The 23rd R&D Meeting

March 13, 2026

Together for a better
healthcare journey

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Index

1. **Initiatives to Realize the Healthcare Journey** — Tomokazu Yoshida, Member of the Managing Board and Senior Executive Officer, Managing Director, CTO

2. **Promotion of Medical DX Utilizing Data** — Kazuya Fukuda, Executive Vice President of Technology Innovation

3. **Deepening of Liquid Biopsy Technology**
   "Toward the staging and stratification of Alzheimer's disease" — Shigeki Iwanaga, Executive Vice President of Technology Strategy

4. **Initiatives Targeting Regenerative and Cellular Medicine** — Kenji Tsujimoto, Executive Officer, Executive Vice President of Next Generation Medical Business Development

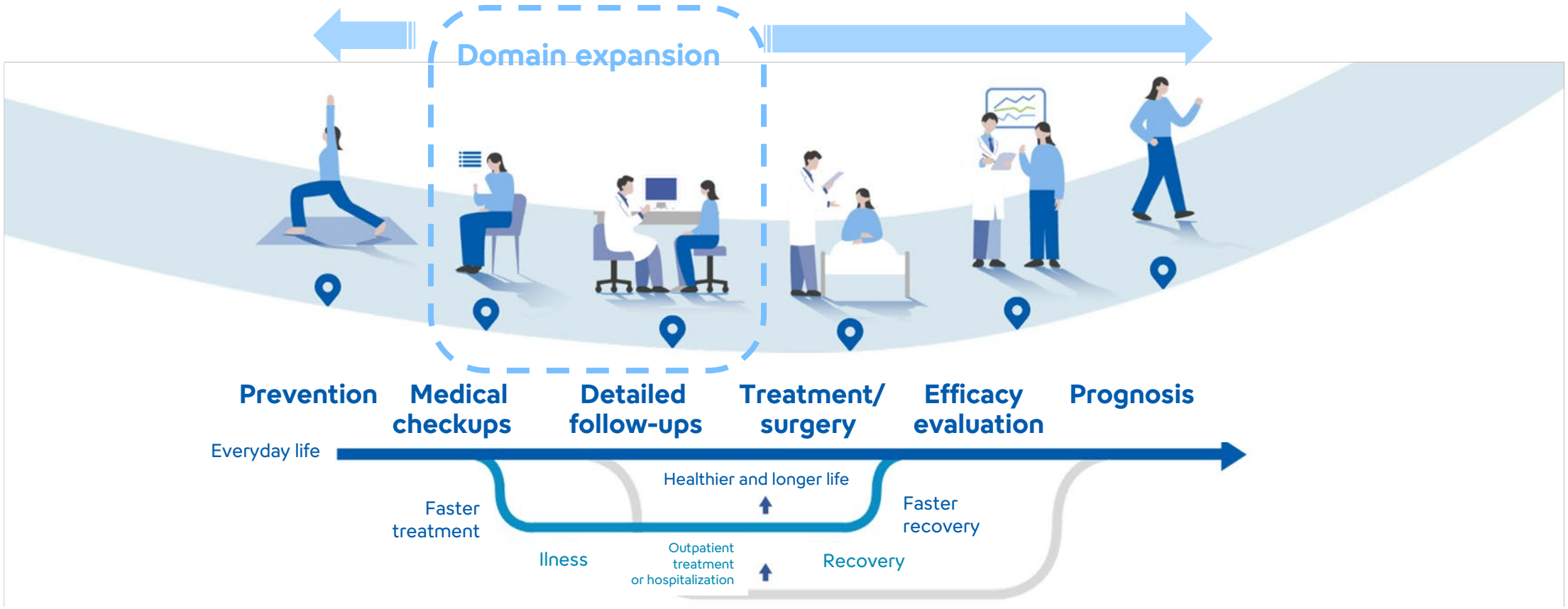
Glossary

1. Initiatives to Realize the Healthcare Journey

Tomokazu Yoshida
Member of the Managing Board and
Senior Executive Officer
Managing Director, CTO

Sysmex's Long-Term Vision

Together for a better healthcare journey



Healthcare Journey and P4 Medicine

Navigating the healthcare journey through the realization of P4 medicine

P4 medicine

- Predictive
- Preventive
- Personalized
- Participatory

Prediction of onset

Pre-disease care and **prevention**

Personalized medicine

Proactive individual **involvement**

“Data Readiness” for the Realization of P4 Medicine

Utilizing test data to guide patients to optimal healthcare pathways, providing optimal intervention options, and driving motivation

- Predictive
- Preventive
- Personalized
- Participatory

Guidance to optimal healthcare pathways

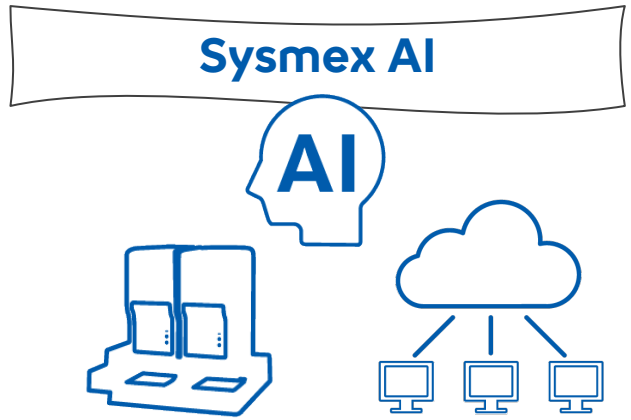
Screening data

Provision of optimal intervention options

Granular data on disease characteristics

Motivation for behavior change

Longitudinal patient data



Circulation of test data
Improvement of prediction accuracy

Achievements (Initiatives) under the Mid-Term Management Plan (1)

Expansion of the product portfolio strengthens the foundation for data collection

Guidance to optimal healthcare pathways: Screening data

Flagship models

Global rollout of the XR™-series

- Next-generation touch-free technology
- Enhanced disease risk assessment

Multiparameter Automated Hematology Analyzer
XR-Series
Medical Device Marketing Authorization No.: 28B1X10014000008

Deployment of the CN™-9000 large-scale automation system in North America

CN-9000 Automated Hemostasis Solution
Automated Blood Coagulation AnalyzersCN-3000
Medical Device Marketing Authorization No.: 28B1X10014000002
Automated Blood Coagulation AnalyzersCN-6000
Medical Device Marketing Authorization No.: 28B1X10014000001

Emerging market models

Expansion of the compact model lineup

XN™-L Series Multidifferential Hematology Analyzer
Medical Device Marketing Authorization No.: 28B1X10014000008

Hematology Analyzer pocH™-120
Medical Device Marketing Authorization No.: 28B1X10014000062

Automated Blood Coagulation Analyzer CN-700
Medical Device Marketing Authorization Number: 28B1X10014000061

UC-1100 Semi-Automated Urine Chemistry Analyzer
Medical Device Marketing Authorization No.: 28B1X10014000064

Achievements (Initiatives) under the Mid-Term Management Plan (2)

Expansion of the product portfolio strengthens the foundation for data collection

Providing optimal intervention options: Granular data on disease characteristics

Alzheimer's disease
- Prediction of amyloid accumulation
- Prediction of tau accumulation

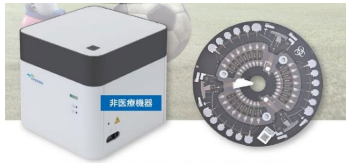
Regenerative and cellular medicine
- Quality control testing utilizing IVD testing technologies
- Automation of manufacturing processes

Genetic testing
- IRD (Inherited Retinal Dystrophy) panel
- Expansion of cancer genomic testing

Surgical intelligence
- Acquisition of surgical support technologies (education)

Motivation for behavior change: Longitudinal patient data

Compact and easy-to-use testing devices
- Expansion into sports applications



MYO equiv（ミオグロビン相当量）を測定
試作段階のイメージ写真のため、外観は変更する可能性があります。

Digital solutions
- Collaboration agreement with Nippon Life Insurance and initiation of joint research (disease risk assessment through the integration of medical and lifestyle data)

JFA PARTNERSHIP PROJECT for DREAM

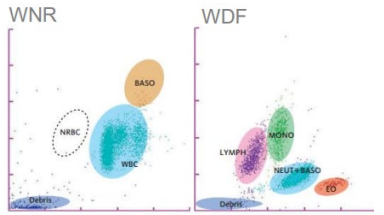
Sysmex is an official supporter of the JFA.

Data Compounding Centered on Technologies and Products

Achieving greater depth in test data through product expansion leads to the creation of new value, and this virtuous cycle increases value exponentially

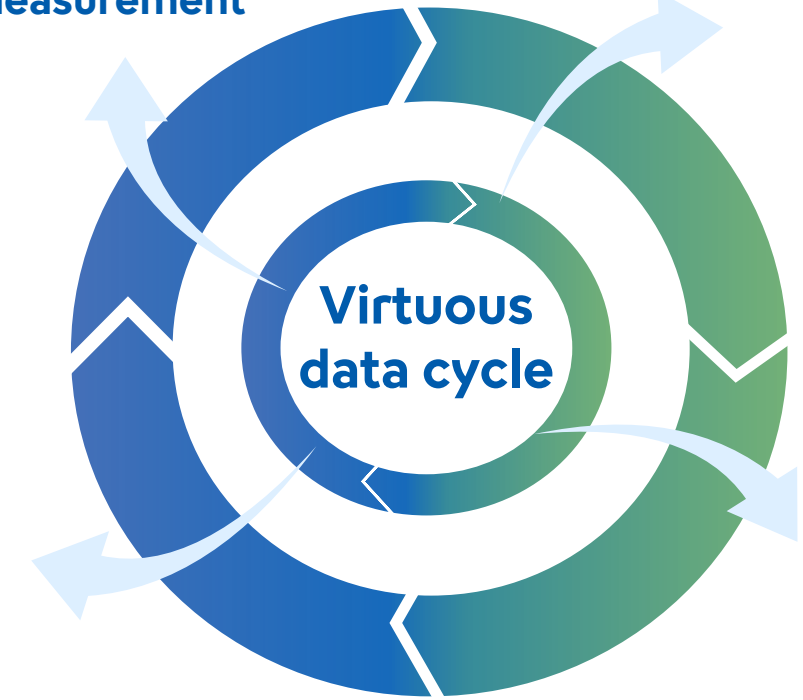
(1) Expansion of the product portfolio and improvement of measurement performance

(2) Generation of high-quality test data from analyzers

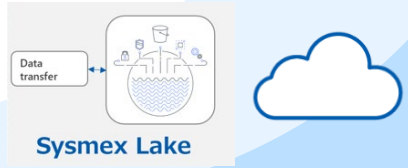


Expansion of value delivered

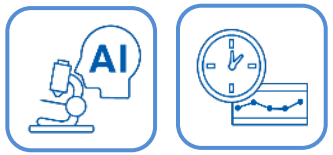
Improvement in the quality and quantity of data



(3) Global data integration and knowledge base expansion



(4) Development of new applications



Product portfolio expansion

Themes Covered Today

2. Promotion of Medical DX Utilizing data

Kazuya Fukuda
Executive Vice President of
Technology Innovation

3. Deepening of Liquid Biopsy Technology

"Toward the staging and stratification of Alzheimer's disease"

Shigeki Iwanaga
Executive Vice President of
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4. Initiatives Targeting Regenerative and Cellular Medicine

Kenji Tsujimoto
Executive Officer
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Next Generation Medical
Business Development

2. Promotion of Medical DX Utilizing Data

Kazuya Fukuda
Executive Vice President of
Technology Innovation

Creating Value Through Data Utilization

Translating test data into information that supports decision-making by healthcare professionals and individuals, thereby improving healthcare quality and efficiency

Data Utilization

Prevention → Medical checkups → Detailed follow-ups → Treatment/surgery → Efficacy evaluation → Prognosis

Intelligence Triage

- Early warning detection
- Personalization
- Prediction of recurrence
- Refined testing

Operational Excellence

- Pursuit of touch-free concept
- Support for hospital and laboratory operations

Population health management

- Visualization of population trends

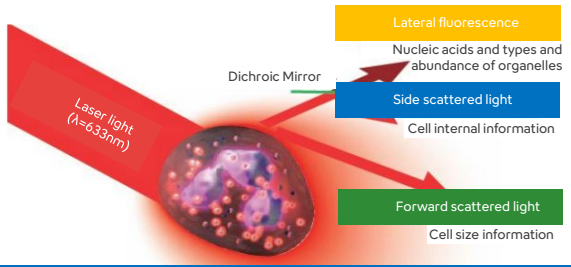
Stakeholders: Administrations, Population, Healthcare professionals, Individuals, Laboratories, Hospitals

Sysmex's Strengths in Medical DX

Expanding the value we deliver by utilizing proprietary data from analyzers, combined with AI and advanced analytics technologies

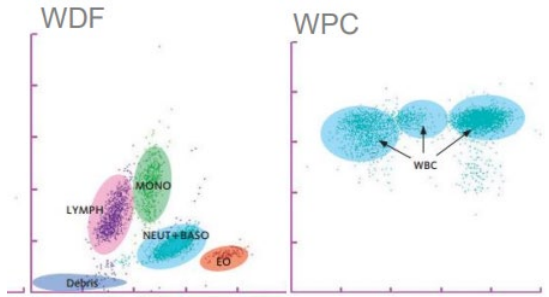
Our proprietary data assets

Detection signals from analyzers
Detection information from optimal measurements and other methods



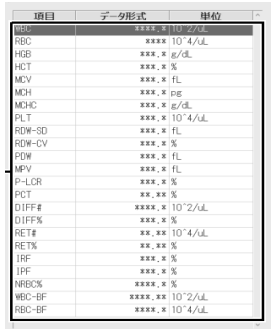
Based on three types of optical information, a three-dimensional analysis is performed and the data is displayed as a scattergram.

Analytical information
Scattergrams and other outputs



Traditional value (provision of test results)

Test data
Measurement results



Laboratory
↓
Doctor
↓
Patient

Greater depth of test data

Increased data volume and quality

Enhanced AI and analytics

Advancement of analytical technologies

- Regional characteristics data
- Longitudinal patient data

New value

- **Refined testing**
- **Early detection**
- **Visualization of population-level trends**

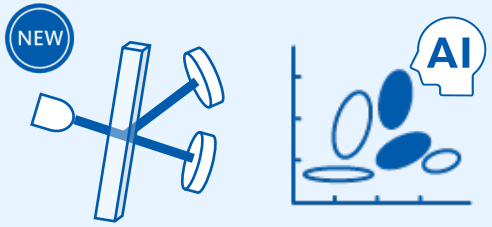
Refined Testing

Refined Testing

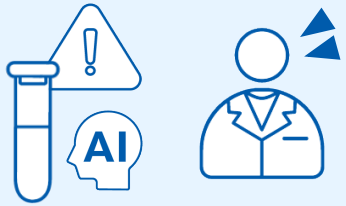
Enhancing analyzer-specific data analytics technology through AI integration and utilization
Leading innovation in testing workflows through testing refinement and efficiency

Next-generation products for the hematology field

Expansion of acquired and analytical information
Refined disease risk assessment



Advancement of abnormality detection algorithms
Refined support for retesting and microscopic examination decisions

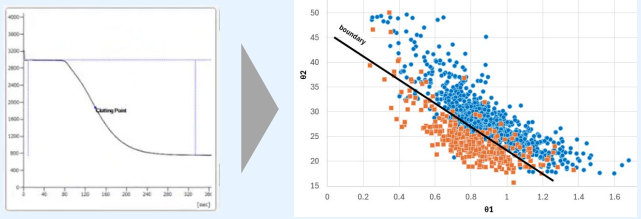


Next-generation products for the urinalysis field

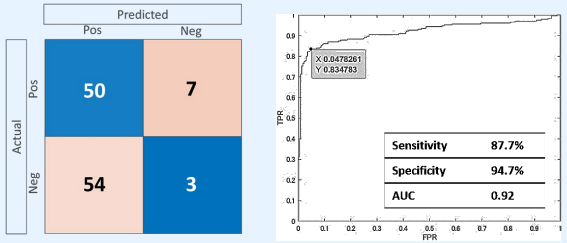
Renewal of detection systems and reagent composition, and advancement of automated component classification
Refined and more efficient disease risk assessment

Next-generation products for the hemostasis field

Automatic detection of sample quality levels
Improved accuracy in decisions on repeat blood collection and retesting



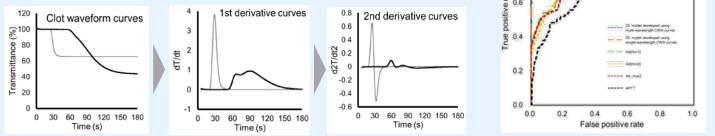
Advancement of abnormality detection algorithms
More efficient selection of additional tests



Citation: Keisuke Nishi, et al. "Development of a machine-learning–based algorithm for detecting in-tube coagulation using APTT clotting waveforms." Japanese Society of Laboratory Medicine Annual Meeting, O-010 (2025).

