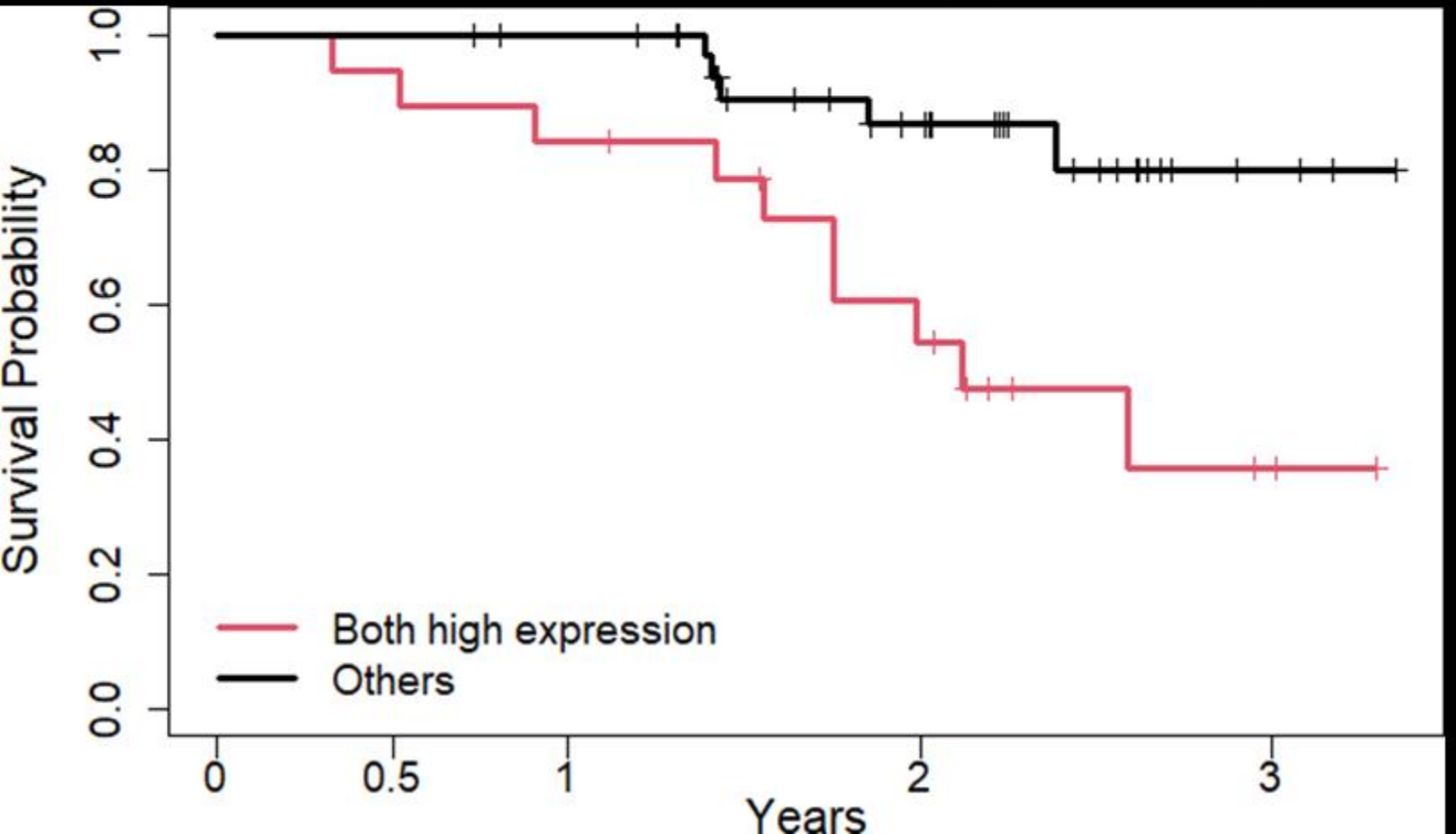
体外診断薬

膵癌NAC-GS効果予測バイオマーカー診断キット



高知大学　谷内恵介

Preoperative Biomarker Kit for Predicting NAC-GS Efficacy in Pancreatic Cancer

- Stratification of Resectable pancreatic cancer using Novel Monoclonal Antibodies for PODXL and ITGB1-

膵癌における術前化学療法（NAC-GS）の治療効果予測バイオマーカー診断キット

-新規モノクローナル抗体を用いたPODXLおよびITGB1発現による切除可能膵癌の層別化-

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高知大学医学部 消化器内科学講座
准教授・谷内 恵介

Executive Summary

- **Objective**: To identify high-risk patients with resectable pancreatic cancer who may experience rapid progression during neoadjuvant chemotherapy with gemcitabine plus S-1 (NAC-GS), the only approved neoadjuvant treatment for this condition.
- **Current Status**: Following the completion of a prospective multicenter trial and the filing of a basic patent in October 2024, the project is advancing toward clinical implementation. The Research Use Only (RUO) kit is scheduled for launch in March 2026, with the production of monoclonal antibodies for In Vitro Diagnostics (IVD) expected to be completed within the same year. Furthermore, following a PMDA consultation, performance evaluation tests for the diagnostic kit are slated to commence in the second half of 2026.
- **Modality**: Immunohistochemical (IHC) diagnostic kit using novel monoclonal antibodies, optimized for EUS-FNA specimens.
- **Target Disease**: Resectable pancreatic cancer.
- **Competitive Advantage**: This biomarker outperforms TNM staging with a 9.11 Hazard Ratio. It identifies the "Others" group (either/both markers low; score ≦ 3 out of a maximum of 6 points) as optimal NAC-GS candidates (81% 2-year survival). Conversely, the "Both-high" group (both markers high; score ≧ 4 out of a maximum of 6 points) shows high resistance (49% survival). With 94% physician support, it serves as a vital clinical gatekeeper.
- **Collaboration Goal**: Partners for IVD medical device approval, kit sales, and global commercialization.

