5.1 New Drug Development and Innovation

Material Topic

Since its establishment, PharmaEssentia has been dedicated to the research and development of new drugs and drug improvement, with the goal of addressing unmet medical needs. We have independently developed the PEGylation technology platform to improve existing drugs and successfully developed a new generation of the PEGylated interferon alpha drug, Ropeg, which has the characteristic of being applicable to multiple indications. It can not only be used to treat indications related to blood diseases, but also tumors and viral infections, creating significant value for patients with solid results.

NT$1.43 billion

R&D spending grew by 12.6% and accounted for 49.6% of sales revenue

GRI 3-3

Management Policy

Internal Policies

- Our company follows internal control research and development cycle regulations, which cover intellectual property patent applications and related measures from early-stage basic research, product technology research, pre-clinical experiments, medium-term drug trial production and phase 1 and 2 human clinical trials, to mature product development and phase 3 human clinical trials. Our goal is to seek new technologies and products with market competitiveness, and explore the development of new drugs for needs that have not yet been met using our own technology
- Internal R&D Control Cycle Regulations and related Management Measures

External Guidelines

- Helsinki Declaration
- Good Clinical Practice Guidelines for clinical trials (ICH-E6-GCP)
- Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP) guidelines for clinical trials, among other international standards

Management Commitment

We are committed to complying with relevant applicable regulations and focusing on four major disease areas. We aim to innovate new biopharmaceuticals with the most refined technology and of the highest quality, and contribute to improving the health of people worldwide by providing innovative and reliable medications

Accountable Units

- New drug exploration is mainly coordinated by the New Drug R&D Department. The Project Evaluation Taskforce, which includes representatives from funtional teams and senior management executives, is the decision-maker for new drug research. The decisions made in the project review meetings are done so jointly. After establishing the R&D project, the project leader will coordinate the project's progress and complete reports on a regular basis.
- The clinical trial part is managed by the Clinical Operations Department
- ECCS - Access to Medicine team

Input Resource

- In 2022, there were 123 R&D clinical personnel in the global network of PharmaEssentia, with a total R&D expenditure of NT$1.43 billion, a growth of 12.6% compared to last year.
- In the early stages of new projects, in-depth data collection is carried out to understand the clinical progress of competing drugs, evaluate unmet needs and commercial development opportunities in the market, and incorporate the development platform to guide drug development processes
- Rolling summarization and feedback of market dynamics of each project are regularly reported to the management task force in biweekly R&D meetings, enhancing the project task force and management task force's understanding of the market and risk assessment capabilities related to R&D projects. The R&D department actively evaluates the possibility of introducing a drug market database for new cases and encourages colleagues to participate in market evaluation-related education and training.

Targets

Short-term Targets for 2023

- Stabilize the development of ongoing projects or technologies, including Anti-PD-1, PEG-GSF, and TCRT, and gradually enter the application for clinical trial permission stage in 2023
- Collaborate on projects related to cell therapy technology and use imported technology to construct a cell factory. Continuously evaluate new drug development directions and apply for clinical trials of a cell therapy product
- Conduct a multinational, multicenter phase III clinical trial for essential thrombocythemia (ET), which is expected to be completed in the first quarter
- Launch various R&D activities of the PharmaEssentia Innovation Research Center Corporation in the United States

Medium-term Targets for 2024-2026

- Continuously promote the multi-center Ropeg (P1101) phase III clinical trial for essential thrombocythemia (ET) and apply for drug license registration
- Actively carry out the PEGylation project of new target proteins, and apply for clinical trial approval
- Develop a new process technology platform to improve production efficiency, reduce costs, and shorten development time; apply the new process technology platform to a new drug product and apply for a clinical trial

Long-term Targets (2026 and beyond)

- Continuously seek licensing collaboration or permission, and jointly develop or introduce new drug candidates with strategic alliance partners to expand the company's product line
- Accelerate the progress of key clinical trials and product drug license registration in various countries to maximize product benefits
- Establish a platform and procedures for R&D and marketing collaborations to promote cross-departmental communication and enhance the market evaluation capabilities of research and development task forces

