

**Nagasaki University Presented Results Of a Specified Clinical Trial On The Use of *L. lactis* strain Plasma For Patients With COVID-19**

**TOKYO, May 11, 2023** – Nagasaki University presented the results of a specified clinical trial on patients with COVID-19 using *Lactococcus. lactis* strain Plasma\*<sup>1</sup> (*L.lactis* Plasma, a postbiotic), researched and developed by Kirin Holdings Company, Limited (Kirin Holdings). The results of this research was presented at the 63rd Annual Scientific Meeting of the Japanese Respiratory Society on Sunday, April 30. Nagasaki University and Kirin Holdings have jointly filed a patent application for the findings of this specified clinical trial.

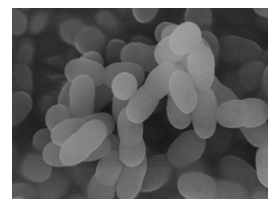
<sup>1</sup> *Lactococcus lactis* subsp. *lactis* JCM 5805 is owned by the RIKEN BioResource Research Center (<https://web.brc.riken.jp/en/>)

**● Current status of COVID-19**

Since December 2019, COVID-19 infections have repeatedly caused pandemics, infecting 676.57 million people worldwide and killing 6.88 million (as of March 10, 2023). With the emergence of Omicron variants, the number of cases in Japan has increased, and the COVID-19 has become a more familiar infectious disease. Although SARS-CoV-2 vaccines have introduced widely and patients with mild illnesses account for a large proportion of the affected population, only a limited number of drugs are available in patients with mild illnesses who are not at risk of developing severe illnesses, and treatment is mainly based on symptomatic therapy.\*<sup>2</sup> Therefore, there is eagerly awaited for an easily accessible, safe, and effective treatment for COVID-19 in the community.

**● What is *L. lactis* strain Plasma?**

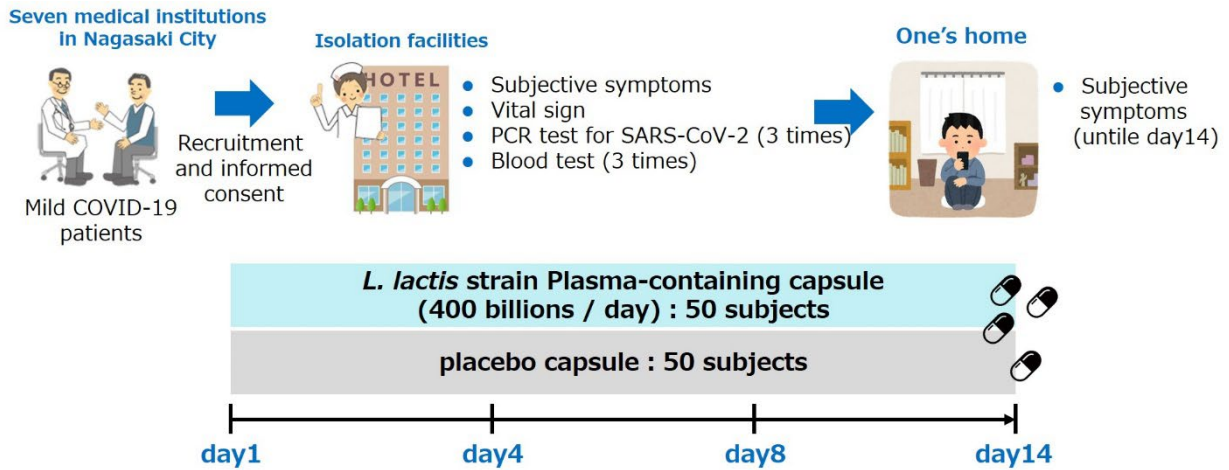
*L. lactis* strain Plasma was discovered by Kirin in 2010 as a lactic acid bacteria that activates plasmacytoid dendritic cells (pDC), which are a leader of the immune system. Previous basic studies showed that *L.lactis* Plasma stimulated pDC to have a first-line defense to viral infectious diseases. Previous clinical studies have also shown that *L.lactis* Plasma stimulated pDC and suppress the onset of an illness from influenza virus, rotavirus, and dengue. These scientific evidence of its immune function brought *L. lactis* Plasma registered as the first\*<sup>4</sup> Food with Functional Claims in Japan on August 2020.

