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To Shareholders,

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Clinical performance test (flash report) for regulatory approval of a software as a medical device (SaMD) using artificial intelligence (AI) to support maintenance hemodialysis

We are developing a software as a medical device (SaMD) using artificial intelligence (AI) to support safe and secure maintenance hemodialysis. In order to evaluate the performance (prediction accuracy) of this programmed medical device, we have conducted a clinical performance test[1)] for regulatory approval at eight medical institutions in Japan, including Tohoku University, St. Luke's International Hospital, etc. We are pleased to announce that the results have been obtained as a flash report.

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[2)] 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.

This project has been selected for the "Medical Device Development Promotion Research Project" by the Japan Agency for Medical Research and Development (AMED) in fiscal year 2023 (the principal research institution is Tohoku University). In addition, in order to utilize this programmed medical device in clinical settings, we have signed a joint development agreement with NIPRO CORPORATION in March 2024 for commercialization.

Clinical performance test results (flash report)

From October 2024, a clinical performance test for regulatory approval of this SaMD was conducted as a multi-center joint verification clinical performance test at eight facilities (Tohoku, Kanto, Chubu, and Western regions in Japan), including Tohoku University Hospital, St. Luke's International Hospital, etc (the coordinating physician was Professor Tetsuhiro Tanaka, Department of Nephrology, Connective Tissue Diseases, and Endocrinology, Tohoku University Graduate School of Medicine).

- A multi-center, retrospective clinical performance test 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 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 90.31 %, 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 average volume of water removal for the subjects in this study was 2,353 mL, so the mean absolute error (MAPE) between the target volume of water removal set by the specialist and the predicted volume of water removal by this product was 5.14 % (<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 117.9 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.

The results of this clinical performance test will be compiled into a summary report, and preparations will be made with NIPRO CORPORATION for practical use.

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) 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.

3) MAPE (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.

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

The smaller the value, the more accurate the prediction.

4) MAE (average 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

The smaller the value, the more accurate the prediction.