Evaluation of Management Policy

Management Evaluation Mechanism

- All R&D projects follow the internal control R&D operation cycle. Every quarter, project progress and execution efficiency management are conducted based on the financial data compiled by the finance department, and project cost control evaluations are conducted every six months. When there are significant R&D achievements or milestones in the project plan, the project task force members will jointly decide whether to continue the project.
- Large-scale projects and annual R&D budgets must be submitted to the board of directors for approval before proceeding with related research and development.
- The auditing unit conducts audits of the R&D cycle management mechanism according to the annual audit plan.
- The Clinical Operations Department reviews the company's clinical trial progress every two weeks at the medical research bi-weekly meeting.

2022 Evaluation Results

- The project task force has regularly evaluated and made decisions regarding various ongoing R&D projects, and the overall management and evaluation has been well-done.
- Results related to Ropeg (P1101)
  - Phase 1 clinical trial recruitment: Clinical trials using this drug followed by anti-PD1 treatment for B or D-type hepatitis have started recruiting subjects
  - Clinical trials at different stages: Clinical trials for the application of this drug in primary thrombocytosis (ET), hepatitis virus infection and tumors are being conducted in 8 countries. The design of phase 3 clinical trials for the treatment of COVID-19 patients using this drug has been significantly modified and approved by the Ministry of Health and Welfare. Preliminary clinical data from the second-phase bridging clinical trial in China for the treatment of polycythemia vera (PV) are available
  - "A+ Enterprise Innovation R&D Program" grant: The "Ropeg (P1101) Treatment of Primary Thrombocythemia (ET) Multinational and Multicenter Phase 3 Clinical Trial Plan" has been fully supported and granted NT$32,918,000 by the Ministry of Economic Affairs
  - Drug Licenses application: An application for market approval for the treatment of PV in Japan has been submitted to the PMDA
- Introducing and developing new drug KX 01 for the treatment of actinic keratosis under authorization from Athenex in the United States
  - Clinical trial: A phase 3 clinical trial has been launched in Japan to meet regulatory requirements for applying for a drug license in Japan
  - Drug licenses application: The drug licenses has obtained marketing authorization in Taiwan
- Establishing the PharmaEssentia Innovation Research Center in the United States

Process Innovation: Creating Value through Innovation - the PEGylation Technology Platform

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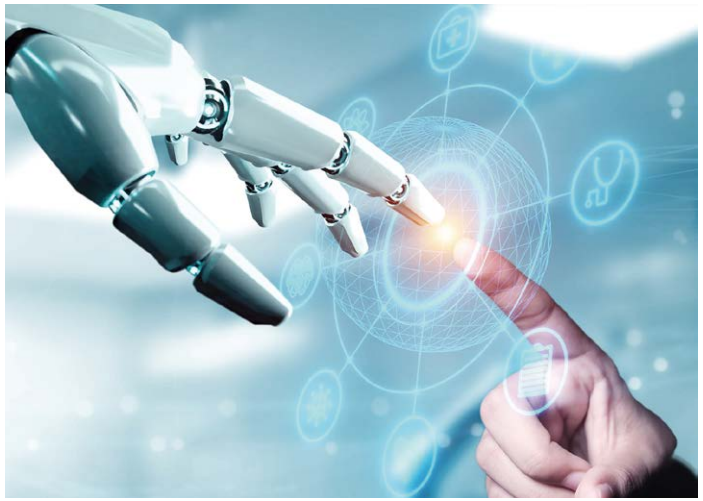


The PEGylation technology platform has been a powerful and core part of R&D at PharmaEssentia since its inception. It is a technology that combines protein drugs with long-chain high molecular weight PEG (polyethylene glycol) to extend the effective concentration time of protein drugs in the human bloodstream. Using this platform technology can significantly reduce R&D costs while improving the tolerability and convenience of the medication. To further expand its R&D innovation capabilities, PharmaEssentia has officially launched various R&D projects through the PharmaEssentia Innovation Research Center (PRIC) in the United States. The projects are expected to combine AI artificial intelligence and machine learning platforms to identify research targets in the early stages of research and reduce development time and costs, accelerating the process of new drug development from research to market.