**● Specified Clinical Research Contents**

Based on the results of Kirin Holdings' research on *L. lactis* Plasma, Nagasaki University, as a research institute with significant achievements in the field of infectious diseases, interested in *L. lactis* strain Plasma which may effect in relieving symptoms in patientis with COVID-19, and has decided to conduct a specified clinical trial from December 2021.

Since December 2021, Kirin Holdings has been engaged in a specific clinical research project led by Dr. Kazuko Yamamoto, a lecturer at the Department of Respiratory Medicine, Nagasaki University Hospital (currently a professor and chair at the Division of Infectious Diseases, Respiratory and Gastroenterological Medicine (First Department of Internal Medicine), University of the Ryukyus Graduate School of Medicine). This is a multicenter, double-blinded, randomized controlled trial conducted at Nagasaki University Hospital as a core facility. The efficacy and safety of 14 days oral intake of 4 hard capsules containing *L. lactis* Plasma (400 billion *L. lactis* Plasma in total) or 4 hard capsules without *L. lactis* Plasma (placebo) was to be evaluated\*<sup>5</sup> by having

50 patients with COVID-19 in each group.



Trial registration number : Japan Registry of Clinical Trials (registration number : jRCTs071210097)

2 Approach to Pharmacotherapy for COVID-19 Version 15.1- the Japanese Association for Infectious Diseases

3 Secrets of Immunity - Kirin's *L. lactis* strain Plasma Research <https://health.kirin.co.jp/en/about/about.html>

4 The first brand in Japan to be registered with the Consumer Affairs Agency as a food with a functional claims for immune function.

5 Yamamoto K, et al. BMJ Open 2022;12:e061172

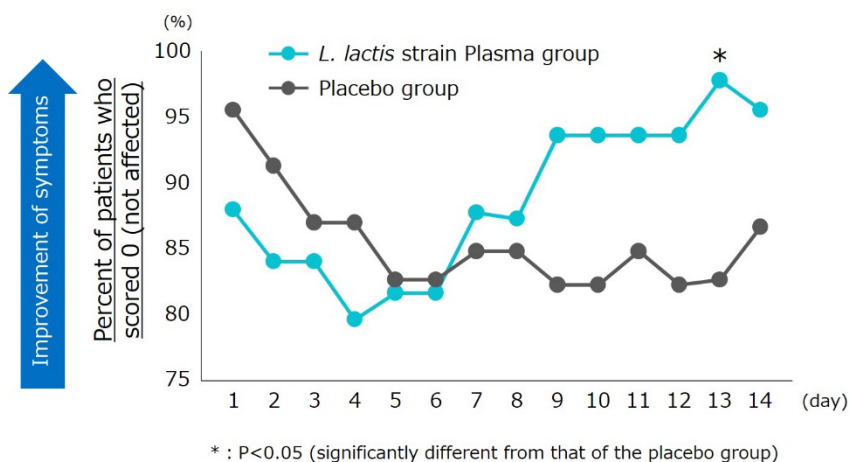
## ● Specified Clinical Trial Results

### 1. Change in subjective symptom overall score (primary endpoint)

The results of an overall score analysis of seven subjective symptoms (Cough, Shortness of breath, fatigue, Headaches, Anosmia and Dysgeusia, Anorexia, and Chest pain) on a 4-point scale (0 points: not affected, 1 points: little effect, 2 points: affected, 3 points: severely affected) showed no difference between the two groups.

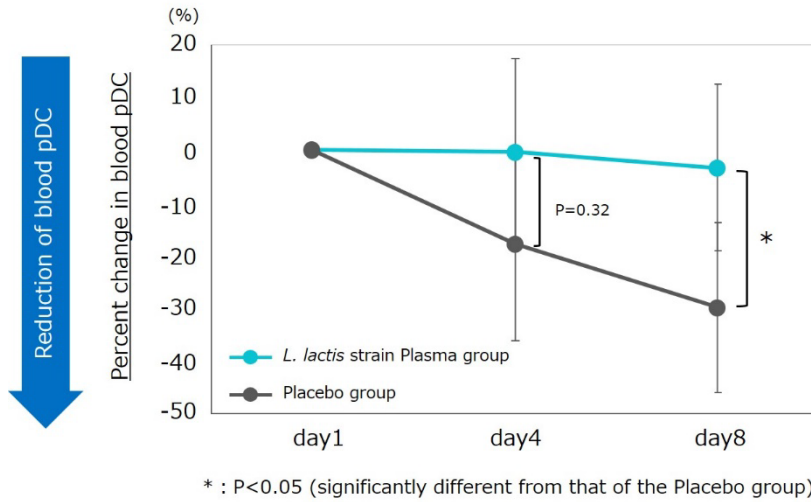
### 2. Anosmia and Dysgeusia (secondary endpoints)