Advancement of waveform analysis technologies
Refined disease risk assessment

Example: Prediction of disease progression using APTT waveform analysis

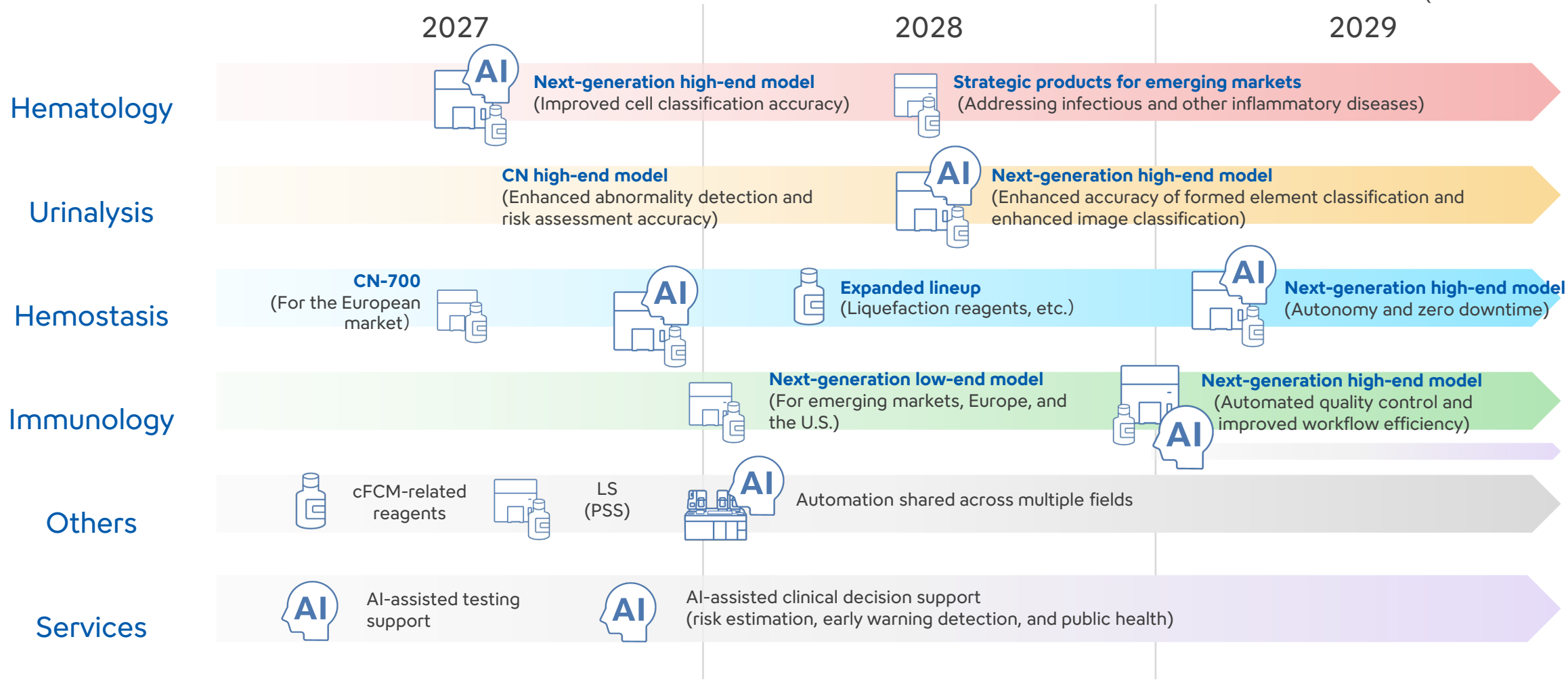


Citation: "Matsuda, M. et al. Deep learning model for screening causes of activated partial thromboplastin time prolongation using clot waveform analysis at multiple wavelengths." Sci. Rep. 15, 32336 (2025).

Refined Testing: Key Product Release Plan

Further improving the quality of and quantity of test data through expansion of the product portfolio and enhanced measurement performance

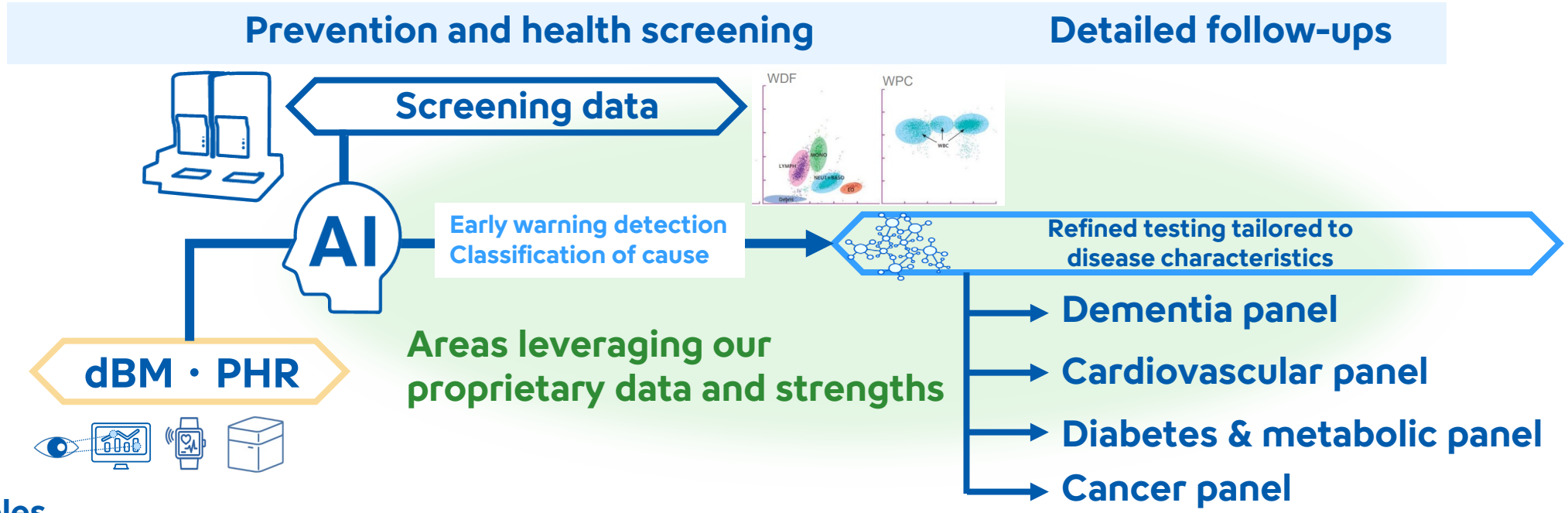
(Years to March 31)



Early Warning Detection

Early Warning Detection

Early detection of functional changes using screening data and digital biomarkers
Triaging potential causes and seamlessly connecting to detailed follow-ups



Examples

Hematopoietic malignancies	CBC/5DIFF + Research parameters				Tumor markers, genetic testing, etc.
Heart failure and sepsis	CBC/5DIFF	Basic coagulation parameters	✖ AI		Cardiac markers and additional coagulation tests, etc.
Dementia	dBM (Gazefinder, etc.)				Dementia-related parameters

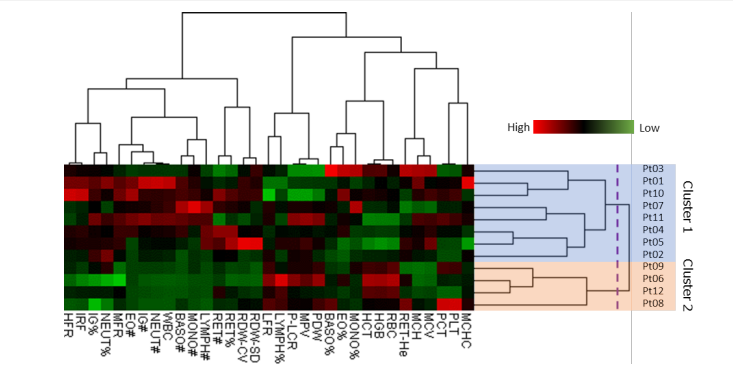
Early Detection of Warning Signs for Hematopoietic Malignancies

Supporting treatment selection by stratifying patients based on predicted treatment response using hematology data

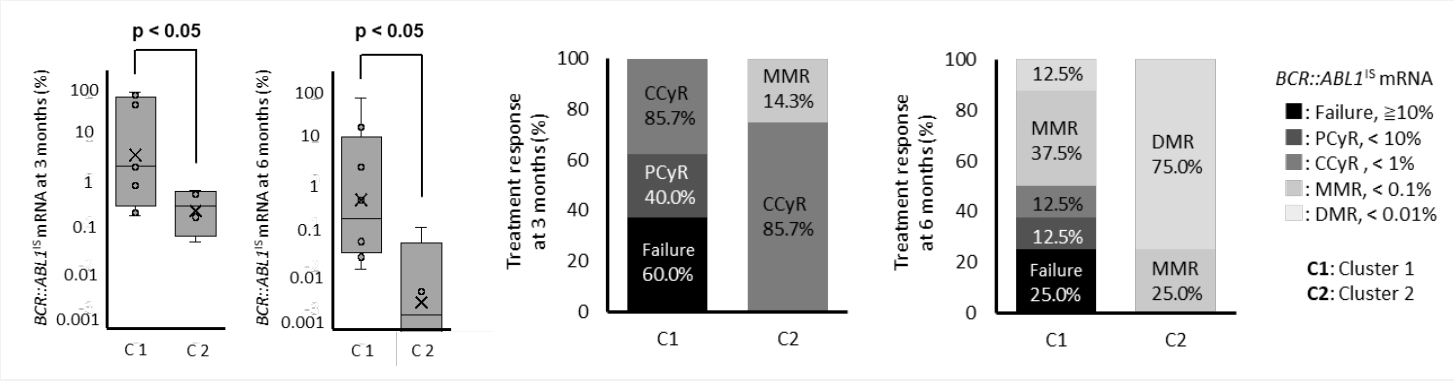
Example: Chronic Myeloid Leukemia*

* Results from joint research with Juntendo University (Source: Suzuki K., et al., *medRxiv,* Jan 21, 2026)

Multivariate analysis of hematology data at diagnosis demonstrated that patients could be stratified into two groups with different treatment responses



Patient stratification using hierarchical clustering analysis



The two stratified groups showed differences in molecular tumor burden and treatment response at 3 and 6 months after treatment

Goal: Supporting treatment selection through prediction of treatment response

Visualization of Population-Level Trends (Public Health)

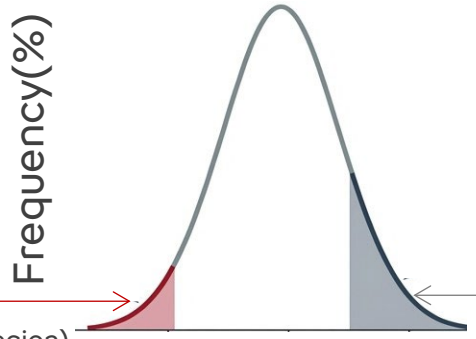
Visualization of Population-Level Trends (Public Health)

Utilizing population-level trend visualization of blood testing data and other applications for public health
Contributing to healthcare systems and local governance in emerging countries

Blood test data

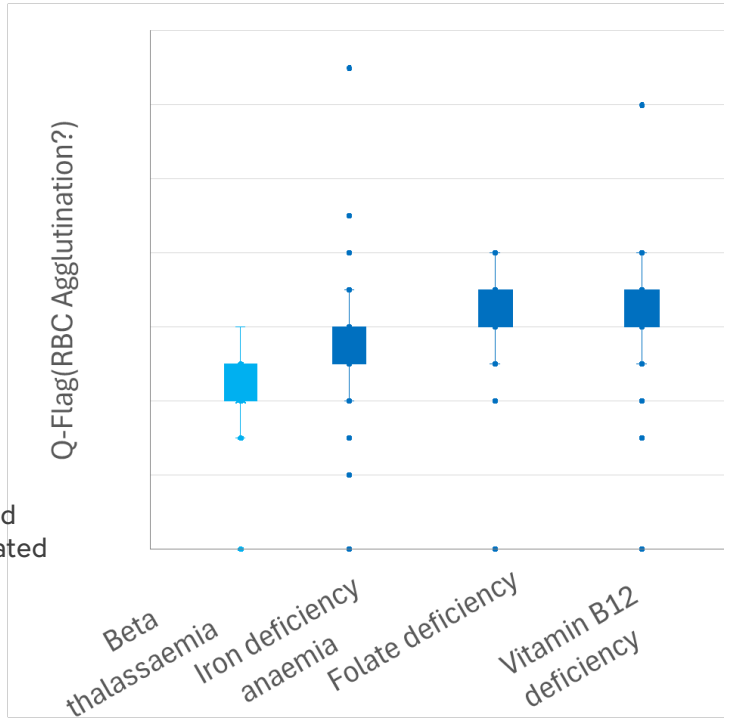
Multiparameter automated hematology analyzer XN-Series
Medical Device Marketing Authorization No.: 28B1X10014000030

Detailed research parameters



Fragments?
(Micro-erythrocyte region)
Reflects fragmented red blood cells caused by hemolysis or ineffective erythropoiesis

RBC Agglutination?
(Macrocytic RBC region)
Reflects macrocytic red blood cells and aggregation associated with vitamin B12 or folate deficiency



- Examination of differentiation between β-thalassemia and iron deficiency anemia in Pakistan
- Using measurement parameters and research parameters* from our XN-Series

*research parameters: For research use only. Not for clinical diagnostic or therapeutic use.

Citation/Adaptation: Muhammad Shariq Shaikh, et al. (2025). "Diagnostic Potential of Q-flag (RBC Agglutination?) and Q-flag (Fragments?) in Beta Thalassemia: A Comparative Analysis with Nutritional Anaemias." XXXVIIIth International Symposium on Technical Innovations in Laboratory Hematology.

Providing information to estimate disease causes from blood test data and enabling potential visualization of population-level trends

Support for Hospital and Laboratory Operations

Support for Hospital and Laboratory Operations

Reducing the workload of healthcare professionals through data and AI
Expanding services that address rising medical expenses, healthcare workforce shortages, stricter regulations, workstyle reforms, and other challenges

Hospital

Improving the quality and efficiency of hospital operations

Examination room | Laboratory

Inquiry response support

Doctors, nurses — Clinical laboratory technologists

DX-enabled communication

Document creation support

Laboratory managers — Clinical laboratory technologists

Automation of document creation and approval workflows

Support for interpretation of imaging data

Clinical laboratory technologists

Assistance with imaging data interpretation

AI for testing support

Data utilized

Publications, outsourced laboratory testing data, etc.

SOPs, guidelines, etc.

Test data, etc.

Documents outside the system, etc.

Inquiry Response Support

Providing immediate answers to doctor inquiries by cross-searching internal hospital documents and test results

Challenge

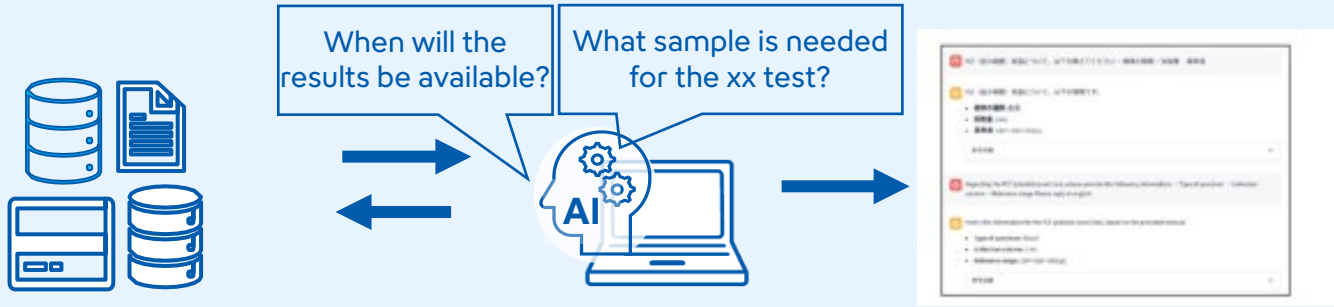
Searching for information and preparing responses takes time

Doctors, nurses　　Clinical laboratory technologists

- Information is scattered
- Preparing response drafts adds to the workload
- Providing manual support outside working hours is difficult

AI-assisted inquiry response support

Searching internal hospital documents and supporting the creation of response drafts



Document Creation Support

Supporting document creation for ISO and other requirements to reduce the workload of indirect laboratory operations

Challenge

Creating documents takes time

- Reviewing corrective actions for ISO and other requirements takes time
- Document creation takes time
- Inconsistent document quality

AI-assisted document creation support

Supporting the creation of document drafts based on established rules

Referencing internal rules and past cases

Supporting proposals for improved measures

Document creation and standardization of quality

- Internal rules
- ISO15189
- Revised Medical Care Act

A test report was missed. Please identify potential causes and propose corrective actions.

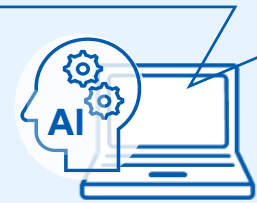


Image Data Interpretation Support

Supporting searches for past cases and medical literature to promote clinical laboratory technologist education and standardized data interpretation

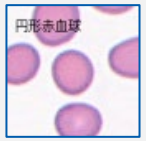
Challenge

Interpreting image data is difficult

Clinical laboratory technologists

What are the characteristics of this blood smear?