Backgrounds (1)

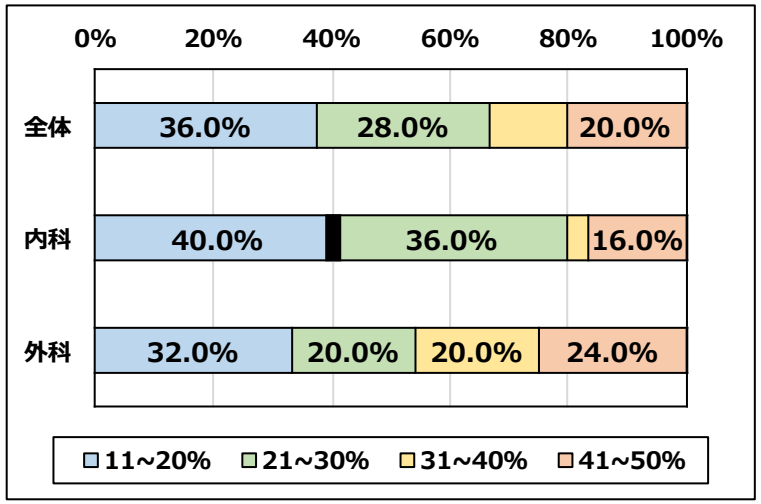
Challenges in the Current Standard Treatment:

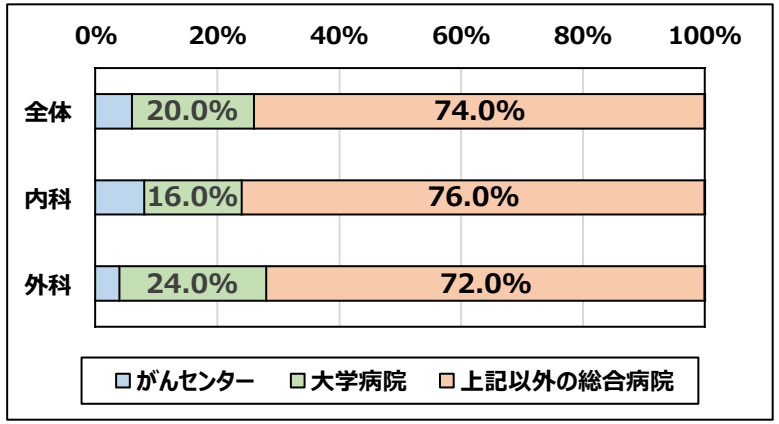
NAC-GS While neoadjuvant chemotherapy with NAC-GS is currently the only approved standard of care for resectable pancreatic cancer, it presents a significant clinical challenge: approximately 10–50% of patients lose the opportunity for curative surgery due to rapid disease progression during the treatment period.

Market Research

- **Target Respondents**: Physicians meeting the following criteria:
  Physicians who have administered NAC-GS therapy to 2 or more cases within one year.
- **Sample Size**: 50 physicians:
  Internal Medicine (Medical Oncology, Gastroenterology): 25.
  Surgery (Gastrointestinal Surgery, Hepato-Biliary-Pancreatic Surgery): 25.
- **Survey Region**: Nationwide (Japan).
- **Survey Schedule**: February 14, 2025 – February 19, 2025.

Q: Percentage of patients whose disease progresses due to the lack of effectiveness of neoadjuvant chemotherapy





In some patients, the therapeutic efficacy of NAC-GS remains limited, and it is not uncommon for individuals to lose the opportunity for curative surgery due to disease progression. The clinical implementation of biomarkers that can accurately predict the response to NAC-GS is highly desired.

Backgrounds (2)

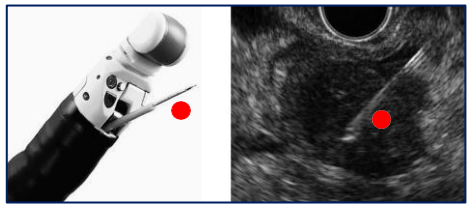
Identification of PODXL and ITGB1 as Prognostic Markers for Resectable Pancreatic Cancer

Increased expression levels of PODXL and ITGB1 in preoperative EUS-FNA specimens independently correlate with poor biological outcomes after surgery.

UMIN000032835： Retrospective clinical study using preoperative biopsy tissue from patients with pancreatic cancer.

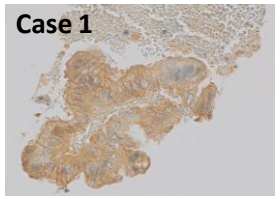
This study included 24 patients with resectable pancreatic cancer and was conducted between 2018 and 2019, prior to the establishment of NAC-GS as the standard neoadjuvant treatment. We used residual pancreatic cancer tissue originally obtained by EUS-FNA for diagnosis.

Preoperative EUS-FNA

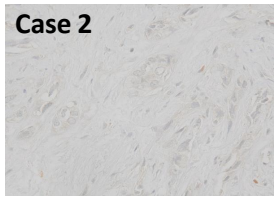


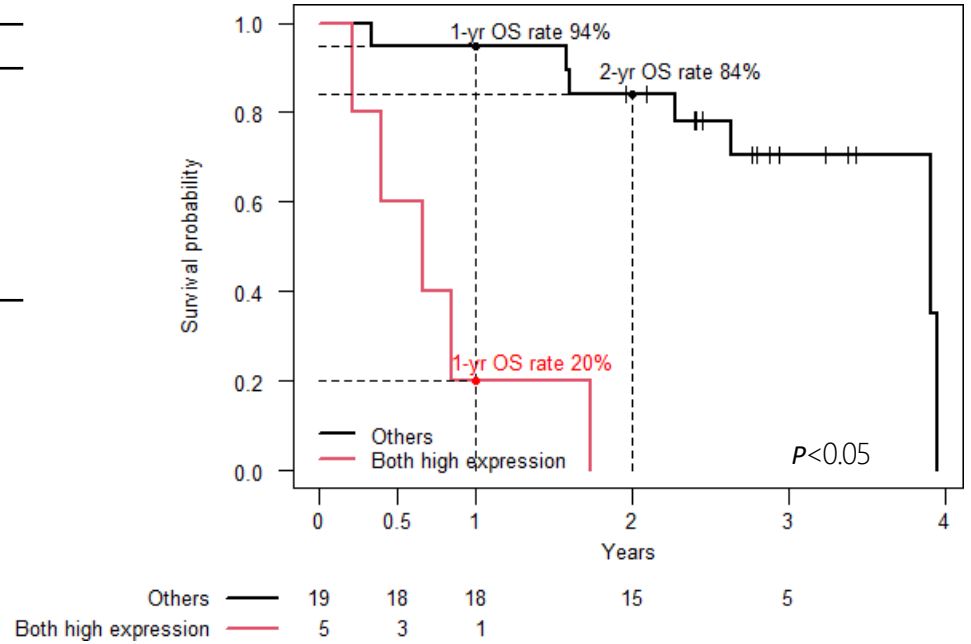
Stage	
IA	n = 4
IB	n = 5
IIA	n = 9
IIB	n = 5
III	n = 1

High expression of PODXL



Low expression of PODXL





Japanese Patent No. 7246731

Others: Low expression of either or both biomarkers
Both high expression: Concurrent high expression of both biomarkers

The combination of PODXL and ITGB1 can accurately predict postoperative prognosis at the preoperative stage.