The percentage of patients who scored 0 (not affected) for smell and taste dysfunction among subjective symptoms were high in the *L. lactis* strain Plasma group compared to placebo group after day 9.



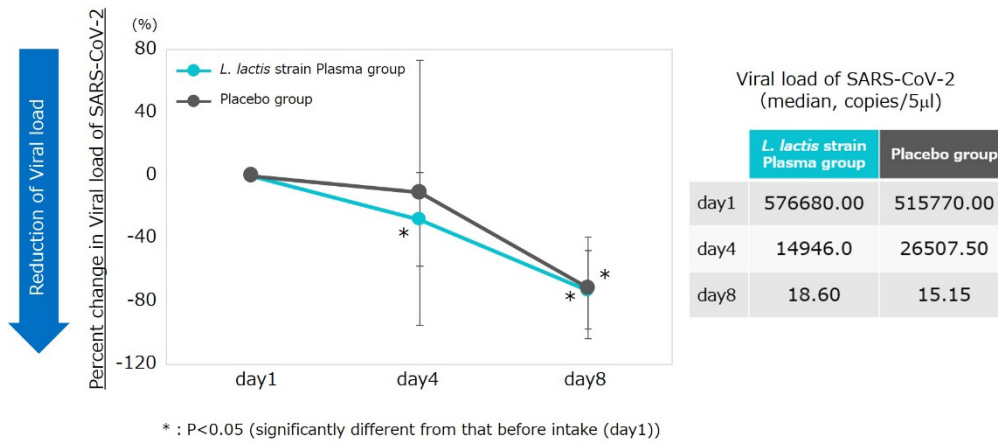
**3. Percent change in blood pDC (secondary endpoint)**

While the placebo group showed a significant decrease in % pDC in the blood during COVID-19 clinical course, the *L. lactis* strain Plasma group maintained % pDC in the blood.



**4. Percent change in SARS-CoV-2 viral load (secondary endpoint)**

The *L. lactis* strain Plasma group showed a significant reduction of SARS-CoV-2 viral load at day 4 of treatment whereas placebo group showed reduction at day 8.



**5. Safety and adverse events**

No critical adverse events of safety were observed in this study.

Although this study did not show an effect on the primary endpoint, the subjective symptom total score, these results suggested that maintained pDC by the intake of *L. lactis* strain Plasma may have resulted in an early reduction of SARS-CoV-2 and early recovery of smell and taste dysfunction.

Nagasaki University and Kirin hope that *L. lactis* Plasma will become one of the new treatment or adjunctive care to patients with mild COVID-19.

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### **About Kirin Holdings**

Kirin Holdings Company, Limited is an international company that operates in the Food & Beverages domain (Food & Beverages businesses), Pharmaceuticals domain (Pharmaceuticals businesses), and Health Science domain (Health Science business), both in Japan and across the globe.

Kirin Holdings can trace its roots to Japan Brewery which was established in 1885. Japan Brewery became Kirin Brewery in 1907. Since then, the company expanded its business with fermentation and biotechnology as its core technologies, and entered the pharmaceutical business in the 1980s, all of which continue to be global growth centers. In 2007, Kirin Holdings was established as a pure holding company and is currently focusing on boosting its Health Science domain.

Under the [Kirin Group Vision 2027](#) (KV 2027), a long-term management plan launched in 2019, the Kirin Group aims to become A global leader in CSV\*, creating value across our world of Food & Beverages to Pharmaceuticals. Going forward, the Kirin Group will continue to leverage its strengths to create both social and economic value through its businesses, with the aim of achieving sustainable growth in corporate value.

\* Creating Shared Value. Combined added value for consumers as well as for society at large.

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