Discocyte (normal RBC)



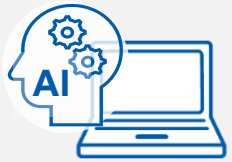
Schistocyte

- Particularly challenging for less experienced technologists

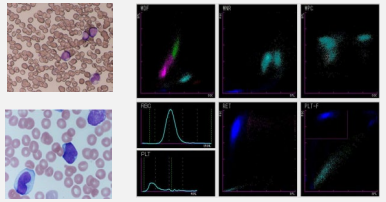
AI-assisted image search support

AI generates responses based on expert knowledge and similar past cases

Image search

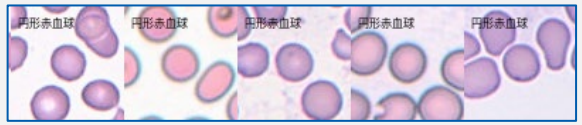


Past case data / expert findings

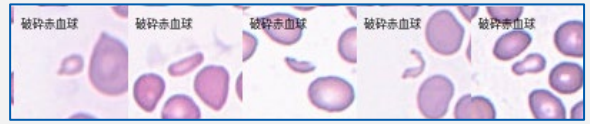


Extracting the top five most similar results

Discocyte (normal RBC)



Schistocyte



3. Deepening of Liquid Biopsy Technology

"Toward the staging and stratification of Alzheimer's disease"

Shigeki Iwanaga
Executive Vice President of
Technology Strategy

“Data Readiness” for the Realization of P4 Medicine

Utilizing test data to guide patients to optimal healthcare pathways, provide optimal intervention options, and drive motivation

Predictive

Preventive

Personalized

Participatory

Guidance to optimal healthcare pathways

Screening data

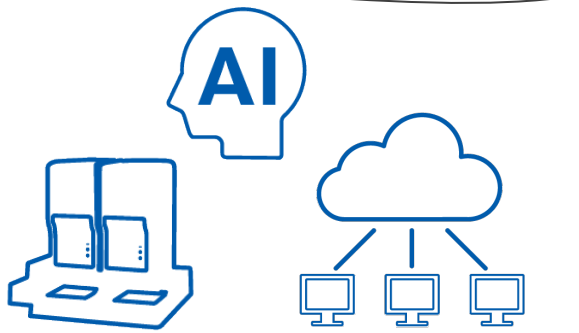
Provision of optimal intervention options

Granular data on disease characteristics

Motivation for behavior change

Longitudinal patient data

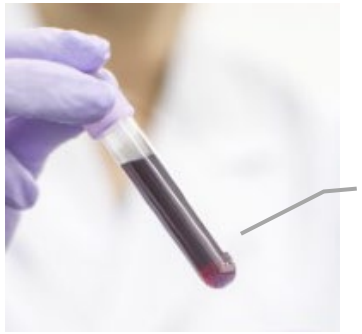
Sysmex AI



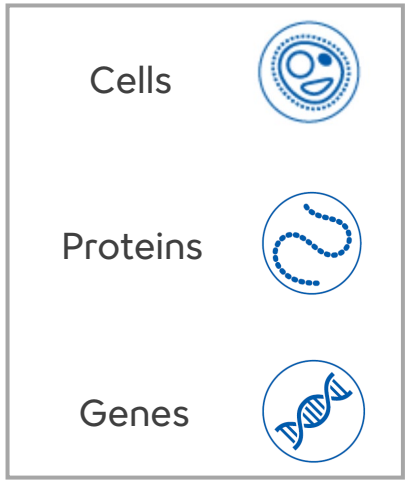
Circulation of test data
Improvement of prediction accuracy

Deepening of Sysmex's Liquid Biopsy Technology

Deepening of measurement technologies



Blood component information (liquid biopsy)



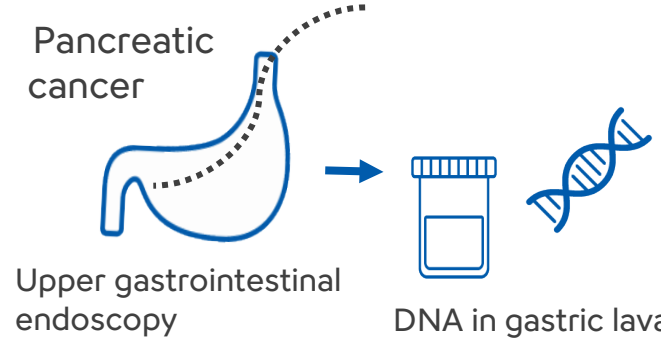
- ✓ Ultra-high sensitivity quantification
- ✓ Specific detection
- ✓ Multiplexing
- ✓ Functional measurements (aggregation, activity, stability)
- ✓ Label-free

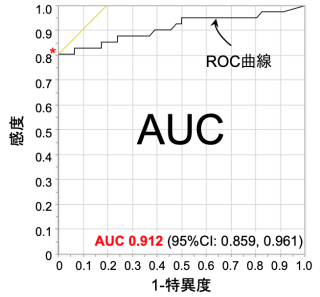
Refined testing

Expansion of target diseases and expansion into early diagnosis and prevention

Cancer

Sensitivity: 80.9%, Specificity: 100%
Detectable pancreatic cancer





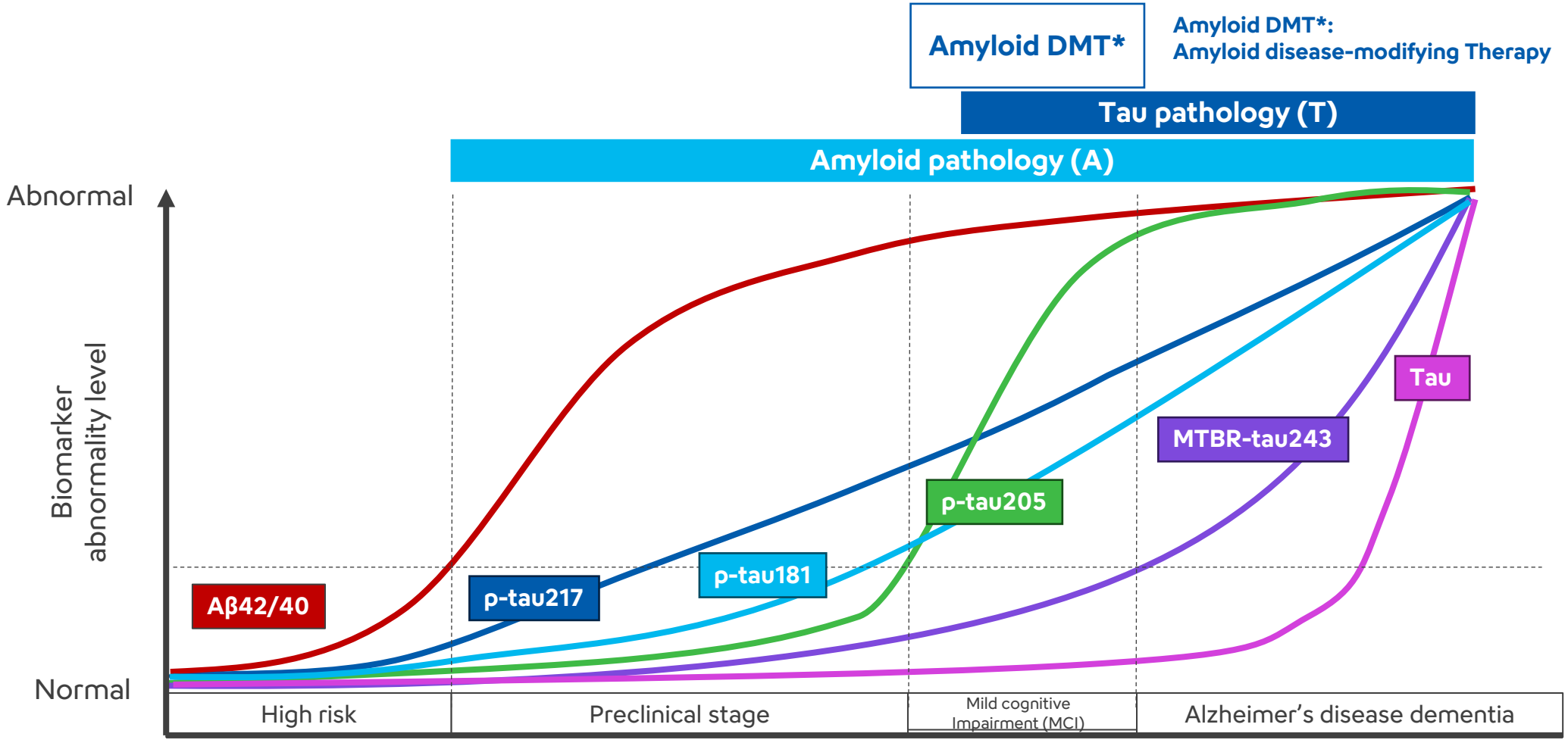
Citation/Adaptation: Shinichi Yachida et al., "KRAS mutations in duodenal lavage fluid after secretin stimulation for detection of pancreatic cancer," Annals of Surgery, 2025 Feb 4.

Cardiovascular diseases
CUC, ATTR

Dementia
Alzheimer's disease

Blood Biomarkers for Alzheimer's Disease

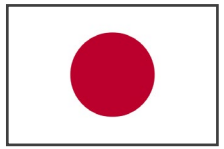
With the advent of disease-modifying drugs, research and development of biomarkers related to amyloid and tau pathologies is progressing



Citation/Adaptation: Gemma Salvadó et al., "Disease staging of Alzheimer's disease using a CSF-based biomarker model," Nat Aging. 2024 May; 4(5): 694-708.

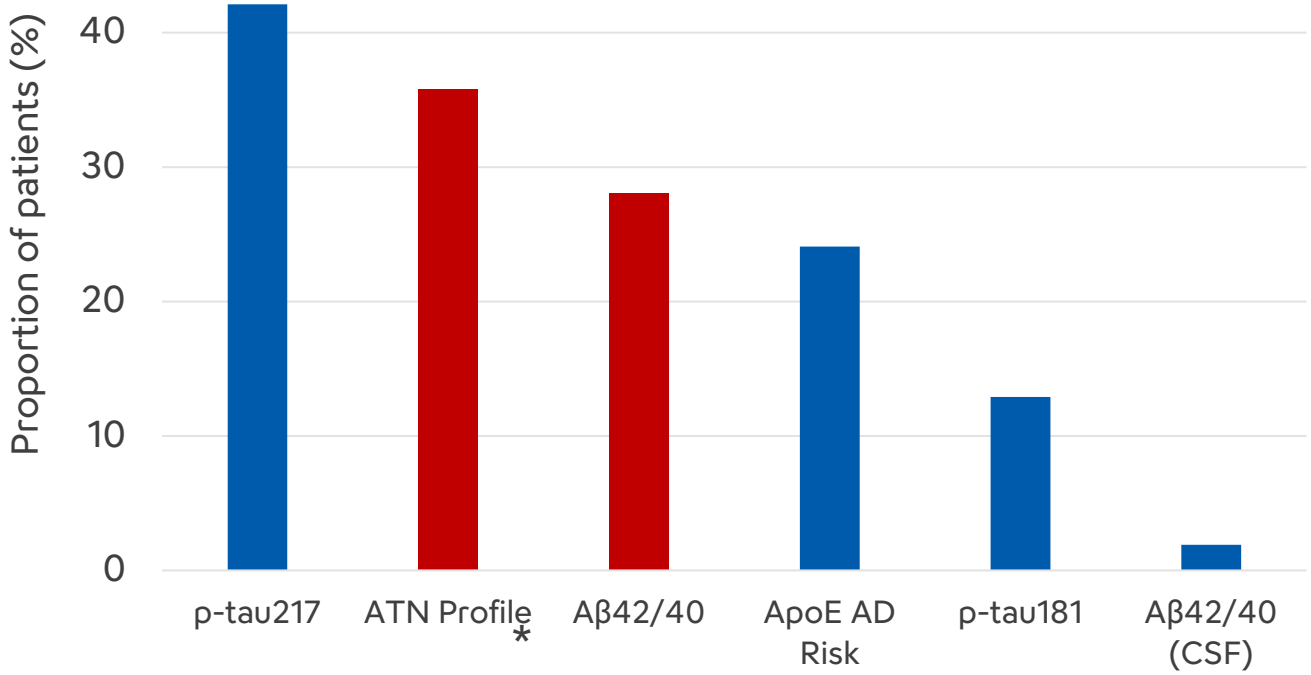
Development Status of Therapeutic Drugs and Blood-Based Diagnosis

Following the rollout of therapeutic drugs around the world, approval of blood-based diagnosis is also progressing.

					
Therapeutic drugs	Leqembi Kisunla	Approved (30 countries)	Approved	Approved	Approved
IVD reagent	**Aβ42/40 (Sysmex)**	**IVDD declared**	**Application in preparation (Launched in Hong Kong and Macau)**	**Approved**	**Application in preparation (LDT in progress)**
	p-tau217/Aβ42 (Sysmex)				**Application in preparation**
	p-tau217/Aβ42 (Fujirebio)	RUO		Pharmaceutical approval (December 2025)	Approved (May 2025)
	p-tau181 (Roche)	IVDR			Approved
	Aβ42/40, p-tau217 (C2N Diagnostics)	IVD (UK)			
	ApoE Gene (Sysmex)	**Application in preparation**		**Approved (June 2025)**	

Status of Blood Biomarker Utilization (U.S. Commercial labs)

Not only p-tau217 but also Aβ42/40 reagents are used in combination.



*Aβ42/40、p-tau181、NfL

Research framework proposed by the National Institute on Aging and the Alzheimer's Association (ATN profile)

Biomarker profile				Stages of dementia (cognitive impairment)		
	A	T	N	Normal	Mild cognitive impairment (MCI)	Dementia
	−	−	−	Normal		Non-AD
	+	−	−			AD-like dementia
	+	−	+			AD and Non-AD
	+	+	−	Preclinical AD	Prodromal AD	
	+	+	+			

Citation/Adaptation：Real-world patterns of Alzheimer's disease biomarker testing: Insights from a large-scale clinical dataset
Citation/Adaptation：Clifford R. Jack, Jr.,et al., A/T/N: An unbiased descriptive classification scheme for Alzheimer disease biomarkers. Neurology® 2016;87:539–547

R&D of Disease-Modifying therapies and Utilization of Blood Biomarkers

Early application of amyloid disease-modifying therapies and progress in research and development of tau disease-modifying therapies. Blood biomarkers are used for clinical trial enrollment

■ Trends in disease-modifying therapies

- **Verification of earlier application of Aβ-targeting disease-modifying therapies**

  Lecanemab, etc.

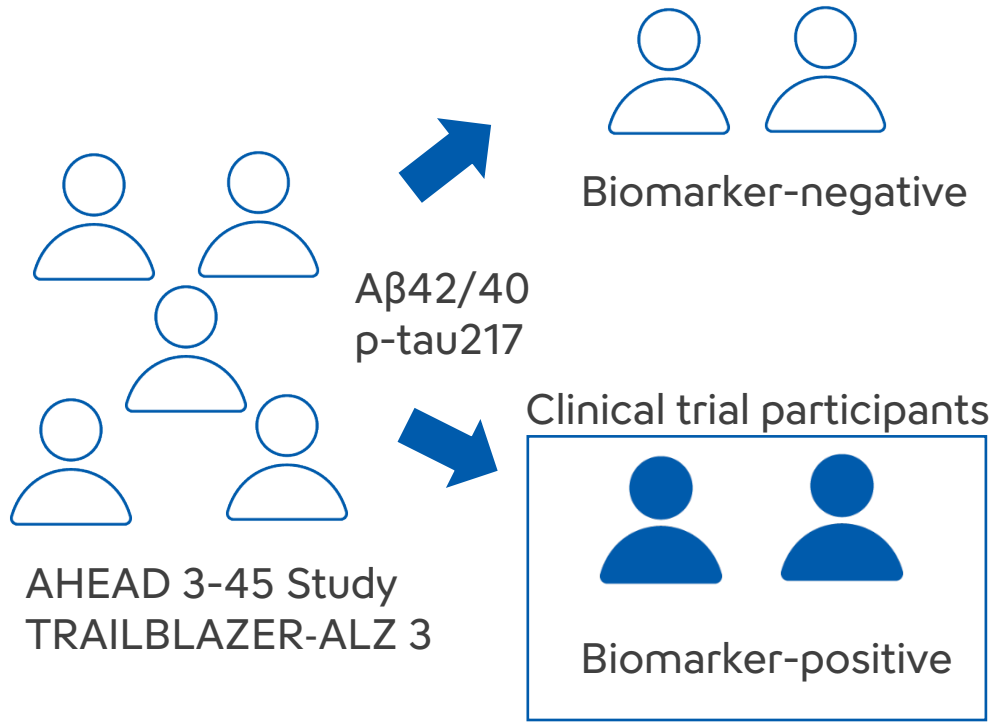
- **Development of tau-targeting disease-modifying therapies**

  Etalanetug,

  BIB080,

  JNJ-63733657, etc.

