Noile-Immune Biotech

News Release

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Noile-Immune Biotech, Inc.
https://www.noile-immune.com

Supplemental Comments on the Termination of the License Agreements for NIB102 and NIB103

Noile-Immune Biotech Inc. ("Noile") has today received the notification from Takeda which will result in termination of license agreements for NIB102 and NIB103, and has timely disclosed the information on December 15, 2023.

As a supplemental information sharing for those investors of interests concerning this matter, Noile would like to share our view on some points which may be requested for clarifications.

- **Is this termination related to the FDA's announcement on November 28 regarding the investigation of CAR-T cell therapy?**

Takeda's decision in this instance is unrelated to any FDA announcements or investigations. As commented in our press-release dated December 1, 2023※, the FDA has announced their decisions to initiate investigations into the risks of T-cell malignancies which have been reported as adverse events in some patients treated with CAR-T cell therapies targeting CD19 or BCMA under circumstance of clinical trials or post-marketing environment. The FDA has stated that the overall benefits patients receive from these products continue to outweigh potential risks. However, they are investigating the risk of T-cell malignancies with serious adverse events such as hospitalization or death, and are evaluating if any regulatory measures are necessary.

Similar to the comments made by the FDA regarding current CAR-T cell therapies for hematologic malignancies, Noile believes that the treatment benefits with our next-generation PRIME CAR-T therapies patients receive should outweigh its potential risks. We continue to focus on progressing development of our pipelines while closely monitoring patients' safety including the risk of secondary malignancies, and also to pay attention to future updates given by the FDA.

※https://www.noile-immune.com/dcms_media/other/20231206_Comment_release_from_NIB_CAR-Ttherapy_EN.pdf

- **Press-release mentioned that Takeda focuses on allogeneic cell therapies. What is the difference between autologous and allogeneic CAR-T cell therapies, and are there any connections to the FDA's announcement?**

In an autologous therapy, CAR-T cells are manufactured with immune cells obtained from the patient's own blood and used for treatment, therefore it requires certain time period until administration. On the other hand, an allogeneic therapy has benefits of timely treatment since CAR-T cells are manufactured with immune cells from non-patient donor and thus kept ready for administration when an eligible patient appears. However, as disadvantage, allogeneic cells derived from non-patient donor induce immunological rejections which results in shorter duration of efficacy due to lack of persistency of CAR-T cells. In order to address this issue of disadvantage, several approaches have been considered for allogeneic CAR-T cells to suppress immune rejections including additional genetic modifications such as genome editing. In particular to the secondary tumor risk mentioned by the FDA, allogeneic CAR-T cells

might seem to have a lower risk due to their shorter persistence, however, with various alternations to enhance the efficacy, including prolonged persistence and additional genetic modifications, the relevant risk may not necessarily be lower.

Noile's PRIME technology enhances the therapeutic effect against solid tumors by enabling CAR-T cells to produce CCL19 and IL-7, encouraging the efficient accumulation and activation of the patient's immune cells in the tumor microenvironment. This means, although allogeneic CAR-T cells have a disadvantage of shorter persistence, combination with PRIME technology could leverage anti-tumor efficacy of patient's own immune cells, potentially reducing the risk of secondary tumors while inducing therapeutic effects. Noile will continue our best efforts on research and development activities to explore PRIME technology in allogeneic CAR-T cell therapies.

- **How the progress to date of the relevant programs seems?**

At present, Takeda has not disclosed information regarding the safety and efficacy outcomes or progress of these programs, and we are unable to provide information. Noile is discussing with Takeda the disclosure of the data from now on.

For the first four cases of NIB102, Takeda presented data at the annual meeting of the Society for Immunotherapy of Cancer in November 2022※.

※https://www.noile-immune.com/dcms_media/other/PR_TAK-102_report_SITC_News_eg_20221125.pdf

- **How will the termination of the license agreement impact Noile-Immune's future business plan?**

While we will retain the rights to NIB102 and NIB103, ongoing discussions with Takeda involve determining the course of ongoing trials, the transfer of data accumulated thus far, the handling of intellectual property, and the settlement of termination fees that may be payable by Takeda. Taking these factors into considerations, we will also be exploring future development strategies and potential new partnerships.

- **What is the future treatment of the Company's shares currently held by Takeda?**

At present, Takeda has not made any decisions regarding the sale of these shares. However, given Takeda's possession of information related to NIB102 and NIB103 as our pipeline, it is generally believed that any actions such as selling may not be taken in the near future.

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