Myeloproliferative neoplasms (MPNs) are rare chronic blood cancers, and patients with such diseases have significant and unmet medical needs. In the same field of true polycythemia vera (PV), we have used the PEGylation technology platform as a basis for the improvement of existing drugs and have successfully developed a new generation of the PEG long-acting interferon alpha drug, Ropeg, which has shown significant results in the treatment of this disease. Our partner, AOP Orphan, conducted a 7.5-year clinical study using Ropeg to treat PV, and found that more than 60% of patients achieved a complete hematological response, confirming the potential of innovative interferon drugs to benefit patient populations.

The near-term value of the "PEGylation technology platform" for the development of original protein drugs.

Improvement of existing drugs - reducing the risk of developing new drugs

By using the **PEGylation** platform to improve existing drugs, a new generation of PEGylated interferon α drugs has been successfully developed, significantly reducing the risk of new drug development failure. The side effects of the new drug are reduced, enabling doctors to provide better treatment options for patients, and creating shared value through drug therapy.

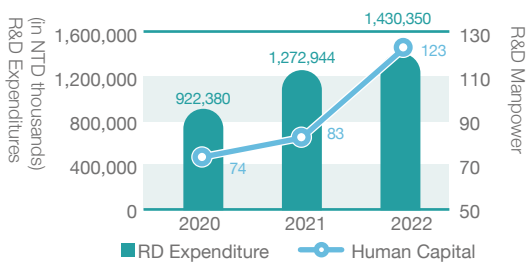
Using the technology platform - effectively developing diverse products

By continuously developing innovative drugs using the technology platform, it can be used in four major areas, including blood-related diseases, with the characteristic of one drug for multiple indications. If the indication is a rare disease, the positive impact of providing patients with the drug after it has been launched is immeasurable.

5 major professional fields

- Analytical Science
- Chemistry
- Cell Engineering
- Pharmaceutical Science
- Process Development

Ongoing growth in research and development (R&D) spending



Competitive advantage in developing new drugs

Ropeginterferon alfa-2b (P1101)
Next-generation PEGylated long-acting interferon alpha drug

- High purity
- High tolerability
- Low side effects
- Stable and single component
- Can treat multiple indications
- Dosing frequency will be reduced to once every 2 weeks

4 major disease areas of focus

- Rare blood diseases
- Viral infection diseases
- Tumor diseases
- Skin diseases

4 R&D products

- Ropeginterferon alfa-2b，Code P1101
- Ropeginterferon alfa-2b (P1101)+ Immune checkpoint inhibitor anti-PD-1 antibody
- Oral paclitaxel Oraxol®
- Kinase inhibitor Tirbanibulin (code name KX01)