■ Utilization of blood biomarkers in clinical trials



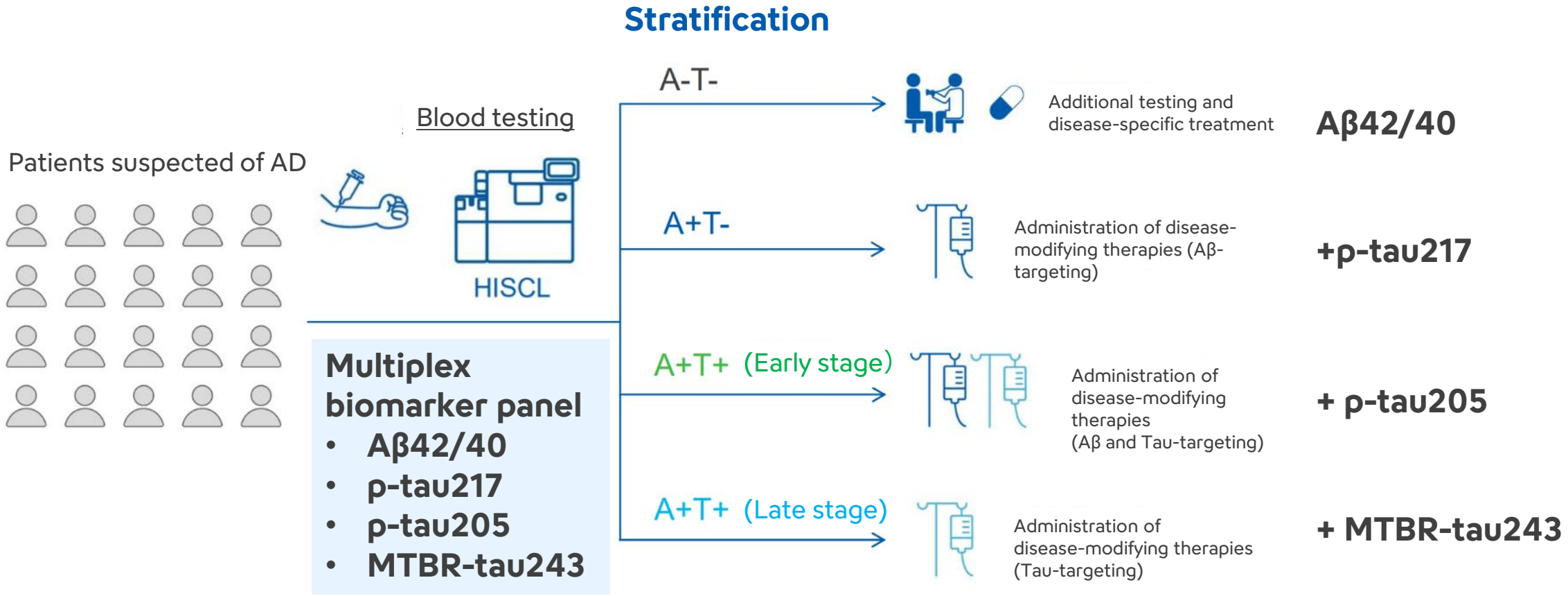
- AHEAD 3-45 Study
- TRAILBLAZER-ALZ 3

Blood biomarkers are expected to be approved alongside disease-modifying therapies

Citation/Adaptation：Viswanath Devanarayan et al., Plasma pTau217 predicts continuous brain amyloid levels in preclinical and early Alzheimer's disease. Alzheimer's & Dementia 2024;20:5617–5628.
Citation/Adaptation：Doris Patricia Molina-Henry et al.,Racial and ethnic differences in plasma biomarker eligibility for a preclinical Alzheimer's disease trial. Alzheimer's Dement. 2024;20:3827–3838.
Citation/Adaptation：Roy Yaari1 et al., Donanemab in preclinical Alzheimer's disease: Screening and baseline data from TRAILBLAZER‐ALZ 3. Alzheimer's Dement. 2025;21:e70662.

Towards staging and stratification of Alzheimer's disease

ATN profile enables selection of appropriate tests and treatments



Towards staging and stratification of Alzheimer's disease

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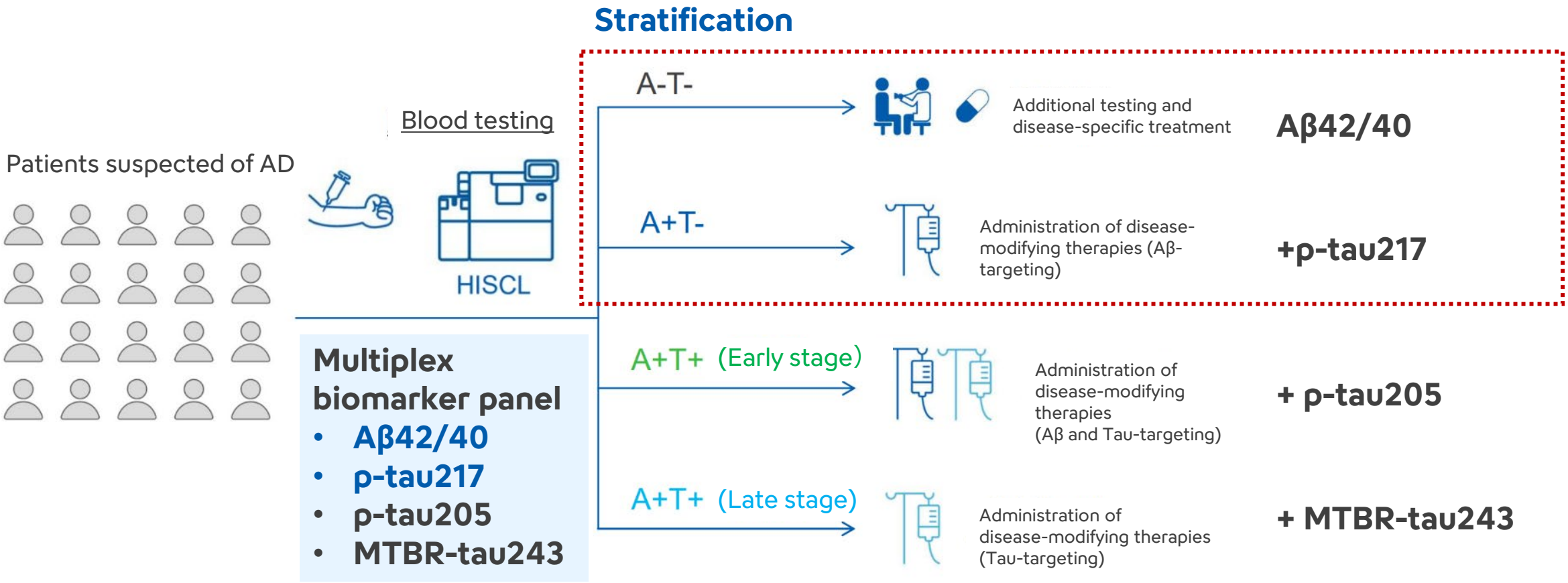
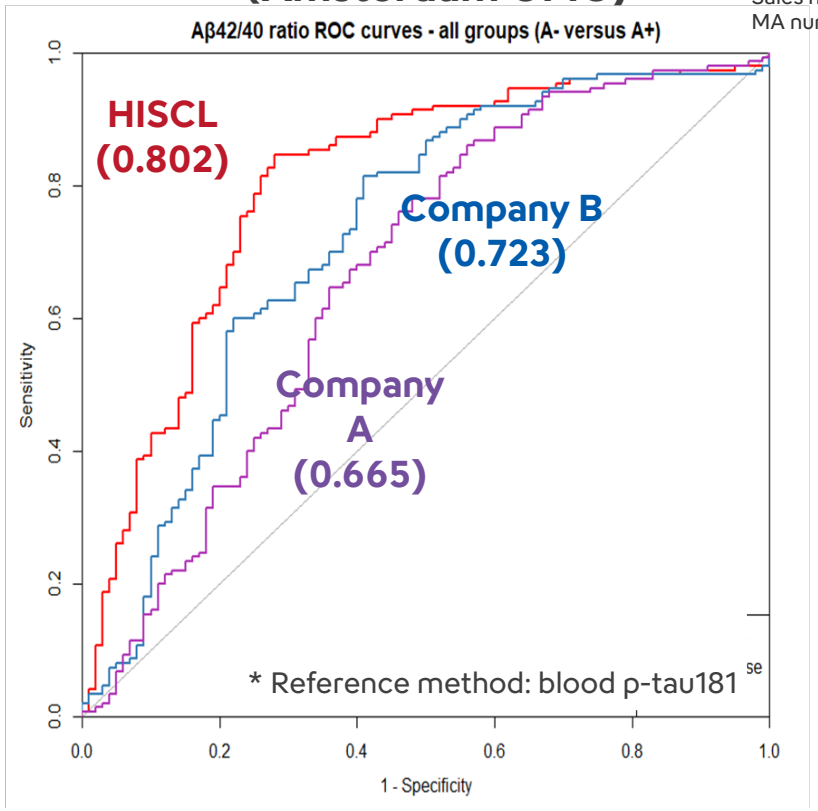


Amyloid Pathology-Based Stratification Using HISCL™ Aβ42/40*

In comparative studies with other companies, our system demonstrated performance superior to that of competing products; for Aβ42/40, our system is the only one that meets the guideline-recommended performance criteria

Heads to Heads study (Amsterdam UMC)

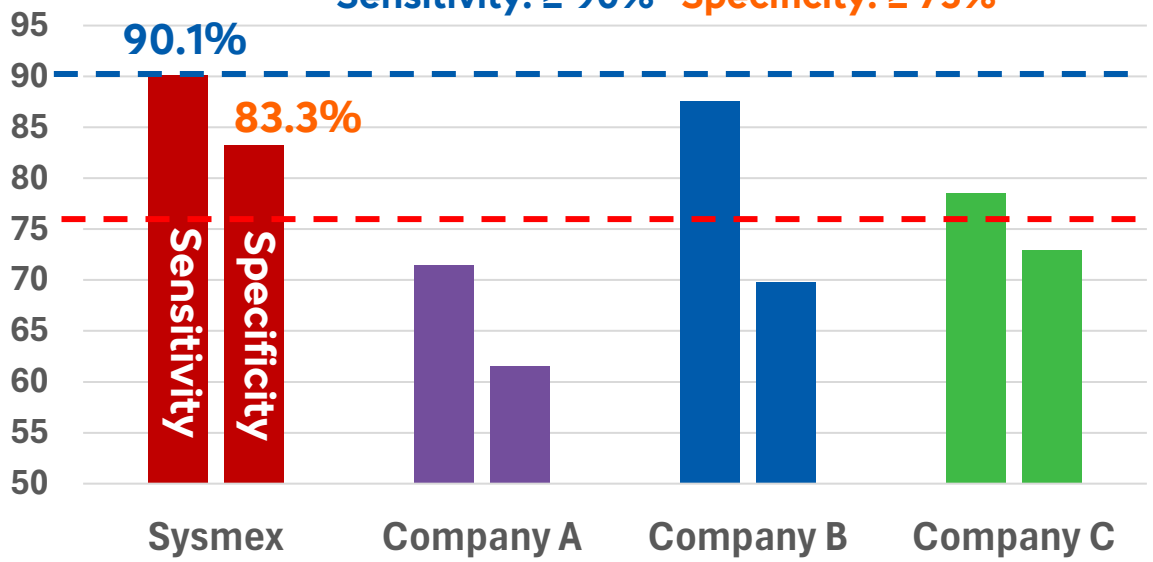


HISCL Aβ42/40*
Sales name：HISCL β-Amyloid 1-40 reagent
MA number: 30400EZX00105000
Sales name：HISCL β-Amyloid 1-42 reagent
MA number：30400EZX00104000

DOI: 10.1002/alz.70535
GUIDELINES
Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

Alzheimer's Association Clinical Practice Guideline on the use of blood-based biomarkers in the diagnostic workup of suspected Alzheimer's disease within specialized care settings

Guideline-recommended performance (triage test)
Sensitivity: ≥ 90% **Specificity: ≥ 75%**



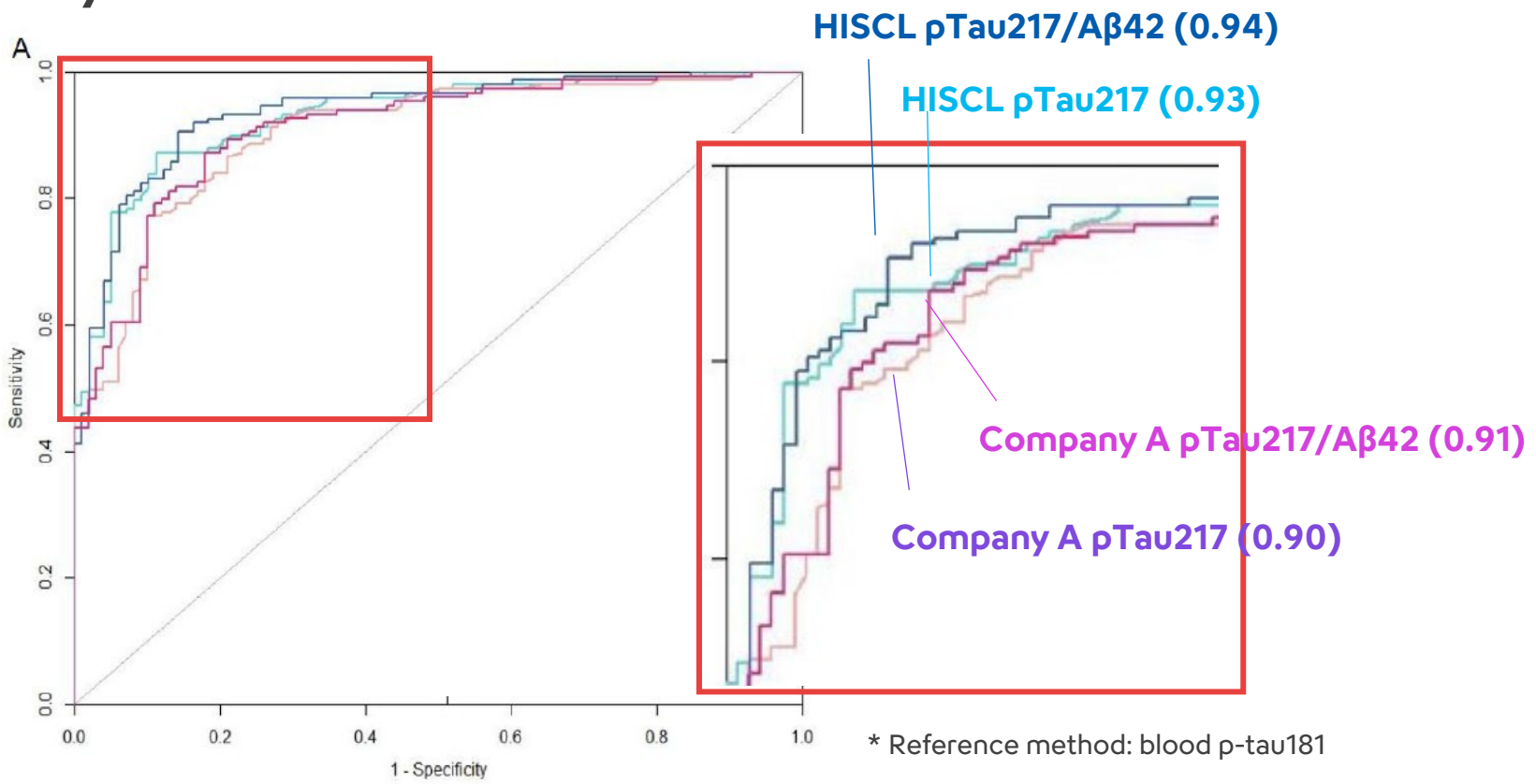
Citation/Adaptation: Inge, V., et al. "High diagnostic performance of the random-access HISCL-5000 pTau217, Aβ42 and Aβ40 plasma assays for detecting amyloid pathology across the Alzheimer's disease clinical continuum." CTAD (2025).

Citation/Adaptation: Sebastian palmqvist et al., "Alzheimer's Association Clinical Practice Guideline on the use of blood-based biomarkers in the diagnostic workup of suspected Alzheimer's disease within specialized care settings." Alzheimers Dement. 21(7), e70535 (2025).

