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To Shareholders,

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Achievement of the primary endpoint in the clinical performance test for regulatory approval of a software as a medical device (SaMD) using artificial intelligence (AI) to support maintenance hemodialysis

A clinical performance test¹⁾ for regulatory approval of a software as a medical device (SaMD) using artificial intelligence (AI) to support maintenance hemodialysis, which we are developing, was conducted from October 2024 at eight medical institutions across Japan (in different regions, including Tohoku, Kanto, Chubu, and Western Japan), including Tohoku University Hospital and St. Luke's International Hospital, and has now been completed (the trial coordinator was Professor Tetsuhiro Tanaka, Department of Nephrology, Connective Tissue Diseases, and Endocrinology, Tohoku University Graduate School of Medicine).

This multi-center, collaborative, confirmatory clinical performance test was published in "Clinical performance test (flash report) for regulatory approval of a software as a medical device (SaMD) using artificial intelligence (AI) to support maintenance hemodialysis" on July 14, 2025. We are now pleased to announce that the final results has been obtained.

Final results of the clinical performance test

- Retrospective multi-center clinical performance test²⁾ was conducted with clinical data from 108 patients who underwent dialysis treatment by a dialysis specialist, comparing the amount of water removal actually prescribed by the specialist (target water removal amount) with the results predicted by this AI (target water removal amount), to prove the non-inferiority

(equivalence) of the AI prediction to the specialist.

- In consultation with the Pharmaceuticals and Medical Devices Agency (PMDA), the primary efficacy endpoint was set as the 'correct rate' when the difference between this AI and the target water removal amount by the specialist was within an acceptable range. The 'acceptable range' was set as the mean absolute percentage error (MAPE) ³⁾ between the target volume of water removal set by the specialist and the predicted volume of water removal by this product being 12 % or less of the physician-determined volume of water removal (with a maximum of 300 mL).
- As a result of the clinical performance test, the accuracy rate (average) obtained was 92.2 %, which was significantly higher than the initial target accuracy rate of 80 % for the primary endpoint, proving the non-inferiority (equivalence) of the AI prediction to that of a specialist. The mean absolute percentage error (MAPE) between the target volume of water removal set by the specialist and the predicted volume of water removal by this product was 5.2 % (<12 %). The mean absolute error (MAE) ⁴⁾ between the target volume of water removal set by the specialist and the predicted volume of water removal by this product was 129.9 mL (<300 mL), which was within the range of about one cup.
- The study targeted maintenance hemodialysis patients visiting multiple facilities in different geographical areas, including Tohoku, Kanto, Chubu, and Western regions in Japan, and showed high accuracy and precision at all facilities.

Consideration

For the primary endpoint, accuracy rate, the expected agreement rate was set at 80%, and the number of patients required to verify that this expectation did not fall below 75% was set at 110. However, anticipating the need for longer-term data and the possibility of many exclusions, the study initiated with a minimum enrollment of 150 patients. After enrolling 150 patients, data review revealed that more dropouts than expected occurred, leaving only 108 patients for analysis of the primary endpoint. However, the prediction accuracy of this AI-programmed medical device was extremely good, adequately verifying non-inferiority.

For MAPE and MAE, the pre-set accuracy targets ($<12\%$ and $<300\text{ mL}$) were fully achieved, with results of 5.2% and 129.9 mL , respectively. These results suggest that this AI-programmed medical device has very high accuracy in predicting fluid removal volume, and the study results are considered to be highly robust.

Background and explanation of this clinical performance test

Approximately 350,000 patients with end-stage renal failure in Japan undergo hemodialysis three times a week to remove water and waste products in place of their abolished kidneys. In hemodialysis, the most important medical issue is "appropriate water removal," and setting the optimal amount of water removal is the issue that doctors struggle with the most. Insufficient water removal impairs cardiopulmonary function, and excessive water removal causes low blood pressure during dialysis, leading to adverse events such as feeling unwell and losing consciousness. In dialysis hospitals, many patients are treated by a small number staff of one doctor, several nurses and clinical engineers, and when adverse events occur, the burden on the staff increases.

