLC;

- For the first-line treatment of unresectable or metastatic hepatocellular carcinoma with no prior systematic treatment;

- For the first-line treatment of unresectable locally advanced, recurrent or metastatic esophageal squamous cell carcinoma; and

- For the first-line treatment of unresectable locally advanced, recurrent or metastatic gastric or gastroesophageal junction adenocarcinoma.

Furthermore, sintilimab's eighth indication, in combination with fruquintinib for the treatment of patients with advanced endometrial cancer with proficient mismatch repair (pMMR) tumors that have failed prior systemic therapy and are not candidates for curative surgery or radiation, was conditional approved by the NMPA in December 2024. And the NDA for sintilimab in combination with ipilimumab as neoadjuvant treatment for resectable MSI-H/dMMR colon cancer is under the NMPA review and has been granted Priority Review designation.

In addition, two clinical studies of sintilimab have met their primary endpoints:

- Phase 2 clinical study of sintilimab monotherapy as second-line treatment of esophageal squamous cell carcinoma;

- Phase 3 clinical study of sintilimab monotherapy as second-line treatment for squamous NSCLC with disease progression following platinum-based chemotherapy.

By Order of the Board
Innovent Biologics, Inc.
Dr. De-Chao Michael Yu
Chairman and Executive Director

Hong Kong, China,
February 24, 2025

As at the date of this announcement, the Board comprises Dr. De-Chao Michael Yu as Chairman and Executive Director and Mr. Ronald Hao Xi Ede and Ms. Qian Zhang as Executive Directors and Dr. Charles Leland Cooney, Ms. Joyce I-Yin Hsu, Mr. Gary Zieziula, Dr. Shun Lu and Mr. Shuyun Chen as Independent Non-executive Directors.

References

[i] http://abstracts.asco.org/239/AbstView_239_267235.html

[ii] Morton D, et al; FOxTROT Collaborative Group. Preoperative Chemotherapy for Operable Colon Cancer: Mature Results of an International Randomized Controlled Trial. J Clin Oncol. 2023 Mar 10;41(8):1541-1552. DOI: 10.1200/JCO.22.00046.

[iii] Wolchok JD, Saenger Y. The mechanism of anti-CTLA-4 activity and the negative regulation of T-cell activation. Oncologist. 2008;13 Suppl 4:2-9. DOI:10.1634/theoncologist.13-S4-2

[iv] Wang J, et al. Durable blockade of PD-1 signaling links preclinical efficacy of sintilimab to its clinical benefit. mAbs 2019;11(8): 1443-1451. DOI: 10.1080/19420862.2019.1654303.