Amyloid Pathology-Based Stratification Using HISCL p-tau217

**For both p-tau217/Aβ42 and p-tau217,
our system demonstrated superior performance over competing products**

Joint study with Amsterdam UMC



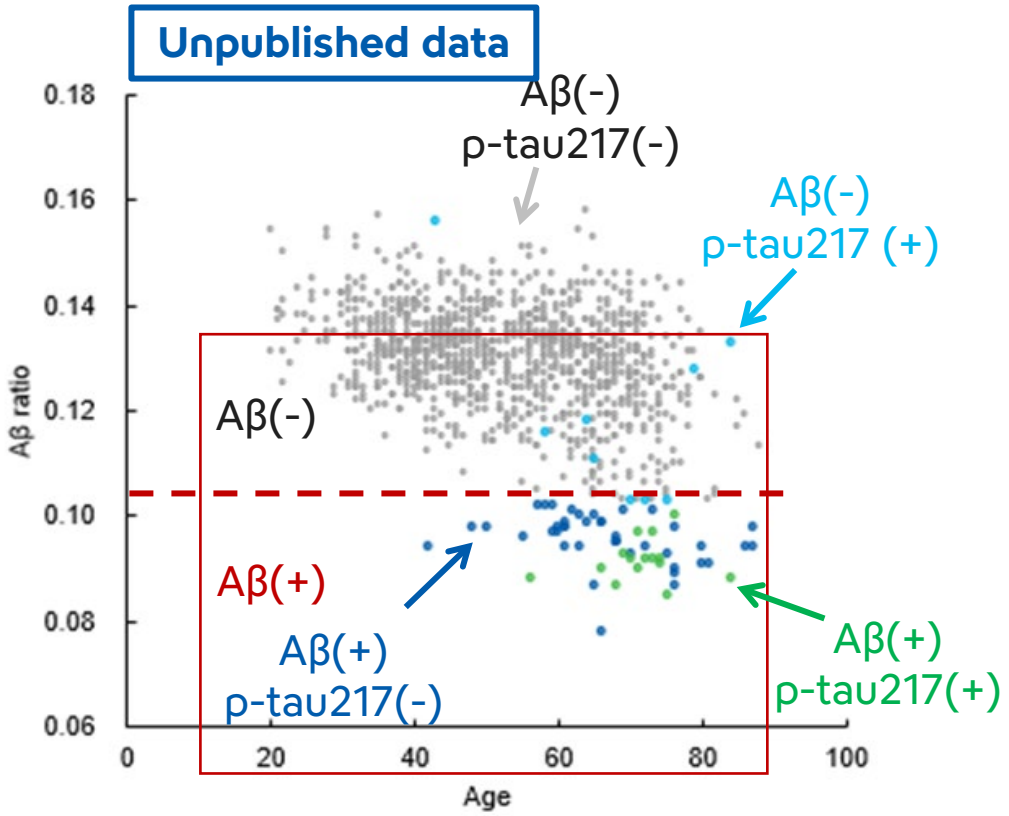
* Reference method: blood p-tau181

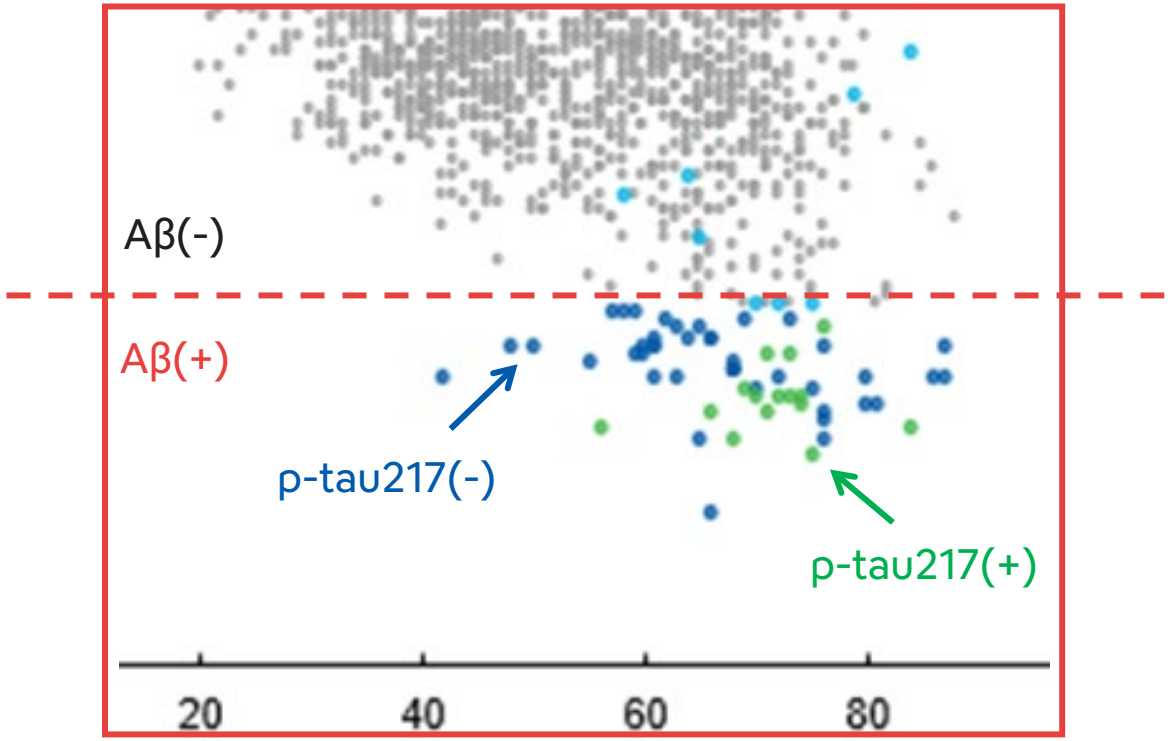
Citation/Adaptation: Inge, V., et al. "High diagnostic performance of the random-access HISCL-5000 pTau217, Aβ42 and Aβ40 plasma assays for detecting amyloid pathology across the Alzheimer's disease clinical continuum." CTAD (2025).

Early Detection of Amyloid Pathology in a Healthy Cohort

p-tau217-negative cases were observed among blood Aβ-positive individuals; these findings suggest that p-tau217 becomes positive following Aβ positivity

Joint study with Hirosaki University





This work was supported by the Japan Science and Technology Agency (JST). Grant Number JPMJCE1302, JPMJCA2201, and JPMJPF2210

Towards staging and stratification of Alzheimer's disease

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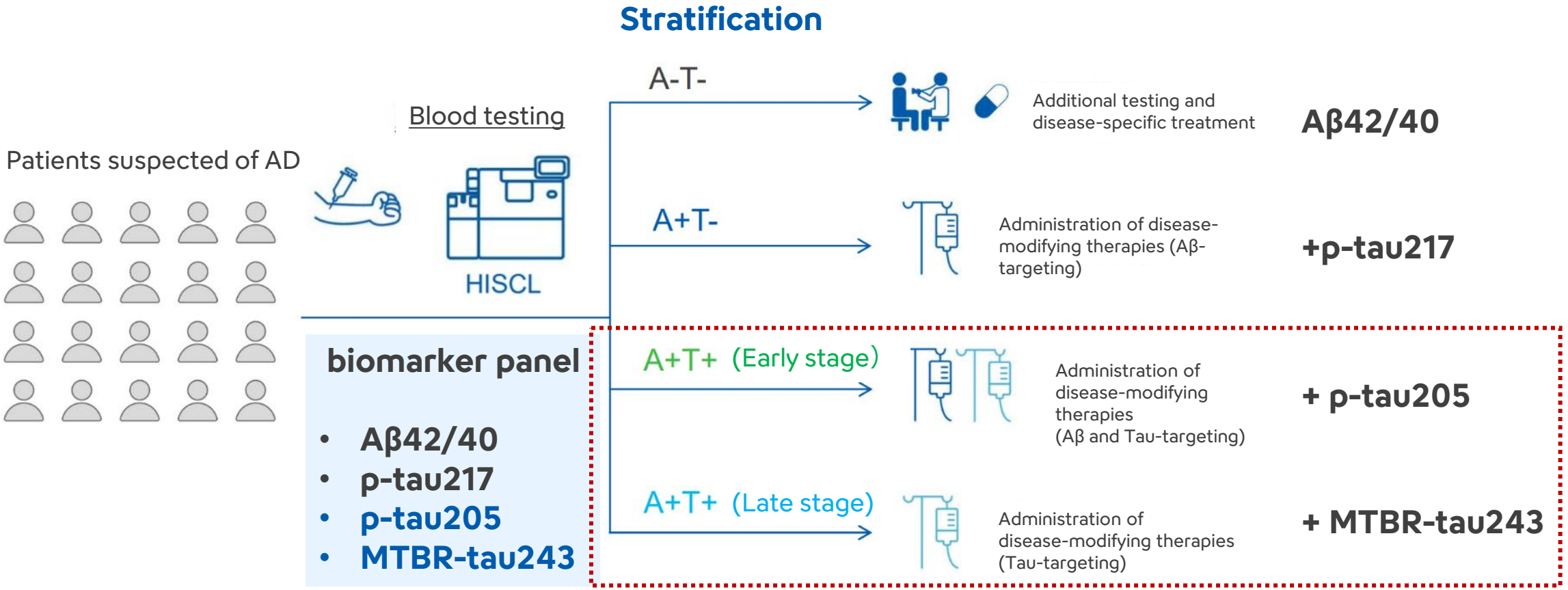
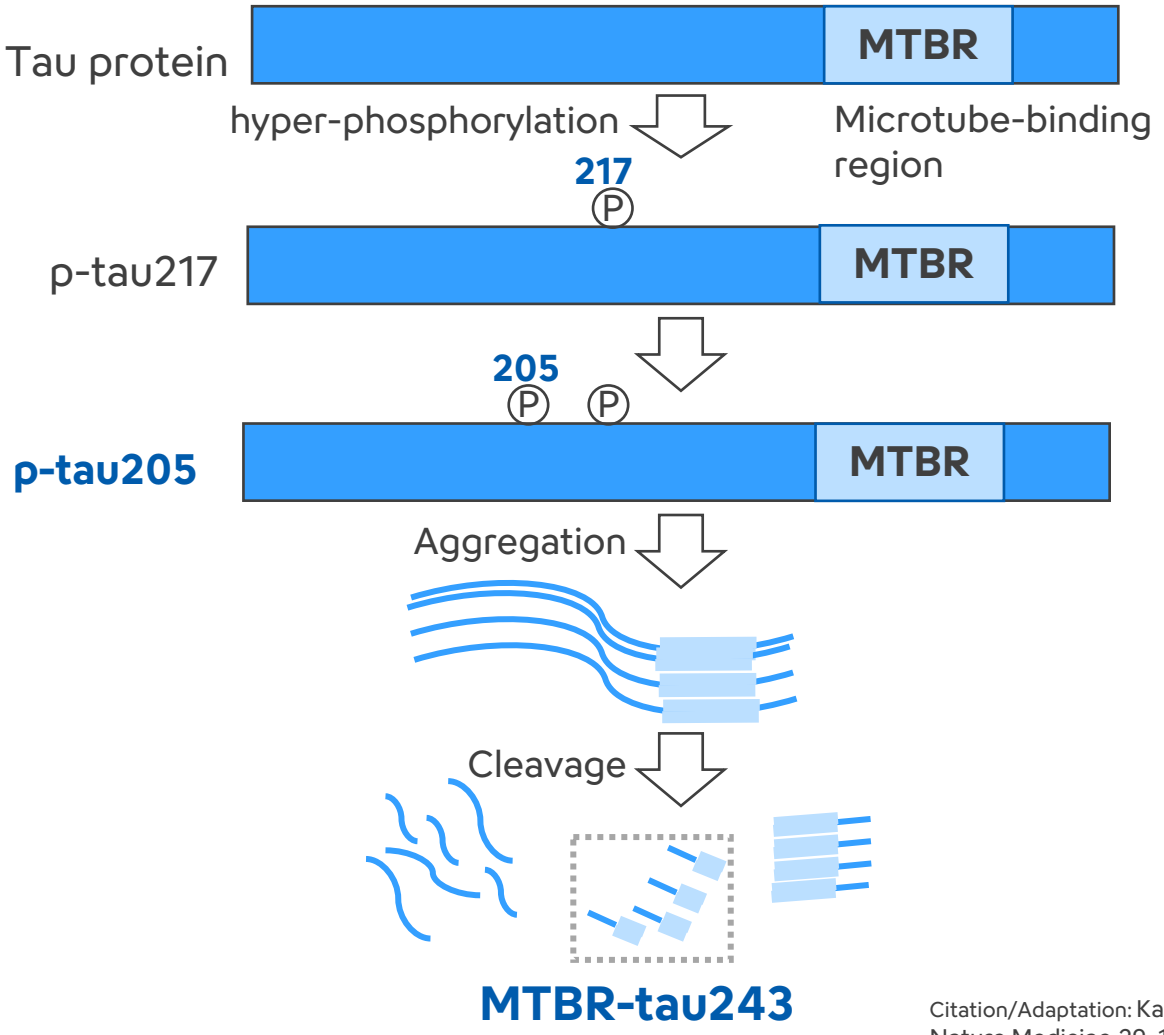
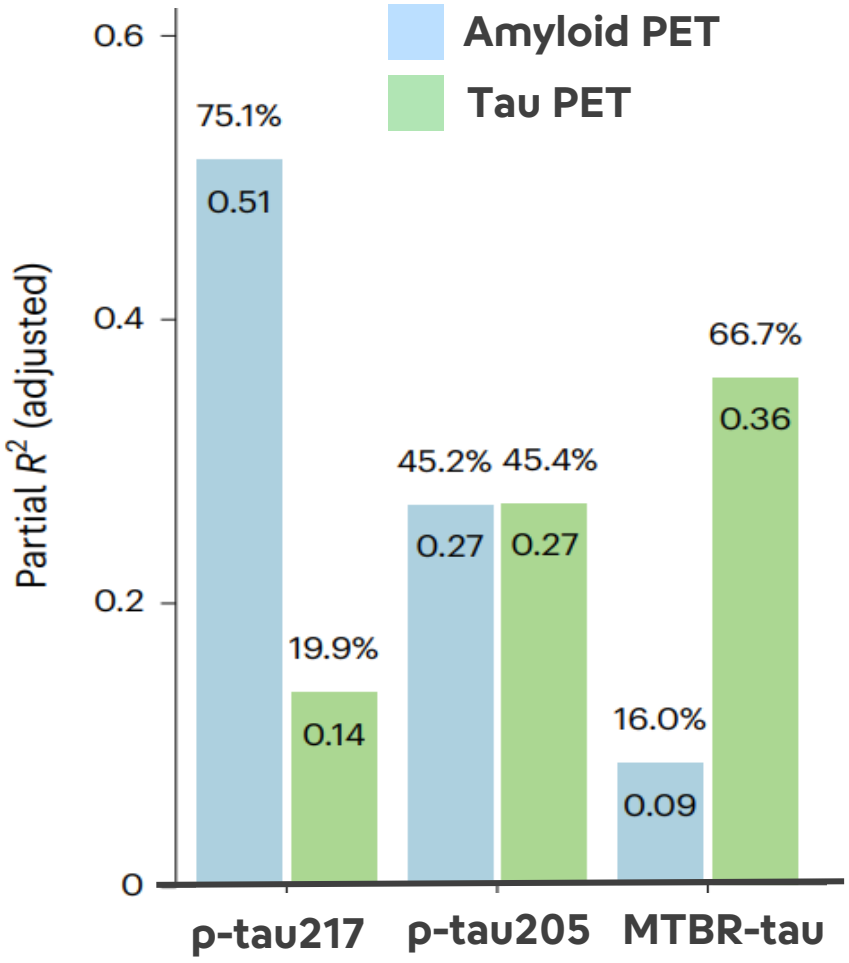


p-tau205 and MTBR-tau243

MTBR-Tau243 are generated by cleavage of tau proteins
Association with tau pathology increases in the order of p-tau217, p-tau205, and MTBR-tau



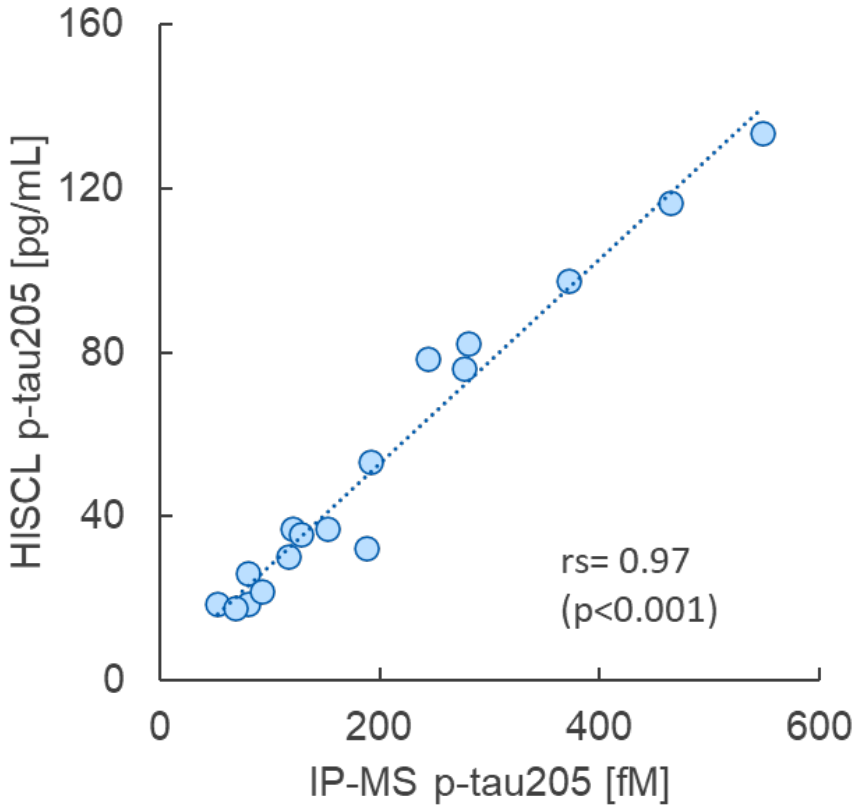


Citation/Adaptation: Kanta Horie et al., CSF MTBR-tau243 is a specific biomarker of tau tangle pathology in Alzheimer's disease. Nature Medicine 29, 1954-1963 (2023)