This program medical device was developed in collaboration with Tohoku University, NEC Corporation (NEC), NEC Solution Innovators, Ltd. (NES), and NIPRO CORPORATION, and imitates and learns the target amount of water removal set by dialysis specialists, and presents the target amount of water removal to non-specialists and other less experienced doctors with the same accuracy as specialists. Experienced dialysis doctors set the amount of water removal based on their experience (tacit knowledge), taking into consideration 1) the weight gain since the end of the previous dialysis, 2) the difference between the set dry weight ⁵⁾ and the weight before dialysis, and 3) the patient's condition (swelling of the face and lower limbs, bowel movement status, sleep, food intake status, etc.). However, while there are 12,000 specialists required for dialysis treatment, there are only about 4,000 actual specialists, and non-specialists are forced to engage in dialysis treatment.

This programmed medical device imitates the treatment of dialysis specialists by having AI learn dialysis treatment information from approximately 3,000 cases (approximately 1% of dialysis patients in Japan), and provides non-specialists with predictions equivalent to those of dialysis specialists. By using this programmed medical device, non-specialists are expected to supplement their

knowledge and experience and contribute to the implementation of appropriate maintenance hemodialysis treatment for dialysis patients. In addition, dialysis with appropriate water removal settings is expected to suppress the occurrence of adverse events such as blood pressure drops, which is thought to reduce the burden on patients themselves and contribute to improving their quality of life.

As announced in the "Announcement of Selection for the Japan Agency for Medical Research and Development (AMED) Medical Device Development Promotion Research Project" dated February 27, 2023, this project has been selected for the Japan Agency for Medical Research and Development (AMED)'s "Medical Device Development Promotion Research Project" for fiscal year 2023. The principal investigator is Tohoku University, and the lead researcher is Professor Toshio Miyata (Chairman and CEO of our company) of the Department of Molecular Pathophysiology and Therapeutics, Tohoku University Graduate School of Medicine. Furthermore, as announced in the "Announcement of distribution of adjustment funds to accelerate practical application of the 'Research on Development of new Medical Devices'" dated September 10, 2025, an additional 143,000,000 yen has been allocated as research funds (adjustment funds) to commercialize this project.

In addition, as announced in the "Announcement of special invited lecture at the 70th Annual Meeting of the Japanese Society for Dialysis Therapy" dated June 27, 2025, a promotional video for this AI-programmed medical device, created in collaboration with NIPRO CORPORATION, a joint research partner, was shown at the Annual Meeting of the Japanese Society for Dialysis Therapy (Osaka International Convention Center).

Outlook

Based on the results of this clinical performance test, we will work with NIPRO CORPORATION, with whom we have a joint development agreement, to advance the development of the final system, with a view to applying for pharmaceutical approval and commercializing and putting it into practical use, while also accelerating preparations for its use in medical settings.

There is currently no impact on the financial results for the fiscal year ending March 2026, but if any matters that need to be disclosed arise in the future, we will disclose them in a timely manner.

¹⁾ Clinical performance test

In order to enable the use of a software as a medical device (SaMD) under development in the medical field, it is necessary to confirm whether the software as a medical device will perform as expected in the clinical field using actual human clinical data. Clinical performance tests are clinical studies conducted for this verification. Based on the performance confirmed in the clinical performance test, an application (pharmaceutical application) will be submitted to the Ministry of Health, Labor and Welfare to manufacture and sell the device as a software as a medical device. This clinical study has a similar nature to a validation test (Phase III trial) for pharmaceuticals.

²⁾ Retrospective multi-center clinical performance test

A study in which multiple medical institutions cooperatively evaluate the clinical performance of medical devices or IVDs using accumulated historical clinical and laboratory data.

³⁾ MAPE (Mean Absolute Percentage Error)

MAPE is one of the indices for evaluating the accuracy of a forecast model. Specifically, it is the average percentage of error relative to the actual value. MAPE is calculated as follows.

$$MAPE = \frac{100\%}{n} \sum \left| \frac{y - \hat{y}}{y} \right|$$

The smaller the value, the more accurate the prediction.

⁴⁾ MAE (Mean Absolute Error)

MAE is one of the indicators for evaluating the accuracy of a predictive model. Specifically, it indicates the average absolute value of the difference between the predicted value and the actual value. MAE is calculated as follows.

$$MAE = \frac{1}{n} \sum_{i=1}^n |y_i - \hat{y}_i|$$

y_i : Actual target water removal volume

$\hat{y}_i$: Predicted target water removal volume

⁵⁾ Dry weight

This refers to the target weight of a dialysis patient, and is the weight when excess water has been removed from the body. Dry weight varies from patient to patient, and is determined taking into account their physical condition, blood pressure, and edema status. Maintaining an appropriate dry weight can reduce the drop in blood pressure during dialysis and the strain on the cardiovascular system.