Product Innovations PharmaEssentia's R&D Pipeline

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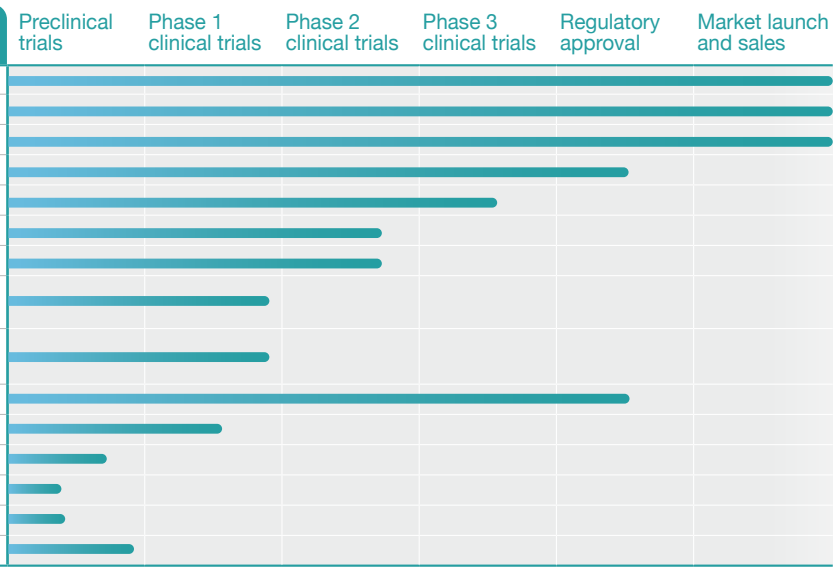
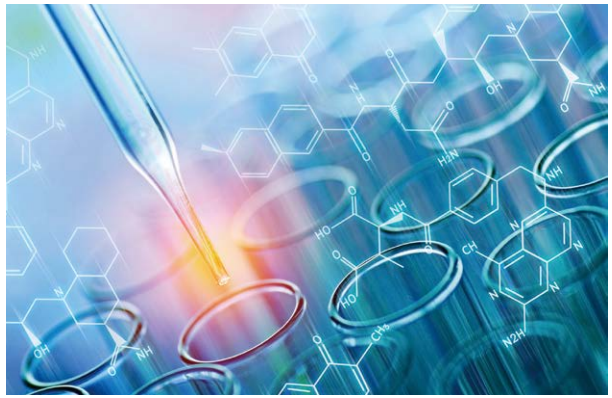
Disease classification	Technology / product	Indications	Market
Blood disorders	Ropeginterferon alfa-2b（P1101）	Polycythemia vera	Europe, Switzerland, Israel
			Taiwan, Korea
			United State
			Japan, China
		Primary thrombocytosis	Global
		Pre-fibrotic myelofibrosis	Global
		Adult T-cell leukemia/lymphoma	Japan, Taiwan、China
Infectious diseases	P1101 + Entry inhibitor	Hepatitis D	United State, Europe, Taiwan
Skin diseases	Tirbanibulin（KX01）	Psoriasis	Taiwan, China, Macau, Singapore, Japan, Korea
		Actinic keratosis	Taiwan, Japan, Korea
Solid tumors	P1101 + anti PD-1	Hepatocellular carcinoma	Global
	PEG-GCSF	Neutropenia	Global
	PEG-IL2	Solid tumors	Global
	PEG-IFN-Gamma	Solid tumors	Global
	TCR-T	Solid tumors	United State, Taiwan



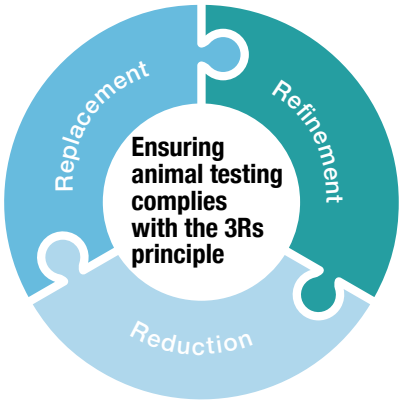
Note: For the latest updates on the R&D product pipeline, please refer to the company website.

Data source : https://hq.pharmaessentia.com/tw/pipeline

Persuit of Animal Welfare of Preclinical Animal Experiments



In order to ensure animal welfare in preclinical animal experiments, our company selects and outsources relevant matters to domestic and foreign research institutions with GLP certification and follow the relevant regulatory requirements of the Institutional Animal Care and Use Committee (IACUC) for animal care and use in experiments. We have commissioned three qualified domestic and foreign institutions to conduct preclinical animal experiments in a humane manner.



A Rigorous Process of Human Clinical Trials

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To ensure the quality of human clinical trials, PharmaEssentia has established more than 20 standard operating procedures (SOPs) for clinical operations, as well as for selecting and managing contract research organizations (CROs). There are audit and review mechanisms at each stage of clinical development, and clinical trials are conducted in accordance with approved trial protocols and local regulations for Phases 1, 2, and 3.

Phase 1 clinical trial
Safety exploration

Phase 2 clinical trial
Preliminary efficacy study

Phase 3 clinical trial
Large-scale confirmatory efficacy study

Study planning

- Evaluate the trial risk based on the clinical trial services and characteristics provided by the CRO.
- Develop a monitoring plan, audit plan, and clinical trial quality management and quality assurance plan according to the level of risk.

