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To Shareholders,

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Achievement of primary endpoint of confirmatory clinical performance test for the artificial intelligence (AI)-based medical software to predict optimal insulin dosage for hospitalized patients with diabetes mellitus.

We are pleased to announce the result of a clinical performance test[1)] for the regulatory approval of 'the artificial intelligence (AI)-based medical software predicting optimal insulin dosage for hospitalized patients with diabetic mellitus', conducted at six hospitals in Japan. We published a preliminary report on the clinical performance study on January 16, 2025, and we would like to inform you that we have now obtained the final comprehensive report.

A summary of the final results is provided below.

[Results of this clinical performance test]

- To verify the non-inferiority (equivalence) of the developed AI-based medical software to diabetes specialists, a multi-center collaborative validation clinical performance test was conducted and the Proof-of-Concept[2)] was obtained.
- The primary efficacy endpoint was the correct rate. The correct rate is the rate of correct answers when the difference between the AI and the prescription unit by the diabetes specialist is considered to be within the acceptable range.
- The average correct rate for the 116 cases analyzed was 85.46, with a confidence interval[3)] of (83.59, 87.34).
- The mean absolute error (MAE[4)]) = |AI prescription unit - specialist prescription unit|) between the insulin dosage unit in the diabetes specialist's treatment and the insulin dosage unit recommended by the AI-software was 1.61 on average.

[Summary]

- This medical device is an AI-based software that has learned the clinical data of hospitalized diabetic patients at Tohoku University Hospital, so in order to ensure its generalization

performance, Yamaguchi University Hospital participated as a facility outside of the Tohoku University medical area. In this study, it showed a high accuracy rate and low MAE at Yamaguchi University Hospital, which is outside the medical area of Tohoku University, suggesting that the test device would show a high accuracy rate and accuracy even outside the medical area of Tohoku University, where the test device was used as learning data.

- ☐ MAE (mean absolute error) was calculated as a secondary evaluation item as an error reflecting the discrepancy between the insulin units in the diabetes specialist's treatment and the insulin units presented by the AI software. As a result, the average MAE of the 116 cases analyzed was 1.61, with a standard deviation of 1.32, and the test device's prediction accuracy was considered to be high even when compared to the results of a preliminary study that examined the variation in insulin dosage units of 10 diabetes specialists.
- ☐ This AI software predicts insulin dosage with the same accuracy as a diabetes specialist, reducing the burden on non-specialists and contributing to improving patients' quality of life through proper blood sugar control.

Details are listed below.

In Japan, among the approximately 10 million diabetic patients, 1 million patients control their blood sugar with insulin treatment. Insulin injection treatment is necessary to strictly control blood sugar level and prevent diabetic complications, but the safe dosage range of insulin is narrow, and excessive administration can cause adverse events such as hypoglycemia. Diabetes specialists set the dosage taking into account tacit knowledge based on experience, but the reality is that it is difficult for non-specialists to do so. Unfortunately, specialists make up less than 2% of all doctors and are unevenly distributed geographically, so currently, diabetic patients do not necessarily have a diabetic specialist as their doctor, and rather often visit a non-specialist. The shortage and uneven distribution of diabetic specialists has the following effects on treatment.

(1) For non-diabetic specialists, the hurdle of insulin treatment to control blood sugar is high, and there are cases where hospitalization is not performed and patients' poor blood sugar control continues, or even if hospitalization is performed, appropriate insulin treatment is not performed.

(2) Even if the main purpose of hospitalization is not blood sugar control, blood sugar control during hospitalization is important. Inappropriate insulin treatment during hospitalization increases the number of deaths during hospitalization, prolonged ICU stays, new onset of infections and acute renal failure, and new onset of respiratory failure requiring ventilator management.

We have developed a ‘software as a medical device (SaMD) that relies on artificial intelligence (AI) to predict optimal insulin dose’ to be used as an assistant for non-diabetic specialists (users) to provide appropriate insulin treatment to hospitalized diabetic patients (target patients). This SaMD was developed with the support of the "Medical Engineering Collaboration Innovation Promotion Project" of the Japan Agency for Medical Device Development (AMED), a national funding agency.

From August 2024, a clinical performance test for pharmaceutical approval of this SaMD has been conducted as a multi-center, clinical performance test at Tohoku University Hospital, Yamaguchi University Hospital, Sendai City Hospital, Osaki Municipal Hospital, Miyagi Prefecture South Core Hospital, and Tohoku Rosai Hospital.
A study was conducted to prove non-inferiority of the drug to the specialist, using clinical data of 116 type 2 diabetic patients who received insulin treatment by a diabetes specialist at the time of hospitalization for the purpose of blood sugar control, using the results of the specialist's actual treatment and the results predicted by the diabetes treatment support AI. As a result, we were able to confirm that the accuracy rate when evaluating the error compared to the diabetes specialist, which is the main endpoint, was approximately 85%, which was 5% higher than the initially set target of 80%. These results demonstrated that it was non-inferior to diabetologists.

Correct rate: Test preliminary value

Number of subjects	116
Correct answer rate (average)	85.46
Confidence interval for the mean	［83.59 , 87.34］

There is currently no impact on the financial results for the fiscal year ending March 2025, but we will disclose any matters that need to be disclosed in the future in a timely manner.

[1)] Clinical performance test
In order for a software as a medical device (SaMD) under development to be used in the medical field, it is necessary to verify whether the software as a medical device will perform as expected in the clinical field using actual human clinical data. A clinical performance test is a clinical study conducted for this verification. Based on the performance confirmed in the clinical performance test, an application (pharmaceutical application) is submitted to the Ministry of Health, Labor and Welfare to manufacture and sell the software as a medical device. This clinical study has a similar nature to a verification test (phase 3 trial) for pharmaceuticals.

[2] Proof-of-Concept (POC)

This refers to confirming the effectiveness of a new device candidate in clinical trials, and if the expected results are obtained, it is said that POC has been obtained.

[3] Confidence interval

A confidence interval indicates the probability that a population parameter (e.g. mean value) is within a certain range. For example, it shows to what extent the mean value calculated from a certain sample data includes the mean value of the population.

[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.