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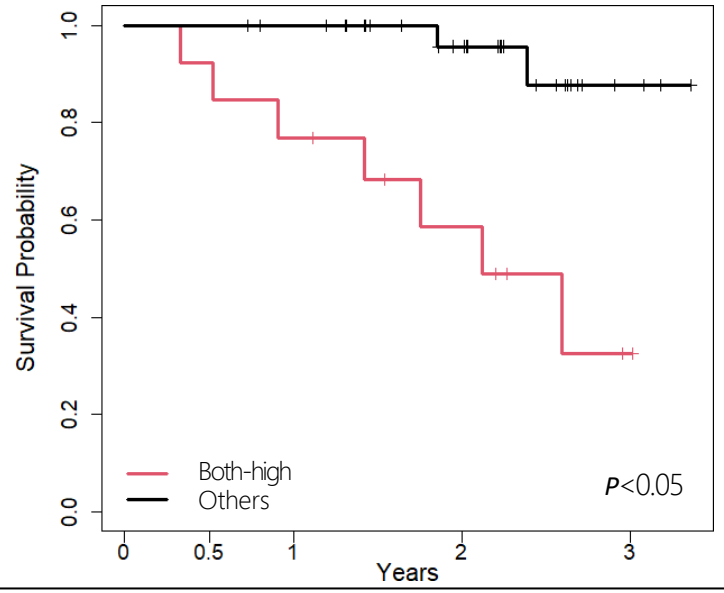
Targeted Goal

Precision Selection for Neoadjuvant Therapy for Resectable Pancreatic Cancer

Implementing molecular stratification to ensure standard NAC-GS for responders while directing high-risk patients toward more intensified treatment strategies.

UMIN000034022： Prospective study on the clinical utility of preoperative and postoperative prognostic markers in pancreatic cancer.

This prospective study included 63 patients who underwent EUS-FNA prior to treatment between 2020 and 2021, comprising 56 with resectable pancreatic cancer and 7 with borderline resectable pancreatic cancer. Among the 56 patients with resectable pancreatic cancer, 45 received NAC-GS followed by surgery, while 11 underwent upfront surgery.



N＝45 (11 cases were excluded due to comorbidities, etc.)

32 cases in the Others group: Cases where the efficacy of NAC-GS is expected.
→ **Indication for NAC-GS followed by surgery.**

Current Issues: Preoperative chemotherapy is currently administered to all patients with resectable pancreatic cancer, provided their general condition is favorable.

13 cases in the Both-high group: Cases where the efficacy of NAC-GS is not expected.
→ **Indication for upfront surgery or alternative neoadjuvant chemotherapy.**

	Both-high	Others
1 year survival rate	0.77 (95%CI 0.57-1.00)	1.00(-)
2 year survival rate	0.59 (0.36-0.95)	0.96(0.88-1.00)

Patent Application No. 2025-130317

Survival rates were comparable to those of surgery-only cases reported in previous literature.

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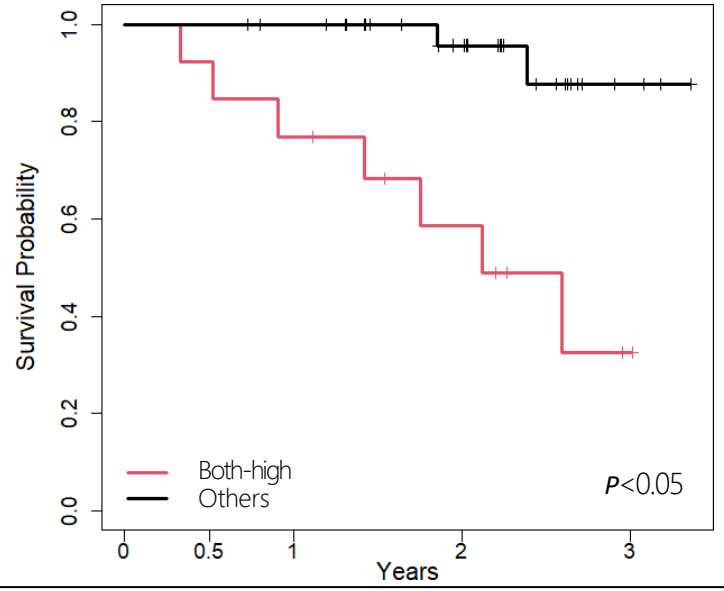
Current Issue; NOT select potential responded patients for preoperative chemotherapy

If the general condition is stable, preoperative chemotherapy is indicated for all cases of resectable pancreatic cancer
➔ If patient selection becomes possible, treatment measures appropriate for each patient can be implemented

UMIN000034022： Prospective study on the clinical utility of preoperative and postoperative prognostic markers in pancreatic cancer.



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Patent Application No. 2025-130317

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Key Data (1): High expression of both PODXL and ITGB1 could have a potential as a strong predictor of resistance to NAC-GS

A Strong Independent Prognostic Factor for Resectable Pancreatic Cancer (Multivariate Analysis)

"Both-high" status (concurrent high expression of PODXL and ITGB1) serves as a potent predictor of resistance to NAC-GS; this group exhibits significantly poorer survival (HR 9.11) and minimal therapeutic benefit compared to conventional clinical staging.

We confirmed the absence of multicollinearity among the following eight variables using the Variance Inflation Factor (VIF) criterion: age, sex, the biomarker (combination of PODXL and ITGB1), clinical stage, ITGB1 alone, preoperative chemotherapy, resectable pancreatic cancer, and CA19-9. Furthermore, variable selection was performed based on the Akaike Information Criterion (AIC).

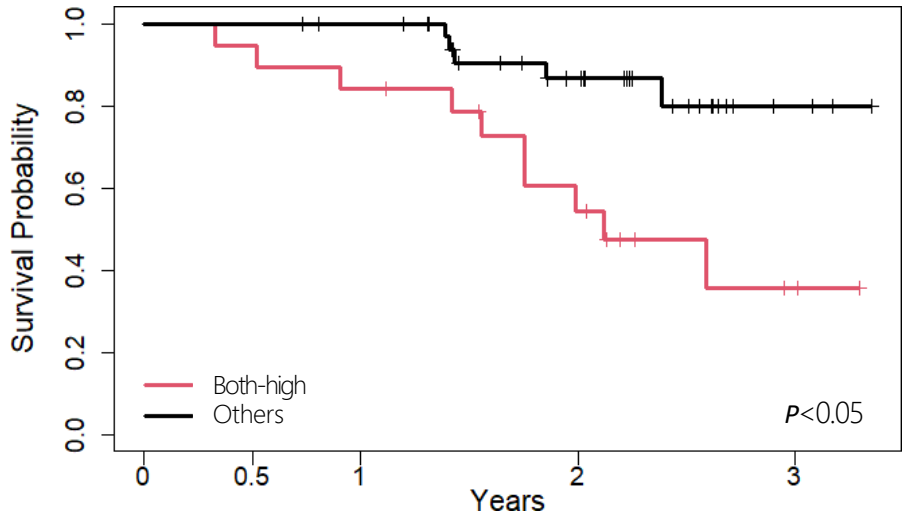
	Hazard Ratio	95%CI	*P* value
PODXL and ITGB1	9.11	[2.58-32.1]	0.0006
Clinical stage	3.29	[1.12-9.67]	0.03
NAC-GS	4.53	[0.87-6.08]	0.09

