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 ACCEPTED THE NEW DRUG APPLICATION FOR IBI311 (IGF-1R ANTIBODY) FOR THYROID EYE DISEASE

This announcement is made by Innovent Biologics, Inc. (the "**Company**", 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 Centre for Drug Evaluation ("**CDE**") of the National Medical Products Administration of China ("**NMPA**") has accepted the New Drug Application ("**NDA**") for IBI311, a recombinant anti-insulin-like growth factor 1 receptor ("**IGF-1R**") antibody, for the treatment of thyroid eye disease ("**TED**").

This NDA was accepted based on the positive results of a Phase 3 registration clinical study RESTORE-1 (CTR20223393) in subjects with TED in China. The primary endpoint of the study was successfully met in February 2024. Significant improvements in proptosis, disease activity, and quality of life of subjects were observed in the IBI311 group compared to placebo group. The overall safety profile of IBI311 was favorable, and no new safety signals were identified during the treatment. Detailed results of the RESTORE-1 study will be presented at medical conferences and journals in 2024.

TED is an autoimmune disease that causes progressive inflammation and damage to tissues around the eyes. The annual incidence of TED is estimated to be 16/100,000 in women and 2.9/100,000 in men[1], with the estimated prevalence of 0.1% to 0.3%[2]. Currently, the use of IGF-1R-targeted antibody has been recommended in multiple clinical treatment guidelines worldwide[3, 4, 5]; particularly, IGF-1R-targeted antibody is recommended as first-line therapy for patients with clinically significant proptosis. In China, no new drugs were approved for a long period, and there is an urgent need for effective, safe and accessible treatment options for TED.

IBI311 is the first anti-IGF-1R antibody with NDA submitted in China. IBI311 has demonstrated favorable safety and comprehensive efficacy benefits in the RESTORE-1 registrational study. The Company will work closely with the regulatory authorities, hoping to provide an effective, safe and accessible treatment option for Chinese TED patients.

About Thyroid Eye Disease (TED)

TED is an autoimmune disease involving ocular tissues and is usually associated with Graves' disease ("**GD**") and is the most common orbit-related disease in adults. TED occurs in approximately 25 to 50% of GD patients and can also be seen in other thyroid diseases, and even in euthyroidism[6].

The annual incidence of TED is estimated to be 16/100,000 in female and 2.9/100,000 in male[1], and the estimated prevalence of clinically relevant TED ranges from 0.1% to 0.3%[2]. According to disease severity, it can be divided into mild, moderate and severe. Although TED appears to affect female more often, severe cases occur more frequently in male. Patients aged 30 to 50 years old are most commonly affected, and severe cases occur more frequently in patients over 50 years old[7]. At present, the pathogenesis of TED is not fully understood, but several studies have shown that orbital fibrous present in muscle fibers, and orbital fibrous connective tissue space are key factors leading to orbital soft tissue enlargement in TED[8].

The natural history of TED is divided into active and inactive phases[9]. The most common symptoms are dry eye, ocular gritty, photophobia, lacrimation, diplopia, and pressure behind the eye, while typical signs include upper eyelid retraction, eyelid edema, periorbital and conjunctival edema, and proptosis. TED is usually mild to moderate, and about 3% to 5% of patients with TED are severe, manifesting as severe pain, vision-threatening corneal ulcers, or compressive optic neuropathy[10]. In addition to potentially affecting vision, TED can have an extremely severe impact on the patient's appearance and social functioning and quality of life.

Currently, the first-line treatment option for moderately severe active TED is intravenous glucocorticoid therapy, which results in unsatisfactory improvement of proptosis and systemic side effects, and second-line treatment includes other immunomodulators, which is also associated with risks related to unclear improvement of proptosis and treatment. Teprotumumab, Tocilizumab and Rituximab are recommended by the Chinese Clinical Diagnosis and Treatment Guidelines for Thyroid Eye Disease (2022)[3], the European Group on Graves' orbitopathy (EUGOGO)[4] and the consensus on thyroid eye disease of the American Thyroid Society and the European Thyroid Society[5] as the second-line treatment options for moderate to severe active TED. Teprotumumab targeting IGF-1R is recommended as first-line therapy for patients with clinically significant proptosis.

About IBI311

IBI311 is a recombinant anti-IGF-1R antibody developed by the Company for the treatment of TED. IGF-1R is a transmembrane tyrosine kinase receptor that plays a role in the development, metabolism, and immune regulation, and is overexpressed in OFs, B, and T cells of TED patients[11]. IBI311 can bind IGF-1R, block IGF-1R signaling pathway activation mediated by IGF-1 and other related ligands or agonistic antibodies, reduce the expression of downstream inflammatory factors, thereby inhibiting the synthesis of hyaluronic acid and other glycosaminoglycan caused by OFs activation, as well as related inflammatory reactions including tissue congestion and edema; and inhibit adipocyte cellularization of OFs, thereby reducing the disease activity of patients with TED and improving proptosis, diplopia, ocular congestion and edema among other symptoms and signs.

In May 2024, the NDA for IBI311 was accepted by the NMPA for the treatment of TED.

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

Hong Kong, China,
May 21, 2024

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, Dr. Kaixian Chen, Mr. Gary Zieziula, Dr. Shun Lu and Mr. Shuyun Chen as Independent Non-executive Directors.

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