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To whom it may concern,

Company name:	Takara Holdings Inc.
Company representative:	Mutsumi Kimura, President
Securities code and stock exchange listings	2531 Tokyo (1st section)
Inquiries:	Takuya Kakemi, General Manager of Investor Relations Dept.
TEL:	(075)241-5124

Notice Regarding Strategic Change in Development of Oncolytic Virus Immunotherapy C-REV from Takara Bio Inc., a Consolidated Subsidiary of Takara Holdings

Takara Bio Inc. (The First Section of Tokyo Stock Exchange, securities code number: 4974), a consolidated subsidiary of the Company, today issued a news release entitled "Strategic Change in Development of Oncolytic Virus Immunotherapy C-REV". For details, please refer to the disclosure materials of Takara Bio.

This decision has less impact on the current fiscal year's financial forecast.

(Attached) Disclosure materials of Takara Bio

TAKARA BIO INC.
Nojihigashi 7-4-38, Kusatsu, Shiga, 525-0058, Japan
Phone : + 81 77-565-6970
Facsimile : + 81 77-501-7017
<http://www.takara-bio.co.jp>

NEWS RELEASE

Strategic Change in Development of Oncolytic Virus Immunotherapy C-REV

Kusatsu/Shiga, Japan — September 27, 2019 – Takara Bio Inc. (Takara Bio) announced today that it has decided to implement a strategic change in the development plan of C-REV (canerpaturev, former HF10) which is being developed as a regenerative medicine product for the treatment of melanoma and pancreatic cancer.

1. Development plan for Melanoma

The new drug application for marketing approval in Japan was submitted on March 29, 2019 based on results from the phase 2 of C-REV in combination with ipilimumab in patients with unresectable or metastatic melanoma after existing therapy. While Takara Bio had meetings with PMDA during the review, it became clear that there exists discrepancy between PMDA and Takara Bio in interpretation of requirement for the conditional/term-limited authorization. On the other hand, the evolution in melanoma treatment changed the position of ipilimumab as the standard of care. Considering these points, Takara Bio decided to retract the new drug application for the treatment of melanoma.

Ref. The news release dated on March 29, 2019
http://ir.takara-bio.co.jp/en/news_all/news_IR/auto_20190329498286/pdfFile.pdf

2. Development plan for Pancreatic cancer

The phase 1 of C-REV in patients with unresectable pancreatic cancer is being conducted in collaboration with Otsuka Pharmaceutical Co., Ltd. The clinical data reported so far was quite encouraging*. Considering the new mechanism action of C-REV and the unmet medical needs, Takara Bio decided to further focus on the development for pancreatic cancer in order to maximize the value of C-REV.

* Hashimoto Y, et al. Results from phase I study of the oncolytic viral immunotherapy agent canerpaturev (C-REV) in combination with gemcitabine plus nab-paclitaxel for unresectable pancreatic cancer. ASCO-GI 2019 (Abstract #325)
* Hashimoto Y, et al. Results from phase I study of the oncolytic viral immunotherapy agent Canerpaturev (C-REV) in combination with gemcitabine plus nab-paclitaxel as first-line treatment of unresectable pancreatic cancer. ESMO 2019 (Abstract #1222)
* Hijioka S, et al. Phase I study of the oncolytic viral immunotherapy agent Canerpaturev (C-REV) with S-1 in patients with stage IV pancreatic cancer. ESMO 2019 (Abstract #1465)

The development plan outside Japan is as follows:

- **Development in South Korea**

Takara Bio entered into a licensing agreement of C-REV with Dong-A ST Co. Ltd. in South Korea in August 2018. Dong-A ST will initiate the clinical trial(s) in South Korea based on the data from Japanese trials.

- **Development outside of Japan or South Korea**

Takara Bio is seeking a partner for the global development of C-REV. Once it is determined, the clinical development will be conducted based on its strategy.

Takara Bio is striving to meet the unmet medical needs and contribute to further increasing the benefits for patients and their families.

This decision has less impact on the current fiscal year's financial forecast.