Patent Application No. 2025-130317

Key Data (2)

Survival Stratification of Resectable Pancreatic Cancer by PODXL/ITGB1 Status

Kaplan-Meier analysis highlights that the "Others" group (patients with low expression of either or both biomarkers) achieves a superior 2-year survival rate of 81% with NAC-GS.
This demonstrates that NAC-GS is highly effective for the "Others" phenotype, whereas the "Both-high" group shows limited benefit with a survival rate of only 49%.



In the 'Others' group, which excludes double-high expression, approximately 70% of patients survived.

N = 56 (including patients who underwent upfront surgery)

Patent Application No. 2025-130317

	Both-high	**Others**
1-year survival rate	0.88 (95%CI 0.75-1.00)	1.00(-)
2-year survival rate	0.49 (0.32-0.74)	0.81(0.69-0.96)
Median OS	1.98 (1.75 – 3.13)	NA (NA-NA)

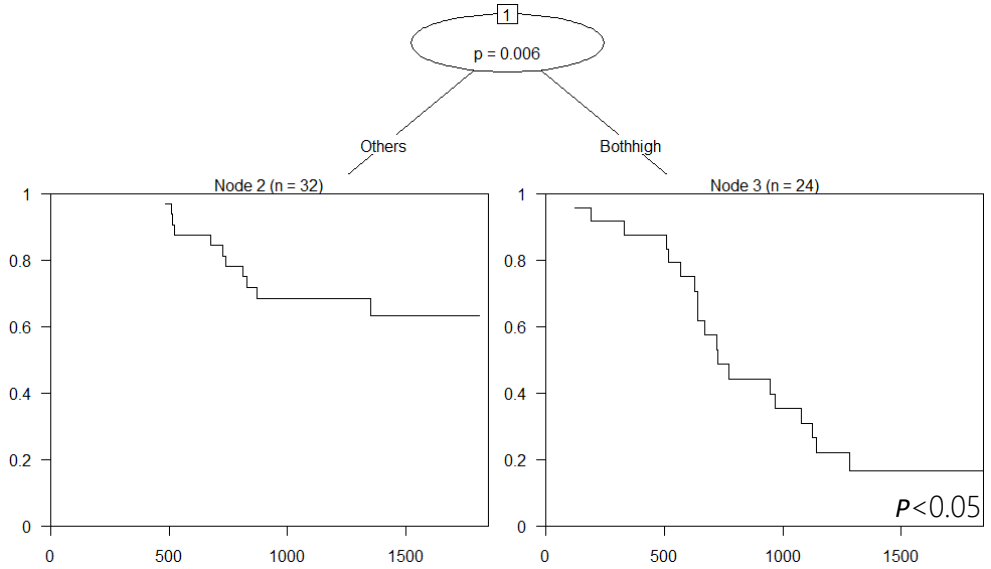
Key Data (3)

Integrated Risk Stratification in Resectable Pancreatic Cancer using CART Analysis

Decision tree (CART) analysis confirms that PODXL/ITGB1 status is the primary predictor of NAC-GS efficacy; it precisely identifies the "Others" group as those most likely to benefit from NAC-GS, while simultaneously isolating the "Both-high" group at the highest risk of treatment failure.

CART analysis was performed using the following eight factors: the combination of PODXL and ITGB1, clinical stage, preoperative chemotherapy, resectable pancreatic cancer, tumor size, tumor location within the pancreas, and CA19-9.

Others: NAC-GS is expected to be effective.



Both-high: No therapeutic effect of NAC-GS is expected.