Pre-trial

- The trial plan and related documents are subject to review and approval by the health authority and the human subjects committee.
- Hold a coordinator meeting to conduct relevant training.
- Obtain written informed consent from the subjects: They must be fully informed and have carefully considered the agreement before signing the consent form to participate in the clinical trial.
- Strictly screen suitable subjects based on the inclusion and exclusion criteria in the trial plan.

During the trial

- The clinical operation department performs collaborative monitoring with the CRO that undertakes the monitoring business.
- The clinical quality assurance department performs audits according to the relevant audit plan to ensure that the CRO's services meet quality requirements.

After the trial

- Compile the efficacy and safety data of the clinical trial.
- Approval for marketing is granted after the health authority's written review and on-site inspection and a risk-benefit assessment.

Assessment of Risk to Ensure the Quality of Clinical Trials

The quality risk assessment and maintenance of clinical trials are conducted by external research institutions. They follow our standard operating procedures and assess the clinical trial risks before and during the trial. Relevant safety education and training on clinical trial products are conducted both internally and externally before conducting the trial. Quality assurance and management activities are also implemented during the clinical trial.

Before clinical trials
Evaluate the potential risks that may be encountered during the trial based on the characteristics of the test drug and the trial design.

Focus of evaluation

Based on the level of risk, develop a case-specific "monitoring plan" and "audit plan" to execute QA and QC items. Ensure that the rights and welfare of subjects are protected, and that the conduct of the clinical trial, data generation, recording, and reporting comply with the trial plan, GCP, and relevant regulations.

Execution process

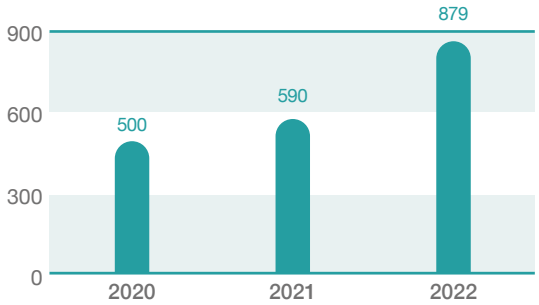
Quality Assurance (QA)
Includes an independent audit system, where any issues found will be appropriately evaluated and tracked, and relevant corrective and preventive measures (CAPA) will be proposed.

Quality Control (QC)
Includes monitoring and collaborative monitoring.

Multinational and Multicenter Clinical Trials Validate the International Competitiveness of Drugs

As of the end of 2022, our company has conducted more than 20 clinical trials worldwide using Ropeginterferon alfa-2b (P1101), benefiting patients from Taiwan, Europe, the United States, Japan, China, Hong Kong, and other regions. The clinical trials covered various indications including PV, ET, hepatitis B and C, as well as mild-to-moderate COVID-19 cases. In 2022, nearly 290 new patients were enrolled, bringing the total number of beneficiaries to more than 850. These multinational and multicenter clinical trials aim to validate the international competitiveness of our drug products.

Number of Benefited Patients in Clinical Trials Phases 1-3



289 New Patients

New P1101 clinical trial participants added in 2022, accumulated to over 850 beneficiaries

Cross-National Industry-Academia Collaboration - Establish Local Research and Clinical Trial Capabilities

In addition, we also collaborated with universities and research institutions in and outside of Taiwan to gain a deeper understanding of global market demand for disease treatment. Through clinical collaboration, we studied relevant diseases and updated our knowledge of the latest technology and techniques in order to jointly develop access to medicine programs that meet the needs of people with different diseases around the world.

2018
Completed a research project in collaboration with a domestic university to develop and apply new drugs in the field of nephrology, with a total investment of nearly NT$2.7 million in Q2 2020.

2019
Sponsored a research project on viral hepatitis in collaboration with domestic medical centers and Japanese academic institutions, with an investment of over NT$1 million, which was completed in Q2 2020.

2020
Collaborated with domestic universities to research hepatitis and anti-PD-1 immunotherapy, investing nearly NT$3 million. Due to the impact of the pandemic, the project was extended to the end of July 2021.

2021
Collaborated with 6 top domestic and international universities on various research projects, with a total investment of over NT$5 million, and all projects are currently ongoing.

2022
Invested about NT$300,000 with a domestic medical university to improve production yield, and the project is still ongoing.