Development of the HISCL p-tau205 Reagent

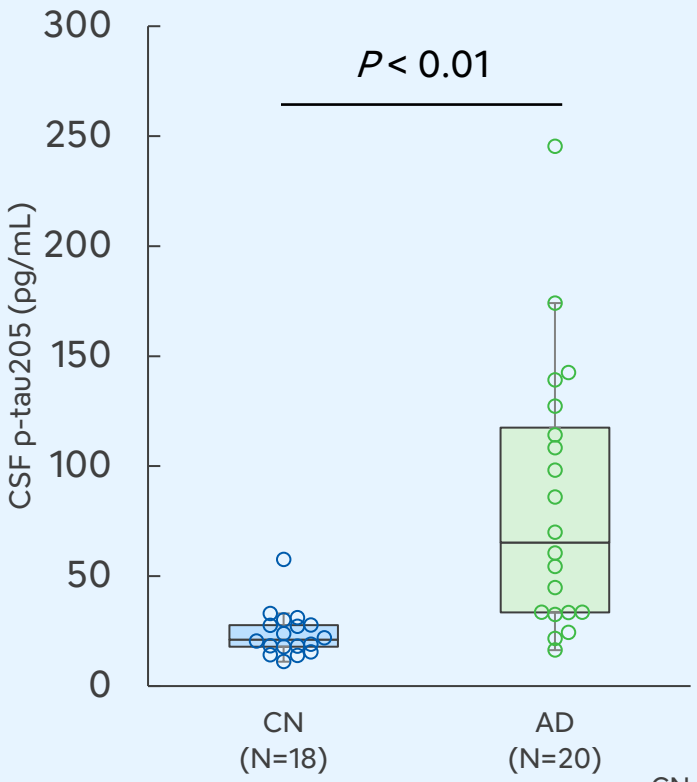
Development of the testing reagent capable of detecting p-tau205 in cerebrospinal fluid and blood

Correlation with immunoprecipitation-mass spectrometry (cerebrospinal fluid)

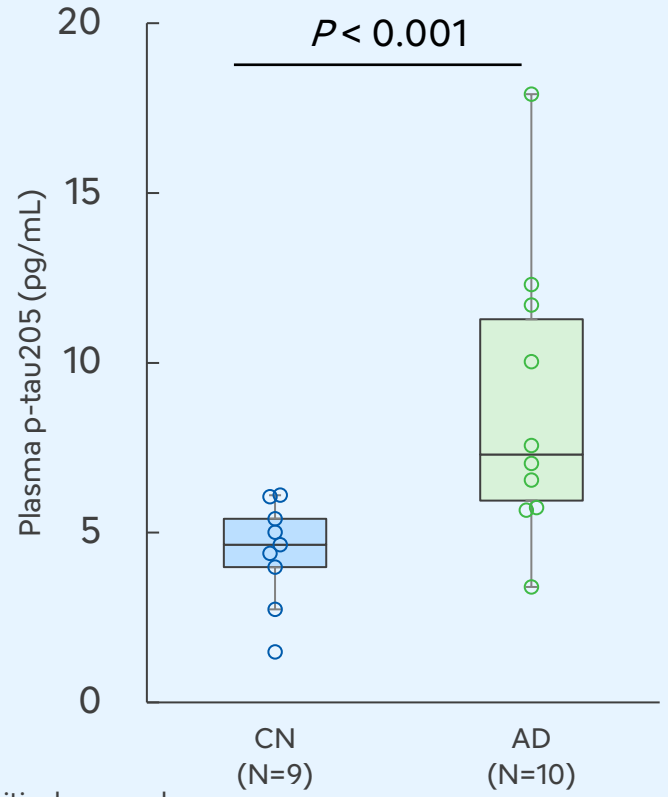


rs: Spearman's rank correlation coefficient

Cerebrospinal fluid



Blood

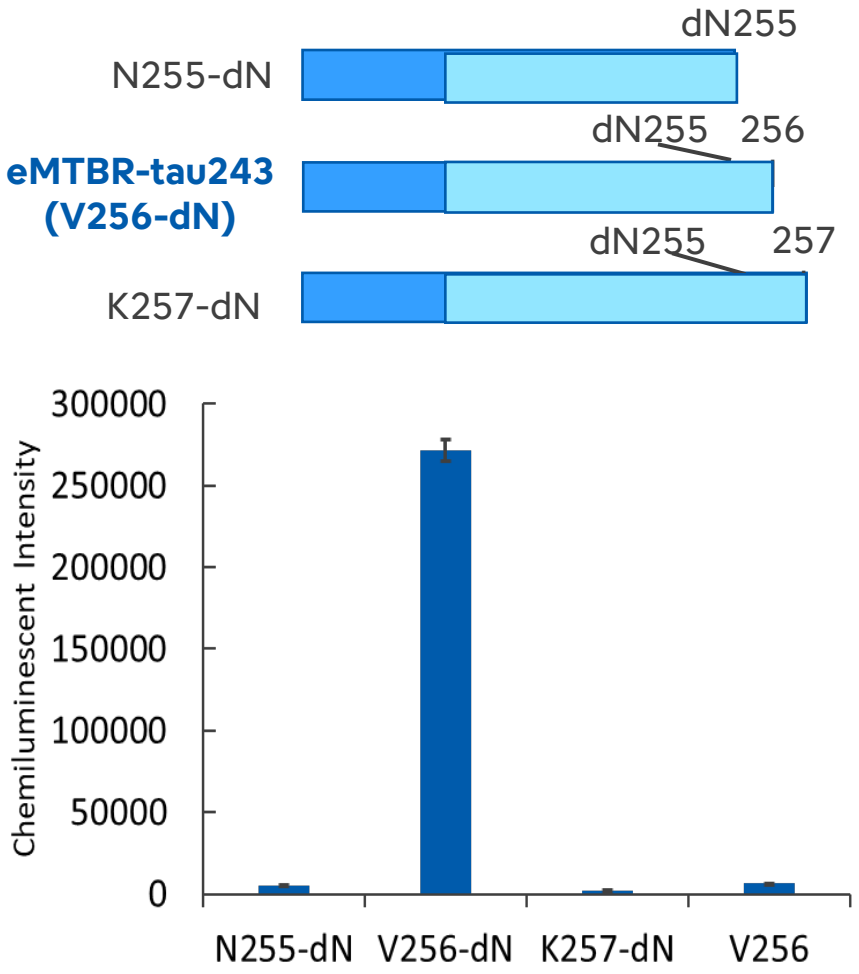


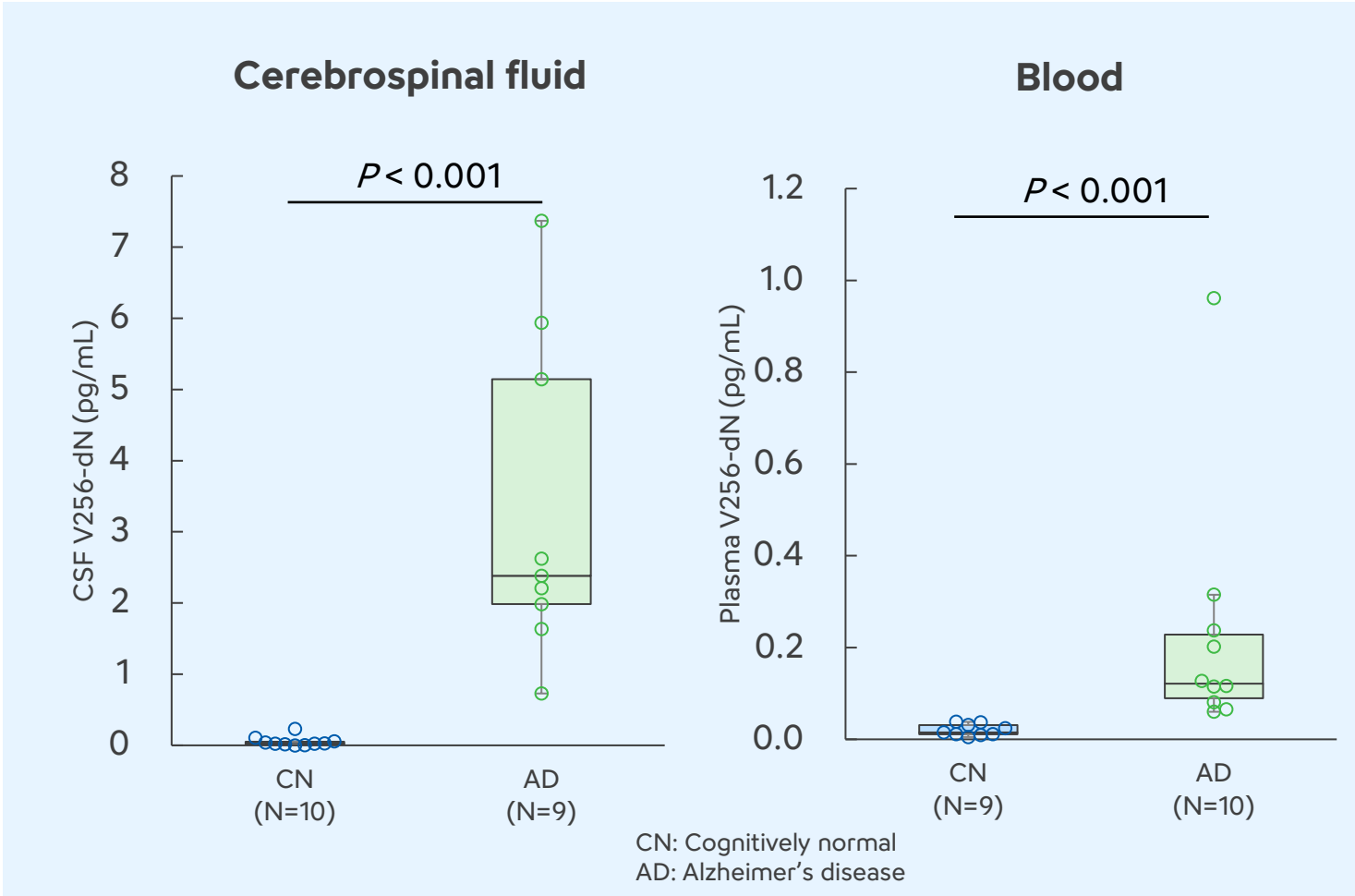
CN: Cognitively normal
AD: Alzheimer's disease

Citation/Adaptation: Ishiki, K., et al., "Development of a highly specific p-tau205 assay using a fully automated immunoassay system." ADPD 2025.
Citation/Adaptation: Murakami, S., et al., "Development of Plasma p-tau205 Assay Using a Fully Automated Immunoassay System." The 44th Annual Meeting of Japan Society for Dementia Research 2025.

Development of the HISCL MTBR-tau243 Reagent

Established the world's first automated immunoassay system for MTBR-tau243





Citation/Adaptation: Murakami, S., et al. (2025). "Development of MTBR-tau Fragment Assay Using a Fully Automated Immunoassay System." CTAD.

Perspective of Technological development for IVD

1. **Establishing staging detection for preclinical, mid-stage, and late-stage Alzheimer's disease. Promoting market awareness activities aimed at insurance reimbursement**
   - Preclinical: Aβ42/40
   - Middle：Aβ42/40・p-tau217
   - Late：p-tau205・MTBR-Tau243
     - ✓ Demonstrating Sysmex's presence in early and late stages by utilizing Aβ42/40 and MTBR-Tau243
     - ✓ Differentiation through biomarker paneling
     - ✓ Accelerating development and clinical research with global KOLs
     - ✓ RUO of p-tau217 (FY26 1Q) , and early IVD development

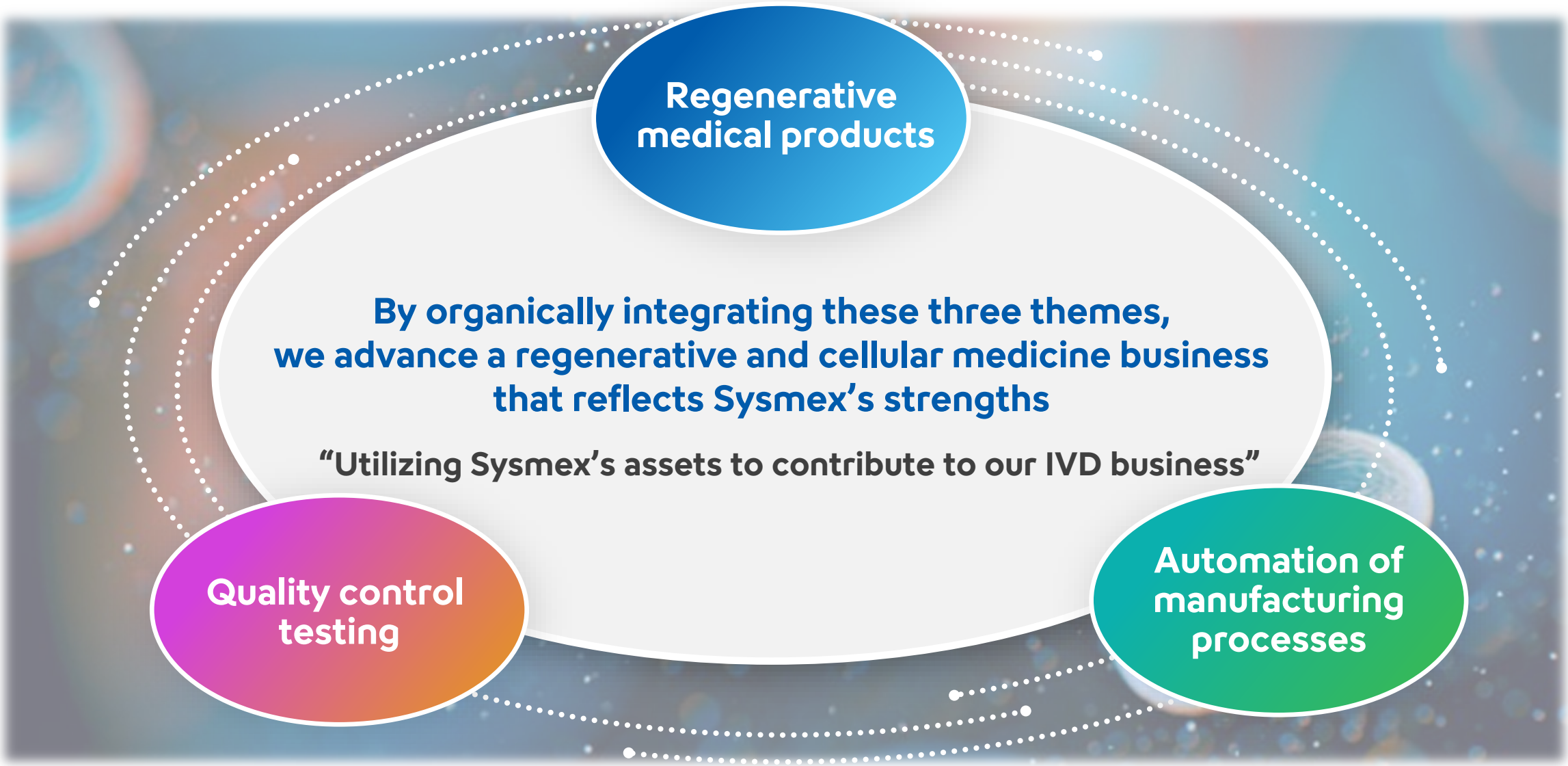
2. **Promote the application of technologies that combine the above markers with previously developed markers (NfL, p-tau181, etc.)**
   Expanding to other dementias (FTD/DLB) and further applying to non-dementia central nervous system diseases (PD/MS/ALS)

FTD: Frontotemporal Dementia
DLB: Dementia with Lewy Bodies
PD: Parkinson's Disease
MS: Multiple Sclerosis
ALS: Amyotrophic Lateral Sclerosis

Initiatives Targeting Regenerative and Cellular Medicine

Kenji Tsujimoto
Executive Officer
Executive Vice President of
Next Generation Medical
Business Development

Three Pillars of the Regenerative and Cellular Medicine Business



Regenerative Medical Product Pipeline

Promoting the development of regenerative medical products that align closely with our business domains

Cell type	Target indication	Clinical value	Submission for regulatory approval (expected)
Inducible inhibitory T-cells AlliedCel	Living donor (liver) transplants	Induction of immune tolerance in recipient T-cells	**Around FY2028**
iPS cell-derived platelets Mega karyon	Thrombocytopenia	Restoration of hemostatic function using highly versatile artificial platelets	Around FY2029

* Cultured hematopoietic stem cells (AlliedCel) are currently being re-evaluated.