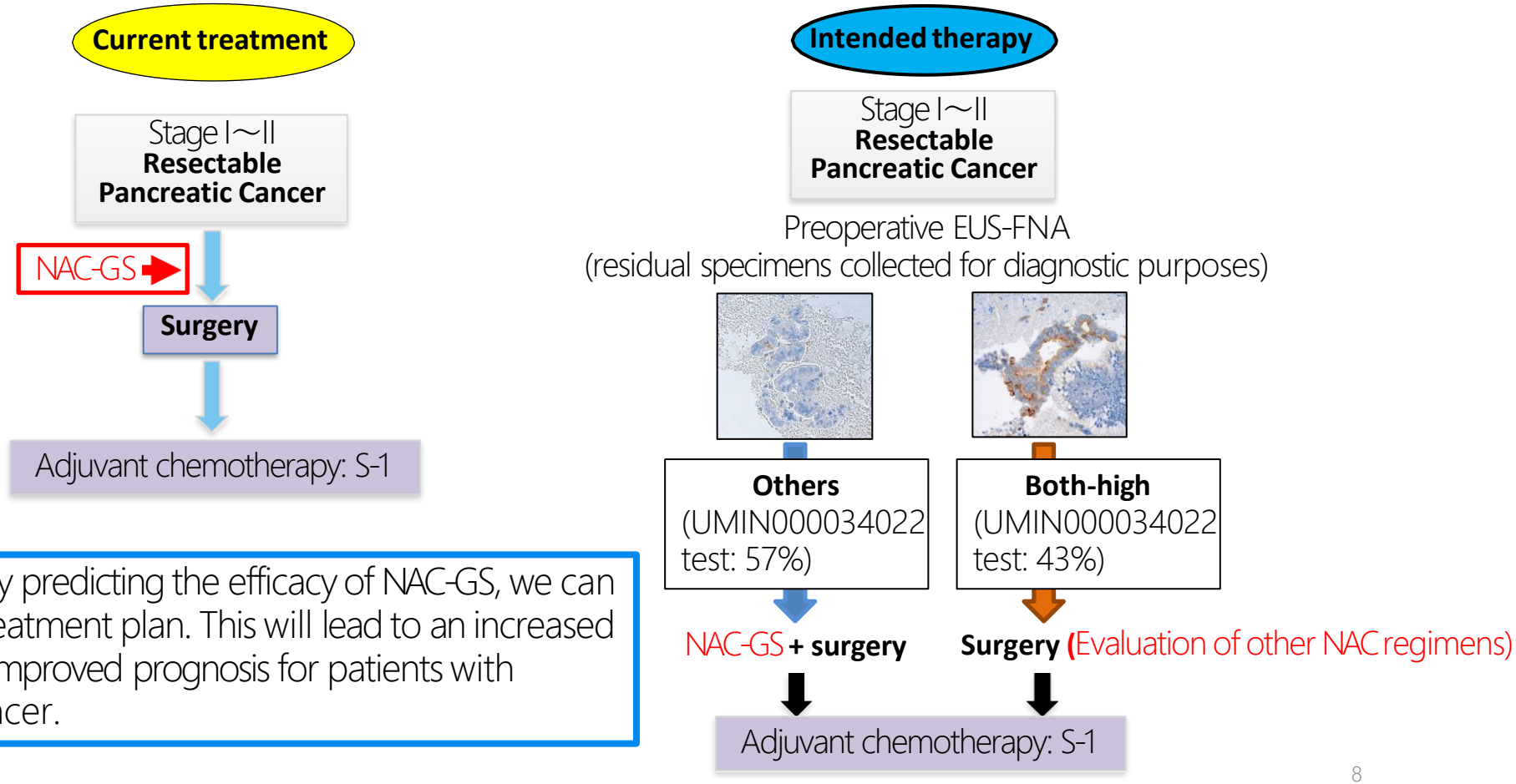
Patent Application No. 2025-130317

The combination of PODXL and ITGB1 most closely correlated with survival after NAC-GS and successfully stratified treatment efficacy.

Competitive Advantage (1);

Superior Accuracy Over Conventional Diagnostic Methods

Unlike CA19-9 or imaging, this IHC-based stratification directly reflects the biological aggressiveness and NAC-GS resistance of the tumor. It provides a robust molecular basis at the time of diagnosis to identify the "Others" group who will benefit from NAC-GS, as well as the "Both-high" group who may require alternative strategies.

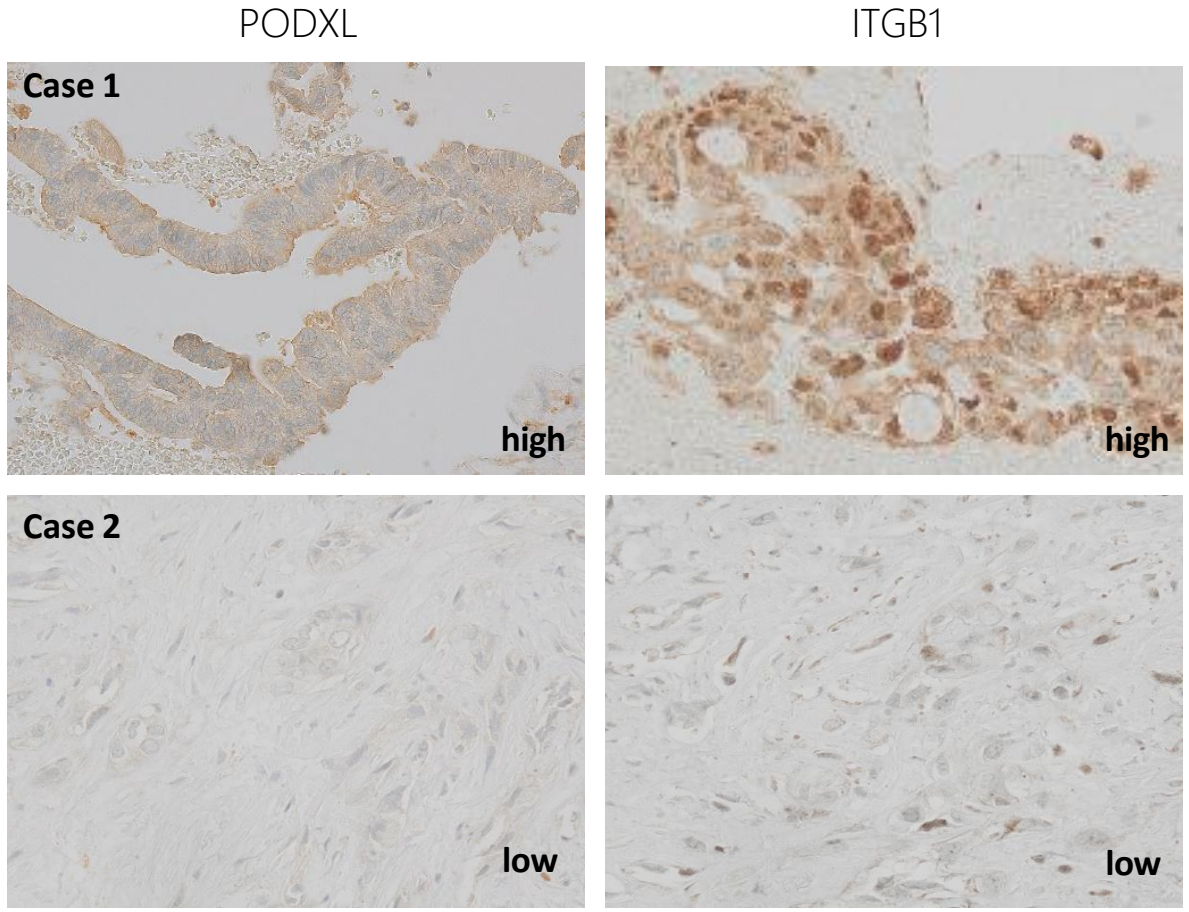


Goal of the Treatment: By predicting the efficacy of NAC-GS, we can determine the optimal treatment plan. This will lead to an increased rate of R0 resection and improved prognosis for patients with resectable pancreatic cancer.

Competitive Advantage (2);

Standardized Workflow and High Clinical Feasibility

The use of novel monoclonal antibodies and automated staining platforms ensures high reproducibility even with small-volume EUS-FNA samples.

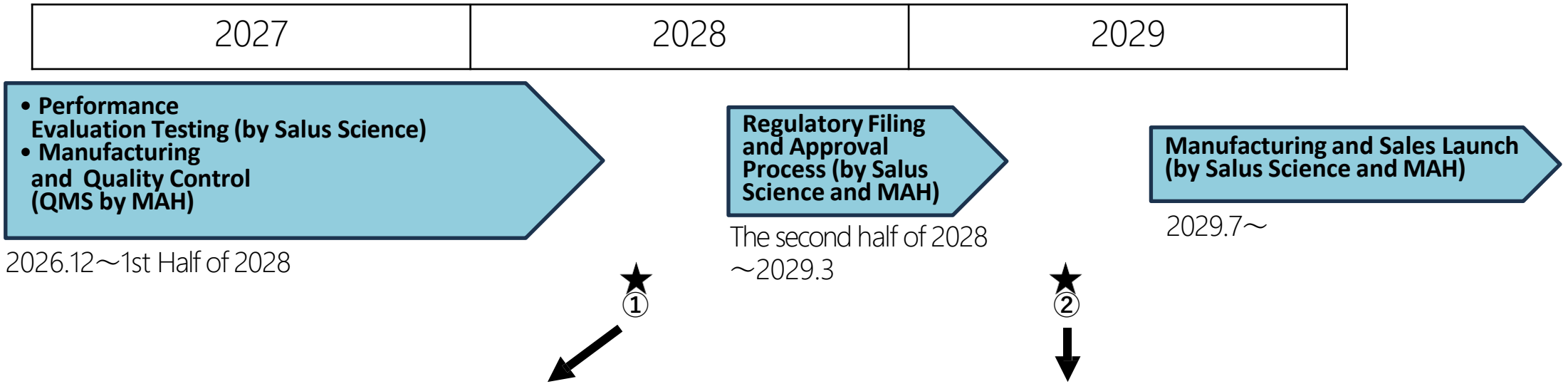


Patent Application No. 2025-130317

Time Schedule

詳細はAppendixに回しました

Regulatory Roadmap: From Performance Testing to Market Approval



① Implementation of PMDA Consultation (at the end of the performance evaluation test)

- Report findings from the prospective study with a view toward regulatory submission.
- Discuss procedures for the regulatory approval application.
- Confirm the application category as Class III In Vitro Diagnostic (IVD).
- Demonstrate the establishment of an appropriate manufacturing and quality control system (QMS).
- Provide a detailed explanation of the completed marketability study.

Preparation for Regulatory Submission

Collaborative preparation of submission dossiers by Salus Science and the Marketing Authorization Holder (MAH) supported by a CRO.

② Obtaining Regulatory Approval (1st Half of 2029)

- Successful completion of PMDA review and official regulatory approval.
- Establish product manufacturing and supply systems immediately following approval.

- **Commercialization**

Reference （Patents / Key Papers）

Patents

1. **Prognostic Biomarker Patent:** A patent titled "Prognostic marker for pancreatic cancer, prognostic diagnostic kit for pancreatic cancer, and method for predicting prognosis of pancreatic cancer" has been filed and registered (**Patent No. 7246731**; Applicant: Kochi University; Inventor: Keisuke Taniuchi). This patent pertains to the use of PODXL+ITGB1 to accurately predict postoperative prognosis for patients with surgically resectable pancreatic cancer at the preoperative stage.
2. **Treatment Efficacy Patent:** In October 2024, a basic patent application was filed titled "Molecular marker for determining the efficacy of Gemcitabine + S-1 therapy (NAC-GS) as neoadjuvant chemotherapy for pancreatic cancer, kit for determining said efficacy, and method for determining said efficacy" (**Patent Application No. 2024-188719**; Applicants: Salus Science and Kochi University; Inventor: Keisuke Taniuchi). This application covers the potential of PODXL+ITGB1 as a biomarker to predict the therapeutic effect of NAC-GS on resectable pancreatic cancer and includes analysis results using research-grade monoclonal antibodies. Furthermore, an updated application incorporating the latest analytical data was filed via a priority claim (**Patent Application No. 2025-130317**; Applicants: Salus Science and Kochi University; Inventor: Keisuke Taniuchi).

Key Paper

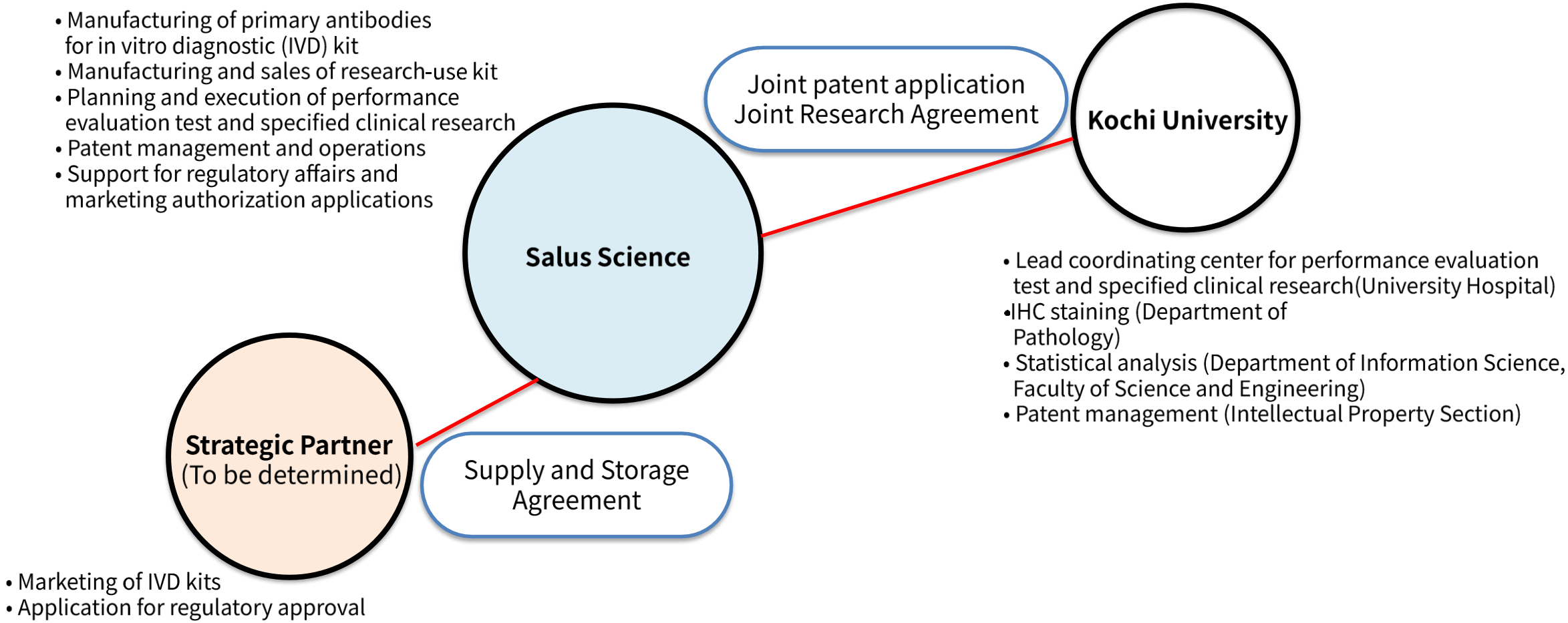
1. Taniuchi K, et al. (Manuscript in preparation) regarding EUS-FNA biomarkers for NAC-GS.
2. Taniuchi K, et al. Upregulation of PODXL and ITGB1 in pancreatic cancer tissues preoperatively obtained by EUS-FNA correlates with unfavorable prognosis of postoperative pancreatic cancer patients. PLoS One. 2022;17:e0265172.
3. Taniuchi K, et al. Overexpression of PODXL/ITGB1 and BCL7B/ITGB1 accurately predicts unfavorable prognosis compared to the TNM staging system in postoperative pancreatic cancer patients. PLoS One. 2019;14:e0217920.