Environment Surrounding Liver Transplants

**Although many liver transplants are performed in Japan,
the costs and side effects of immunosuppressive therapy remain challenges**

Annual number of living-donor liver transplant surgeries (Japan)

350–400 cases

* Source: Japanese Liver Transplantation Society, “Liver Transplant Registry Report”

Lifetime drug cost for immunosuppressive drugs per patient

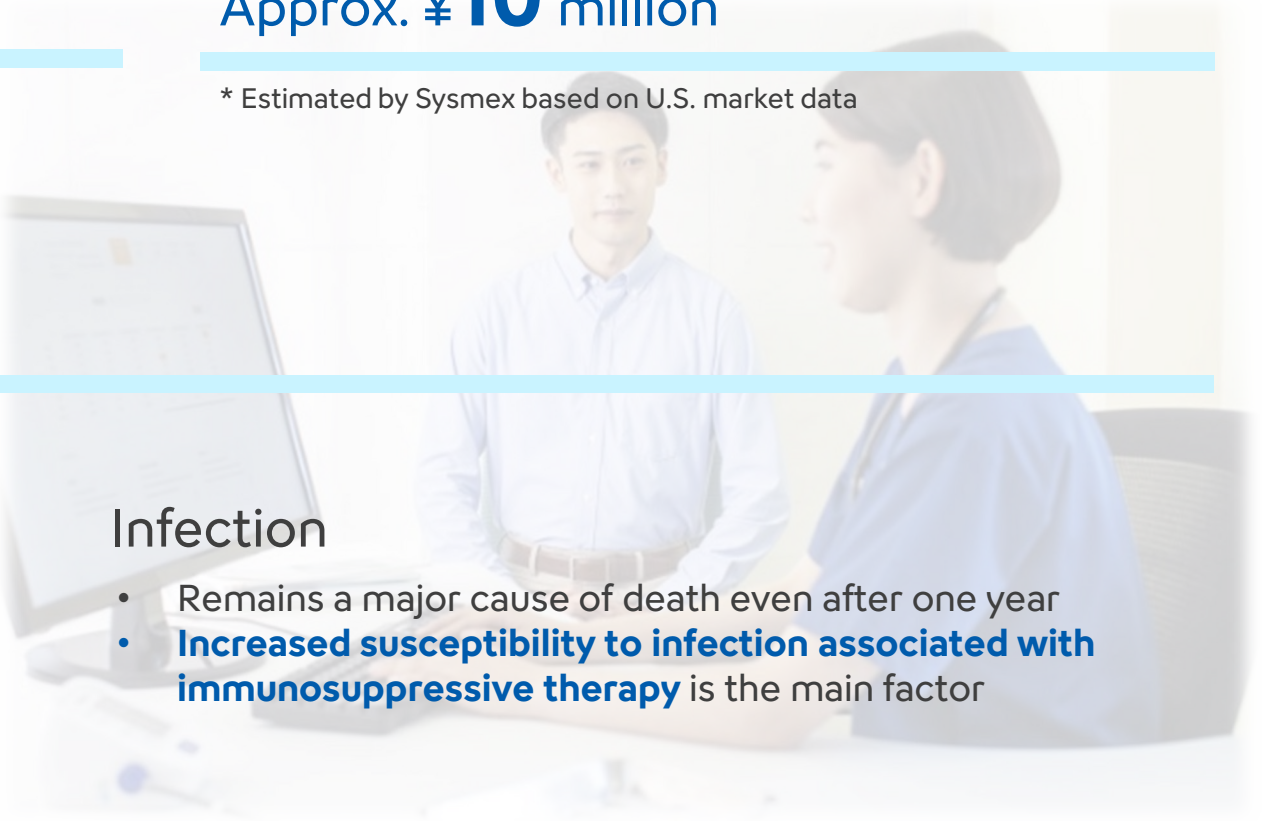
Approx. ¥**10** million

* Estimated by Sysmex based on U.S. market data

Leading causes of death among patients who survived one year after liver transplant (Top 2)

Malignancy and infection

* Rana et al., “Annals of Surgery 2019”



Malignancy

- Most common cause of death
- Attributed to **increased cancer risk associated with immunosuppression**

Infection

- Remains a major cause of death even after one year
- **Increased susceptibility to infection associated with immunosuppressive therapy** is the main factor

Global trends in the reduction and discontinuation of immunosuppressive therapy in organ transplantation

Minimization of immunosuppressive therapy: Progress toward establishing a framework for international standardization

Preparation for international consensus building

- There is growing international recognition of the need to define and evaluate **immunosuppression minimization** in "a standardizable manner" to balance reduction of long-term immunosuppression-related complications (such as infections, malignancies, and nephrotoxicity) with effective prevention of rejection.
- At **major KOL meetings,** efforts are underway to establish common definitions, endpoints, and application criteria for minimization, **accelerating discussions toward consensus building**.
- The **Japanese Society for Transplantation is also preparing to align consensus documents, KOL statements, and related materials with topics for regulatory consultation and communications**, aiming to establish a "common language" that can support future academic and clinical frameworks.

Principles of immunosuppression minimization

- **Safety-first:** Evaluate rejection control and safety (infection, tumors, renal function) within the same framework.
- **Risk-stratified:** Clearly define application criteria according to immunological risk, organ type, and post-operative time course.
- **Measurable & reproducible:** Define measurable indicators for dosing (dose/number of agents/duration) and outcomes.

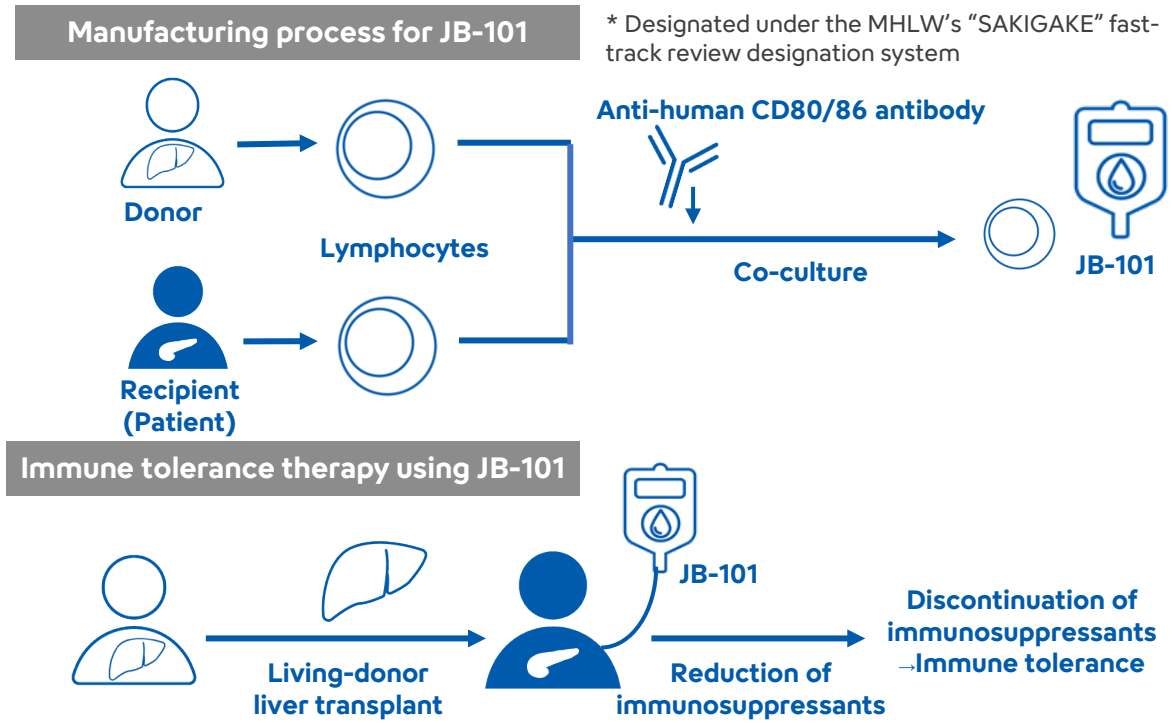
Collaboration with transplantation societies

- **Development of common definitions:** Harmonizing the terminology for minimization (dose, combination therapy, duration) and defining application criteria.
- **Candidate new endpoints:** Combining rejection, infection, renal function, and related factors, along with defining measurement frequency.
- **Study of standard immunosuppression and adverse event:** Stratification, safety evaluation, follow-up duration, and comparative frameworks

Inducible inhibitory T-Cells (Investigator-Initiated Clinical Trial Underway)

This has the potential to become the world's first cellular therapy to induce sustained immune tolerance in organ transplants, and may also enable the development of tests to monitor immune status

Inducible inhibitory T-cells (JB-101*) are cells designed to prevent rejection of transplanted donor organs by the patient's immune system



Significance of immune tolerance therapy

- **Improved graft survival rate through the induction of immune tolerance**
- **Reduced risk of complications through reduction or discontinuation of immunosuppressants**
- **Lower healthcare costs through reduction or discontinuation of immunosuppressants**

Immune status monitoring will be key, creating opportunities for our IVD testing technologies

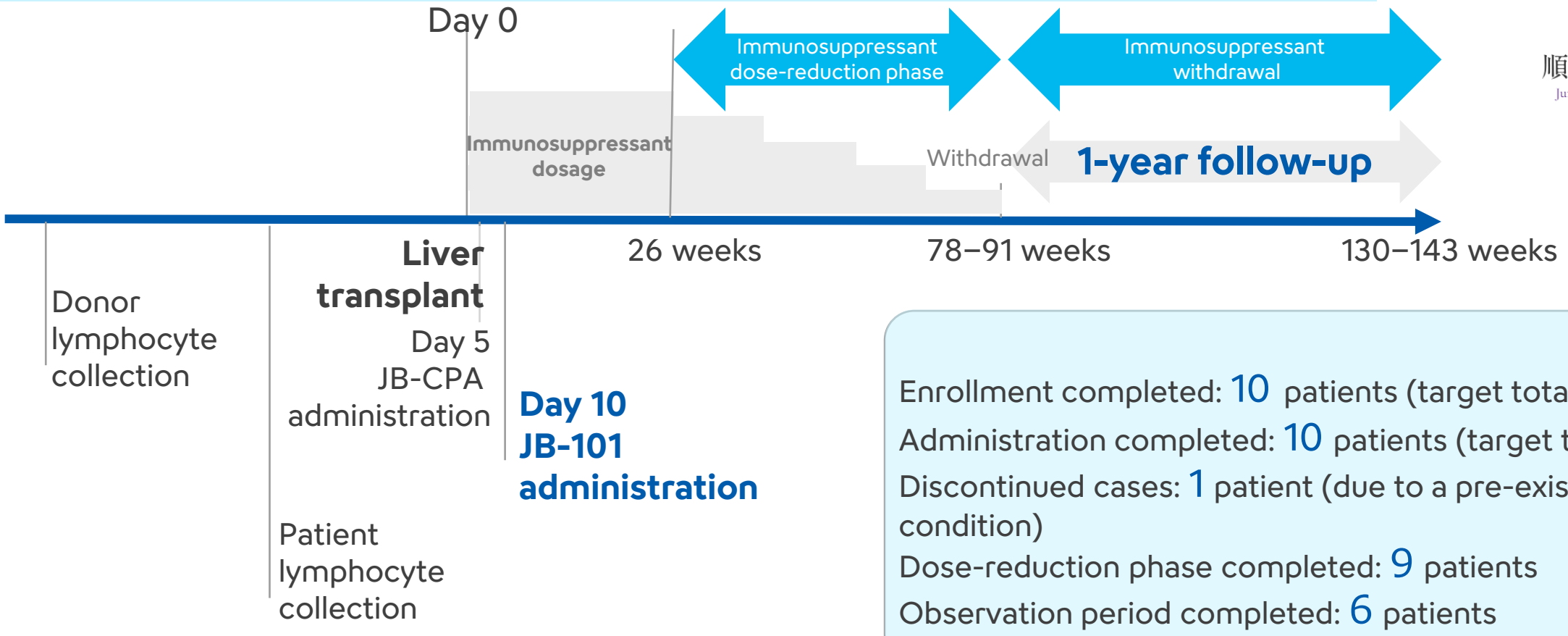
Inducible inhibitory T-cells belong to the same Treg subset as regulatory T-cells recognized by the 2025 Nobel Prize and may attract increasing attention as a therapeutic technology in the future

Progress of the JB-101 Investigator-Initiated Clinical Trial

Target enrollment: The immunosuppressant dose-reduction period for the 10 enrolled patients has been completed.
Future regulatory submission plans are under consideration through prior consultation with PMDA.

Overview of the investigator-initiated clinical trial led by Juntendo University

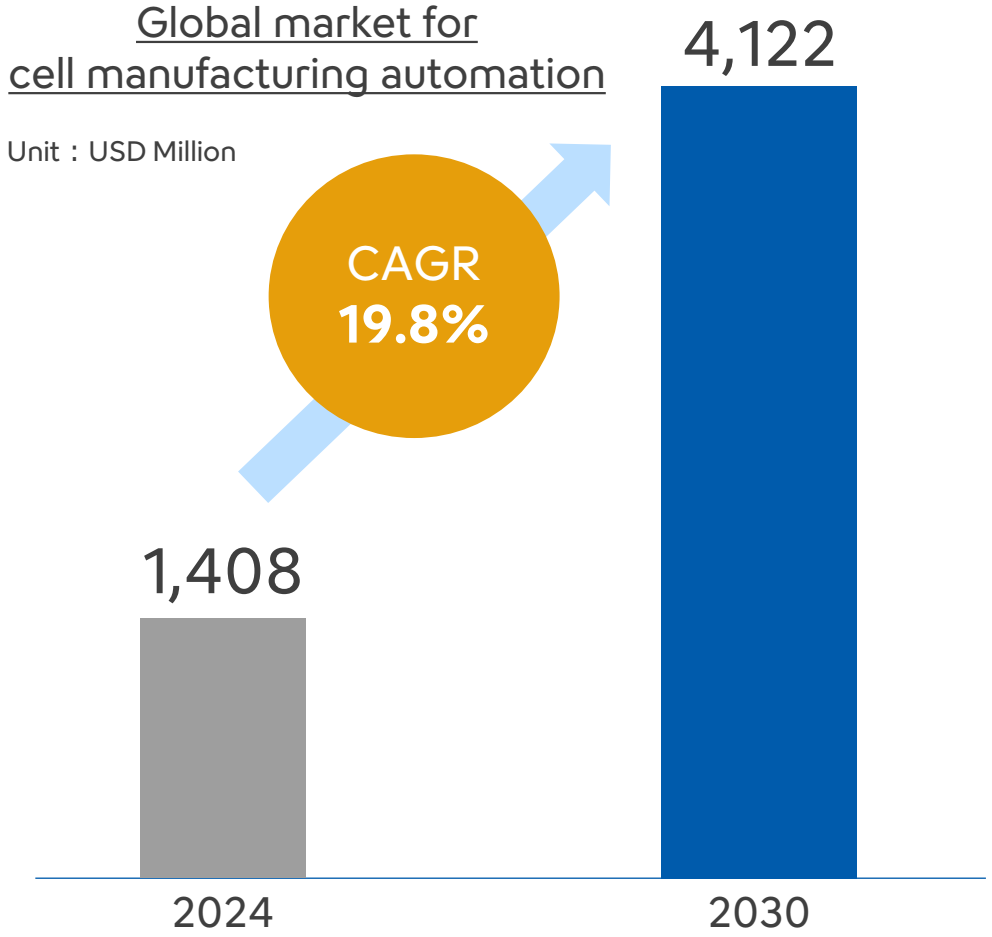
順天堂大学
Juntendo University



Enrollment completed: 10 patients (target total)
Administration completed: 10 patients (target total)
Discontinued cases: 1 patient (due to a pre-existing condition)
Dose-reduction phase completed: 9 patients
Observation period completed: 6 patients

Changes in the Environment Surrounding Regenerative and Cellular Medicine: Automation of Manufacturing Processes

The global market for automation in cell manufacturing is expected to expand, and relevant government agencies are strengthening support



Source: Automated and Closed Cell Therapy Processing Systems Market Estimates & Trend Analysis from 2018 to 2030

Manufacturing challenges arising from the use of living cells as raw materials

- Complex manufacturing processes still centered on manual operations drive up costs **(labor accounts for approximately 70% of total manufacturing costs)**
- IoT adoption remains limited, and data are not centrally managed

The value of automation is increasingly recognized

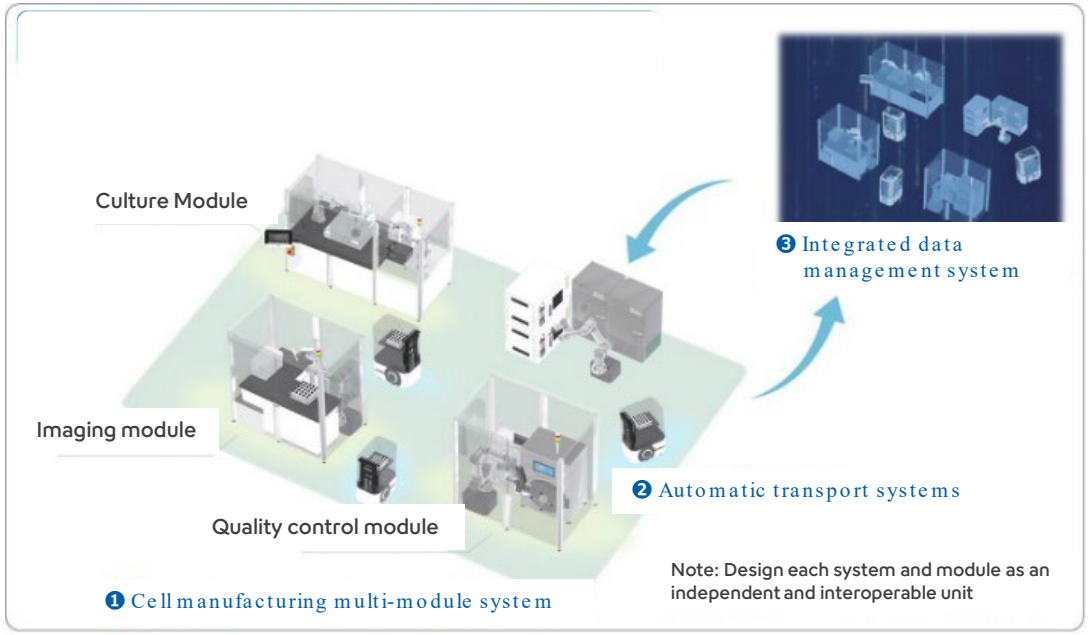
- In cell culture processes that rely heavily on manual work and show high variability, robots and AI that provide **reproducibility, precision, and consistency** are highly valued, with some cases being **recognized by the FDA as advanced manufacturing technologies**

The government supports manufacturing automation through subsidy programs

- **The FY2024 supplementary budget allocated ¥10 billion** to newly establish the “Subsidy Program for Investment in Manufacturing Facilities for Regenerative Medicine, Cell Therapy, and Gene Therapy.”
- **In FY2025, ¥3.9 billion** was allocated **to the “Fundamental Technology Development Program for the Industrialization of Regenerative Medicine and Gene Therapy.”**

Concept of an Automated Cell Manufacturing System

Leveraging our technologies and open innovation with partner companies,
we have conceptually designed and completed a prototype of a “modular cell manufacturing system”



1 **Realization of an automated cell manufacturing system with end-to-end functionality and high versatility** through a multi-module system

2 **Realization of cell and material transport between modules** through the adoption of an automated transport system that maintains cleanliness

3 **Realization of an integrated data management system** based on internationally compatible communication protocols and data formats

Facilitating seamless technology transfer from academia to startups, CDMOs, and pharmaceutical companies

Allowing manufacturing staff to focus on creative activities while attracting young and cross-disciplinary talent

Providing safe and effective treatments to patients through stable product quality

Changes in the Environment Surrounding Regenerative and Cellular Medicine: Quality Control Testing

In regenerative and cell therapy, where living cells are used as raw materials, the importance of quality control testing to ensure scientific validation and safety is increasing

In March 2025, the Japanese Society for Regenerative Medicine defined "explorative therapy" and explained its importance

There is a recognized responsibility to **clearly distinguish scientifically validated treatments** from **those that have not undergone sufficient scientific verification.**

Explorative Therapy

A form of treatment using processed cells, nucleic acids, or other materials that have not obtained marketing approval under the Act on Pharmaceuticals and Medical Devices. Clinical data are accumulated in an independent third-party registry, and **validation studies are conducted before and after treatment**.