Our Team

Multidisciplinary Collaboration for Clinical Implementation

- **Academic**: Kochi University.
- **Industrial**: Salus Science* and Strategic Partner

*: SU company, Co-founder / Dr. Taniuchi



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Proposed Partnership Scheme;

Market Opportunity: High Clinical Demand and Strategic Partnership for Pancreatic Cancer Biomarker Implementation

1. Executive Summary: Overwhelming Professional Endorsement

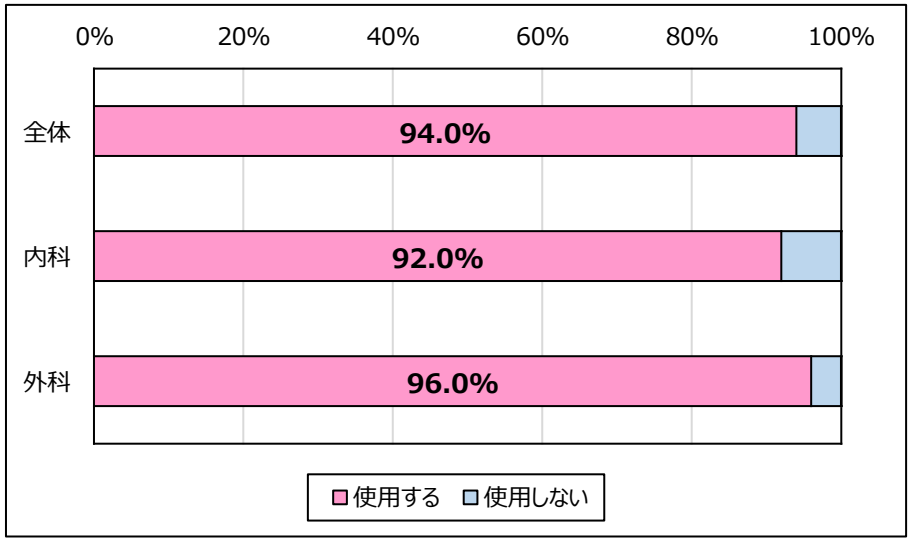
Market research indicates an exceptional clinical need for this biomarker among pancreatic cancer specialists, with nearly universal intent for facility-level adoption.

Q1: Clinical Utility

- **94.0%** of all specialists (n=50) expressed the intent to use this biomarker in a clinical setting.
- High demand across disciplines: **92.0%** in Internal Medicine and **96.0%** in Surgery.

Q2: Routine Implementation

- **100%** of respondents (n=47) who would use the biomarker confirmed they would implement it as a routine diagnostic method at their own facility.



2. Strategic Partnership Scheme

To transition from academia to global clinical application, Salus Science seeks a synergy between our innovative technology and established corporate expertise.

3. The Path Forward: Accelerating Patient Access

We are seeking strategic partners to bridge the gap between academic innovation and commercial scale. By combining our biomarker with your infrastructure in regulatory affairs and commercialization, we aim to enable precise prediction of therapeutic efficacy for NAC-GS in resectable pancreatic cancer, ensuring the most appropriate treatment selection for each patient.

Taniuchi et al. are currently preparing a specific clinical trial at Kochi University Hospital for patients with resectable pancreatic cancer. In this study, the 'Others' group will receive surgery following NAC-GS, while the 'Both-High' group will undergo surgery after an alternative neoadjuvant chemotherapy regimen. The trial is expected to commence in the first half of 2026.

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Market Opportunity; **Market survey showed high preference**

Executive Summary of Market Suervey

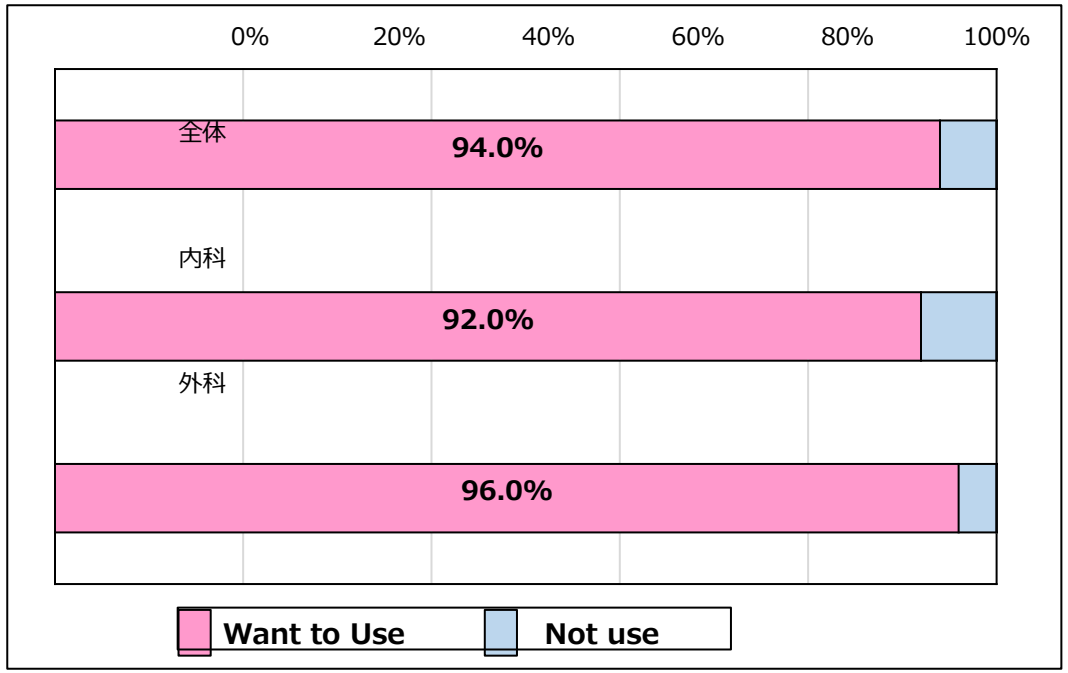
Market research indicates an exceptional clinical need for this biomarker among pancreatic cancer specialists, with nearly universal intent for facility-level adoption.

Clinical Utility

- **94.0%** of all specialists expressed the intent to use this biomarker in a clinical setting.
- High demand across disciplines: **92.0%** in Internal Medicine and **96.0%** in Surgery.

Routine Implementation

- **100%** of respondents who would use the biomarker confirmed they would implement it as a routine diagnostic method at their own facility.



Executive Summary

- **Objective**: To identify high-risk patients with resectable pancreatic cancer who may experience rapid progression during neoadjuvant chemotherapy with gemcitabine plus S-1 (NAC-GS), the only approved neoadjuvant treatment for this condition.
- **Current Status**: Following the completion of a prospective multicenter trial and the filing of a basic patent in October 2024, the project is advancing toward clinical implementation. The Research Use Only (RUO) kit is scheduled for launch in March 2026, with the production of monoclonal antibodies for In Vitro Diagnostics (IVD) expected to be completed within the same year. Furthermore, following a PMDA consultation, performance evaluation tests for the diagnostic kit are slated to commence in the second half of 2026.
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- **Collaboration Goal**: Partners for IVD medical device approval, kit sales, and global commercialization.

Appendix

Goal and its Plan for Research and Development

Roadmap Toward IVD Approval by 2029

- **2026: Launch RUO (Research Use Only) kit.**
  We have created an immunohistochemistry staining kit line featuring **mass-producible rabbit monoclonal antibodies**. The lineup includes versions for research use and in vitro diagnostics (IVD). The research-use version will be launched in March 2026 through Salus Science Co., Ltd.

- **2026: Conducting Specified Clinical Research.**
  Resectable pancreatic cancer patients at Kochi University Hospital will be stratified by biomarker profile: "Both-High" cases receive **NAC-GnP** plus surgery, and "Others" receive **NAC-GS** plus surgery. The study aims to verify the prognostic value of the PODXL/ITGB1 combination in optimizing patient outcomes, using OS and RFS as endpoints. Biomarker analysis will be conducted using the **IVD kit**.

- **2027: Conduct performance and stability testing for the IVD kit.**
  The study will assess its efficacy in assisting treatment decisions for NAC-GS using residual biopsy tissue from resectable pancreatic cancer patients.

- **2029: Regulatory approval, manufacturing, and marketing.**
  Salus Science Co., Ltd. will internally produce the rabbit monoclonal antibodies for the IVD kit. We will file for regulatory approval in collaboration with a strategic partner (to be determined) that will handle the kit's manufacturing and commercialization.

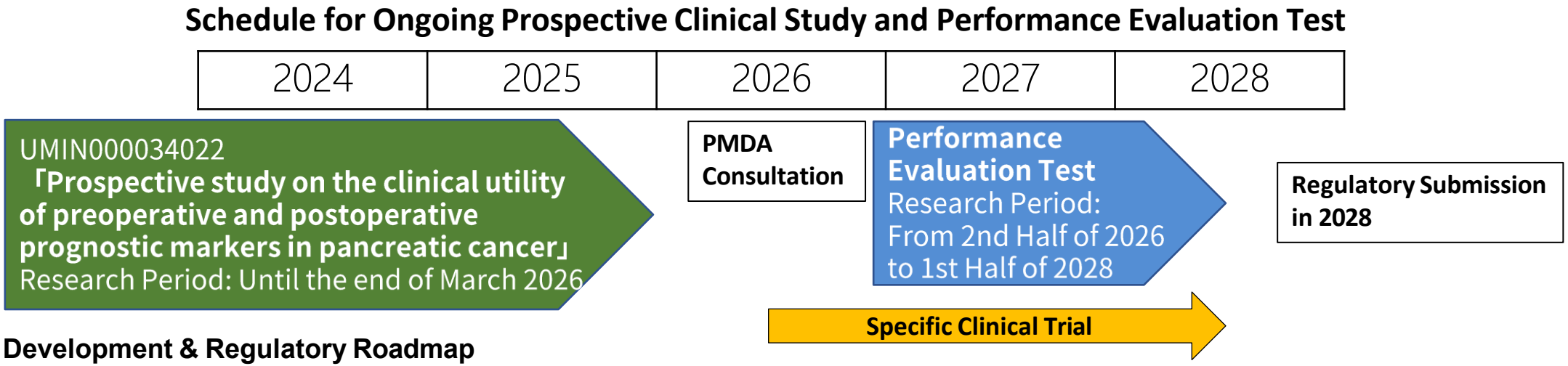
Challenges to achieving the goal

Clinical Validation and Market Expansion
Validation across global regimens (e.g., Gemcitabine plus nab-paclitaxel (GnP)) and establishment of a robust, QMS-compliant manufacturing system for international markets.

A multicenter clinical trial to evaluate the efficacy of **NAC-GnP** in patients with resectable pancreatic cancer is being conducted across multiple institutions, led by Kochi University Hospital in collaboration with Hokkaido University Hospital and Sapporo Medical University Hospital.

Study Title	A clinical study aimed at validating biomarker performance to predict the efficacy of neoadjuvant chemotherapy using biopsy specimens.
Launch Date	April 2026 (Ethics Committee Approved)
Regimen	NAC-GnP (Gemcitabine + nab-paclitaxel)
Primary Endpoint	Overall Survival (OS)
Secondary Endpoint	Recurrence-Free Survival (RFS)
Observation Period	2 Years

Time Schedule



1. Product Development & Regulatory Roadmap

- **IHC Kit Completion (2026):** We expect to complete the development of an Immunohistochemistry kit in 2026. This IVD kit consists of monoclonal antibodies compatible with major automated staining platforms.
- **System Compatibility:** The secondary antibodies are designed to work with standard anti-rabbit antibody reagents already equipped on various IHC staining systems, ensuring seamless integration into existing laboratory workflows.
- **Regulatory Status:** Following a PMDA General Consultation, we have been advised to proceed to a Face-to-Face Consultation to finalize the protocols for performance evaluation tests.
- **Manufacturing & Approval:** Sarus Science Inc., the patent holder for the UMIN000034022 trial results, will handle the synthesis of the IVD monoclonal antibodies. The application for regulatory approval (planned for 2029) will be conducted in collaboration with a partner company responsible for quality control and distribution.

2. Market Opportunity & Clinical Impact

- **Target Population:** The kit targets patients with resectable and some borderline resectable pancreatic cancer who are candidates for surgery. The potential market size is estimated at up to 18,000 new patients in Japan per year.
- **Unmet Medical Need:** Currently, there are no established biomarkers to predict the therapeutic efficacy of NAC-GS therapy (Neoadjuvant Chemotherapy with Gemcitabine and S-1).
- **Market Dominance:** Our Immunohistochemistry kit, capable of detecting PODXL and ITGB1, addresses this critical gap in clinical practice. As a first-in-class diagnostic tool, it has the potential to monopolize the market for pancreatic cancer treatment selection.