The importance of rapid quality control testing is increasing, and demand for it is growing rapidly

In response to **adverse events and the need to ensure long-term safety,** the Ministry of Health, Labour and Welfare issued the "Guideline on Microbiological Safety of Specified Cell-Processed Products" in October 2025.

The MHLW, FDA, and EMA have issued the **latest guidance supporting the introduction of rapid microbiological testing**

- Technical Guidance on Quality, Non-clinical Studies, and Clinical Studies for Regenerative Medical Products (Human Cell-Processed Products) (June 14, 2016, Yakki No. 0614043)
- USP <1071> Rapid Microbial Methods for Release of Sterile Short-Life Products
- Ph. Eur. 5.1.6 Alternative Methods for Control of Microbiological Quality

Source: Citation from the Japanese Society for Regenerative Medicine, "YOKOHAMA Declaration 2025."

Deployment of Our Quality Control Testing

Our quality control testing is used across various quality control processes in regenerative and cellular medicine, and our track record continues to expand both domestically and internationally

Raw material acceptance testing

- Infectious disease screening
- Raw material cell evaluation
- Reagent and culture media evaluation

In-process testing

- Cell quality testing
- Culture environment testing
- Process-specific testing (e.g., cytokine measurement)
- Safety screening

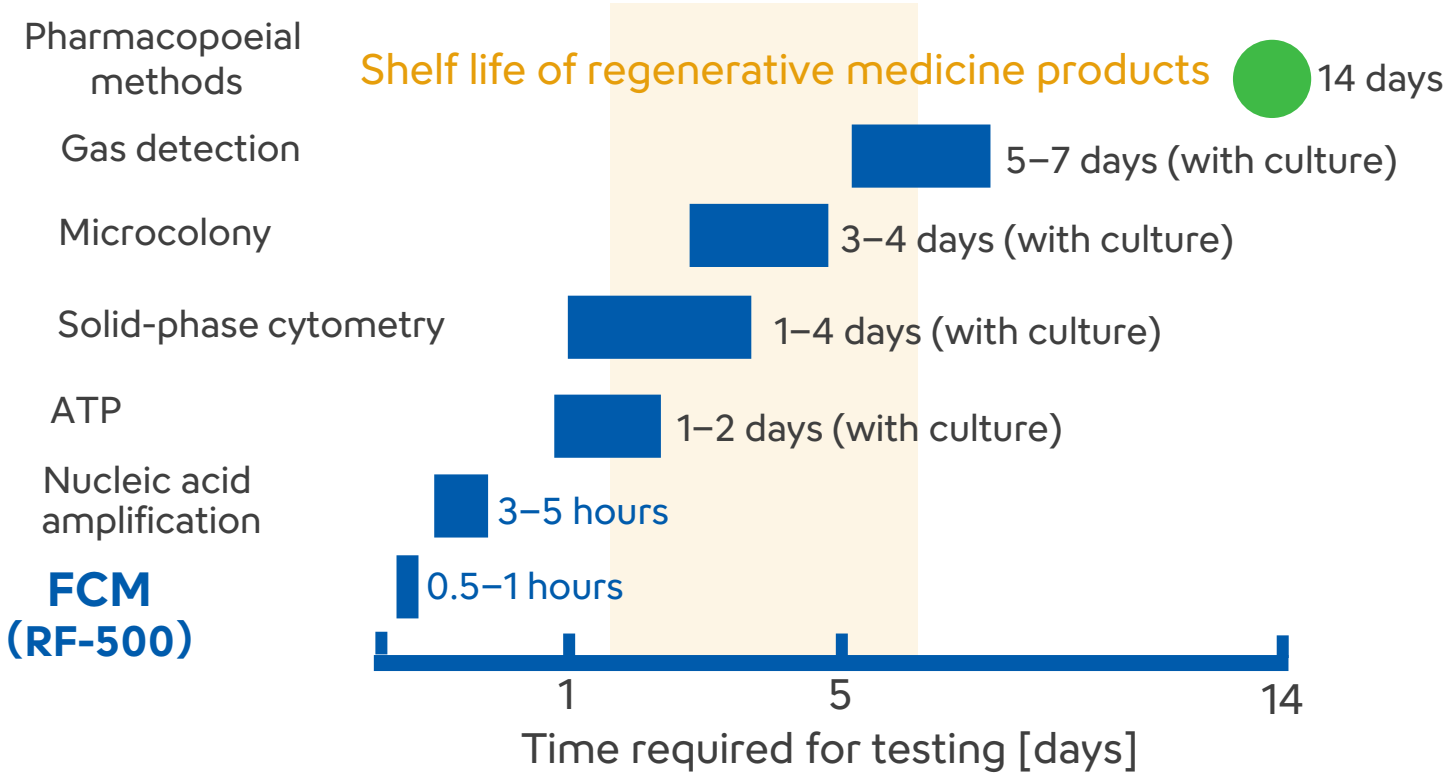
Release testing

- Safety evaluation (sterility testing)
- Identity evaluation (e.g., surface marker measurement)
- Purity evaluation (residual testing)
- Potency evaluation
- General characteristics evaluation

Development of Rapid Sterility Testing

Rapid sterility testing using flow cytometry is gaining attention, and we are developing a rapid sterility testing method using our proprietary instruments. After validation with actual samples, commercial launch is planned for FY2026.

Testing time for rapid sterility testing methods (reference methods)



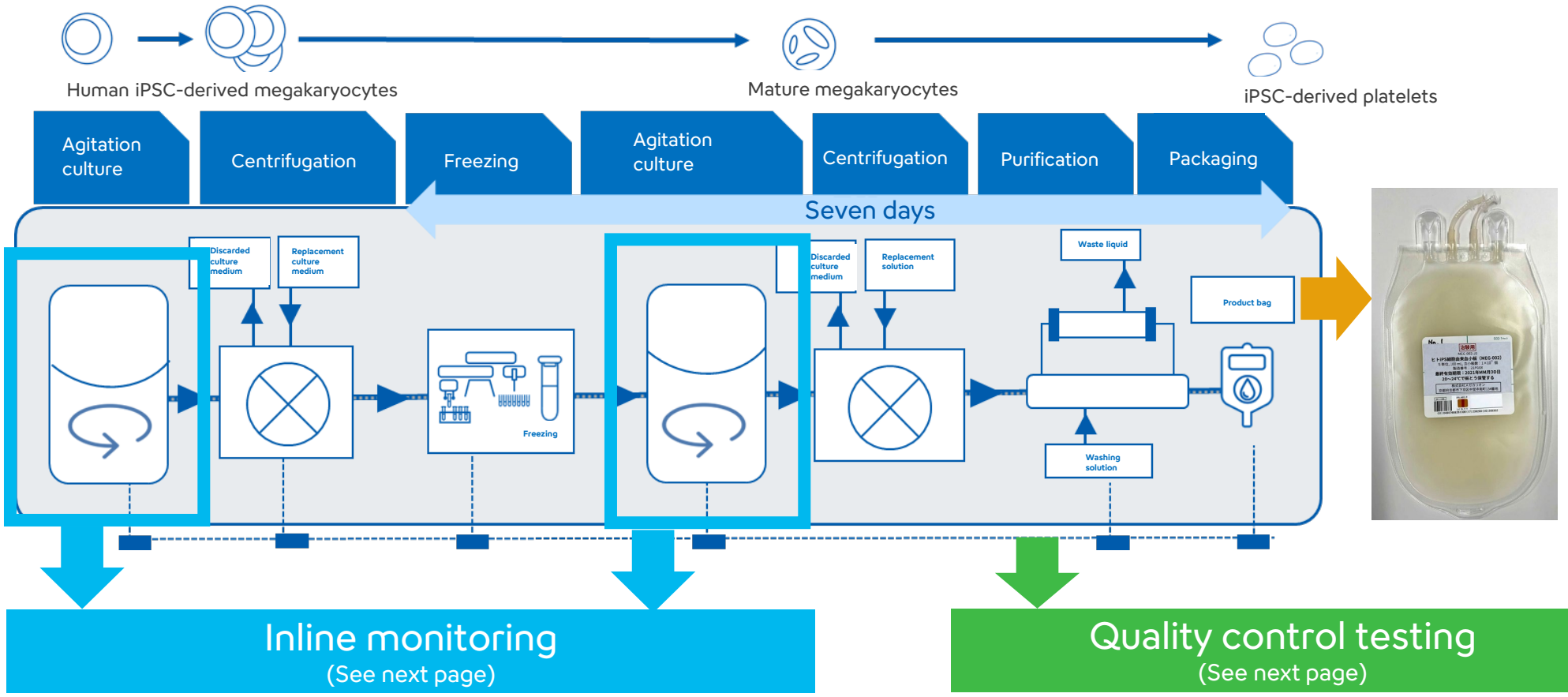
Source: Arita et al., "Regenerative Therapy," 31,101043 (2026).

Key Features of sterility testing using the RF-500

1. Capable of differentiating between live and dead microorganisms
2. Measurement time is one-fifth that of nucleic acid amplification methods
3. When combined with microbial concentration technology, detection sensitivity is equivalent or higher
4. Detects a wider variety of microorganisms than nucleic acid amplification methods

Example of Our Quality Control Testing in Practice: Megakaryon (1/2)

Sysmex technologies are planned to be introduced for process development and quality evaluation in platelet production

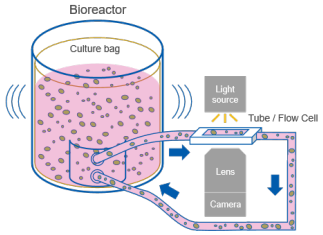


Example of Our Quality Control Testing in Practice: Megakaryon (2/2)

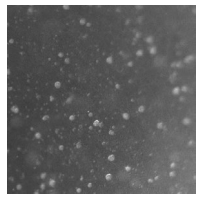
Fully automated testing instruments developed by Sysmex for its diagnostics business demonstrate value in regenerative and cellular medicine as well, expanding the potential applications of our testing technologies

Inline Monitoring System

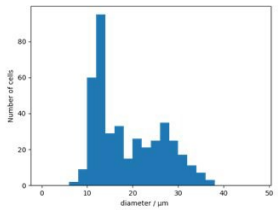
Microscopic observation



Microscopy images



Histogram of cell size vs. cell count



Non-destructive,
real-time evaluation of the culture process

Continuous, label-free tracking of multiple parameters, contributing to process development

No sampling required,
reducing contamination risk

Cell counting

XN/XR Series

Quality evaluation

FCM（XF/RF）

Aggregation ability evaluation

CN Series

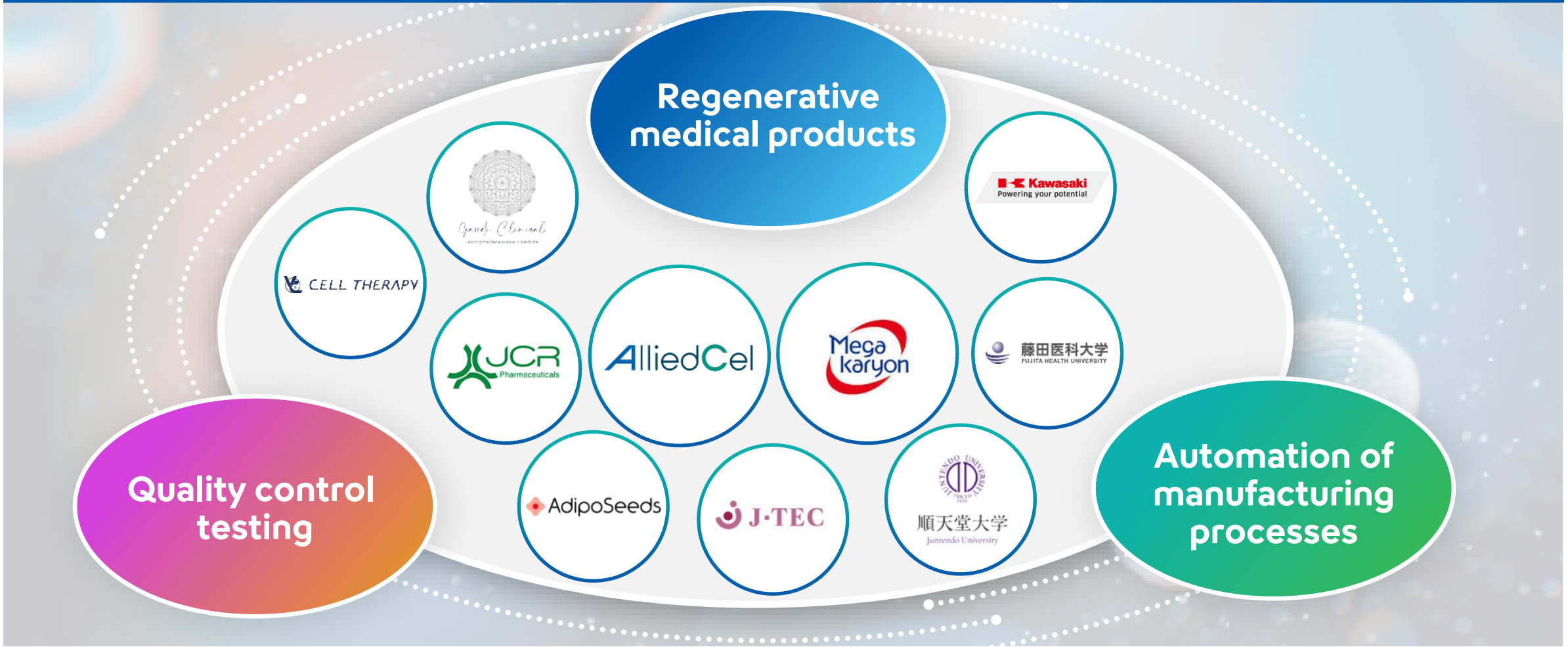
Standardization of testing independent of manual procedures

Reduced testing time
(approximately one-twelfth for cell counting)

Shortened testing time leads to reduced lead time
before product release

Open Innovation

Expanding our business around three pillars through open innovation with affiliates and partners



Glossary

Glossary

Amyloid-β (Aβ)	A key constituent of senile plaque, a pathological characteristic of the brain tissue of patients with Alzheimer's disease, composed of around 40 amino acids.
APOE Gene	The gene that encodes apolipoprotein E (ApoE), which is involved in lipid metabolism and transport.
ATTR	This is a disease in which TTR amyloid, formed by aggregation of transthyretin (TTR), deposits in the heart, causing myocardial dysfunction.
CUC	An acronym for "cholesterol uptake capacity," CUC means the ability of HDL to take up cholesterol.
Cultured hematopoietic stem cells	Hematopoietic stem cells which expanded and cultured in-vitro in the presence of proprietary growth factors, compounds, etc.
Immune tolerance	Immune-system's state of unresponsiveness to substances that would otherwise trigger an immune response.
Inducible inhibitory T-cells	T cells that suppress immune responses to specific antigens induced by antigens and anti-CD80 and anti-CD86 antibodies.
JB-CPA	Cyclophosphamide Hydrate for Injection.
NfL	Neurofilament light chain (NfL) is a neuron-derived protein, which is used as a biomarker for cognitive function.
Recipient T cells	T cells of a patient who receives a transplant operation.
Schistocyte	Red blood cell fragments that have been mechanically damaged and fragmented by external physical forces in the circulating blood.
Tau	A microtubule associated protein that exists in neuronal cells. Along with senile plaque, inordinately phosphorylated deposits of tau protein can be observed in the brains of patients with Alzheimer's disease.
β thalassemia	A hereditary hemolytic anemia caused by reduced or absent production of the hemoglobin beta chain due to mutations in the beta-globin gene.

Together for a better
healthcare journey