3.1 Drug Quality and Safety Management GRI 3-3

PharmaEssentia is focused on independently developed R&D technologies which not only represent breakthroughs in the biomedical industry, but also improve patient wellbeing. All stages from new drug R&D, production, manufacturing, transportation, and launch rigorously and comprehensively adhere to complex regulatory and quality requirements. To maximize the life cycles of core products, PharmaEssentia conducts constant patent mining and enables comprehensive protection for innovative R&D technologies, and has established various intellectual property protection measures. We also manage post-marketing risks through continued monitoring and reporting of drug safety information as part of our responsibilities to protect patient interests.

Material Topics

- New Drug Research & Development and Innovation Management
- Drug Quality and Safety Management
- Business Integrity and Ethical Management

Main Stakeholders

- Patients
- Medical Personnel
- Commissioned Research/ Experiment Units
- Shareholders and Investors
- Suppliers and Business Partners
- Local Communities
- Government and Competent Authorities
- Media

Material Topics

PharmaEssentia MATERIALITY

New Drug Research & Development and Innovation Management

Description of Impacts

PharmaEssentia independently built a PEGylation technology platform. PEGylation is a type of technology that can maintain the stability of protein-based drugs in the human bloodstream, thereby prolonging the duration of therapeutic concentration. We used this technology to improve on existing protein-based drugs and successfully developed a new-generation long-acting interferon BESREMi (Ropeginterferon alfa-2b, Ropeg, P1101), which can be used for multiple indications. Apart from already obtained drug permits for PV, we are also working on multiple new indications to benefit more patients.

Policies and Commitments

PharmaEssentia is committed to solving unmet medical needs. After achieving breakthroughs in the MPN domain, we adhered to the spirit of the Access to Medicine Index and continued to invest in research on blood disorders and solid tumors. We are also working with external research institutes and biotechnology companies to jointly develop cell therapies. PharmaEssentia screens domestic and international research institutes with GLP, ISO 17025 (non-compulsory), and AAALAC certifications to ensure that research personnel rigorously adhere to all relevant regulations during R&D processes for new drugs and use humane procedures when conducting preclinical animal trials.

Responsible Unit

Research and Development of New Drugs center: Responsible for new drug discovery, and has established the "Project Evaluation Team" to serve as the research decision-making unit. Team members include colleagues and senior managers from different departments. Projects are initiated following approval at "Project Review Meetings," and project supervisors coordinate project progress and make regular progress reports.

Clinical operations department: Responsible for managing clinical trials

The Executive Center for Corporate Sustainability Access to Medicine Team: Responsible for compiling and managing material sustainability issues

Response Measures and Management Actions

Invested resources:

Manpower resources: A total of 165 R&D and clinical personnel around the globe, a reduction of 16.2% compared to the previous year

Financial resources: R&D investments: In 2024, PharmaEssentia invested a total of NT$2.59 billion to build R&D momentum, an increase of 16% compared to the previous year

R&D:

- Important R&D projects included use of PEG-IL-2 to treat inflammatory and immune diseases; many other products which are in Phase 1, Phase 2, Phase 3, or post-marketing Phase 4 clinical trials; and a number of IITs in collaboration with physicians
- Joint development of TCR-T cell therapies with external partners

Prospective projects:

- Combine AI (artificial intelligence) and ML (machine learning) to expand R&D capabilities
- Continue to recruit professional scientific talents with expertise in drug development, and utilize AI/ML technologies to enhance the efficiency of early drug development, design, and optimization stages

Evaluation Mechanisms

(Channels and Systems for Tracking Effectiveness of Response Measures and Management Actions)

- New drugs have to pass feasibility studies, preclinical animal trials, clinical trials, product manufacturing, and market authorization reviews before launch, and all R&D processes have product quality assurance, drug safety and efficacy, and regulatory compliance mechanisms that serve as a basis for determining whether development should be continued
- Our R&D department manages and reviews schedules for all R&D projects each month and makes quarterly reports to the Board
- Our R&D expenditures were approved by the Board in December 2023. The finance department tracks actual and budgeted expenditures of R&D projects every quarter, and reports on discrepancies to the Board
- Our auditing departments conducts audits on R&D cyclical management mechanisms each year in accordance with annual audit plans

Targets and Achievements in 2024

Number of drugs in development: 13

In 2024, our headquarters completed investigational new drug (IND) applications for PEG-GCSF and Anti PD-1, and conducted 5 new clinical trials for PEG-GCSF, Anti PD-1, TCRT-ESO-A2, HOPE PMF, and ATL.

- Submitted IND application for PEG-GCSF Phase 1 clinical trials and completed Phase 1 clinical trials
- Completed patient recruitment for EXCEED-ET and ECLIPSE-PV clinical trials in March and June of 2024
- Completed multinational, multicenter ET Phase 3 clinical trials, and completed Topline data analysis at the end of December
- Obtained government scientific subsidies of NT$10,428,000 for ET Phase 3 clinical trial
- Initiated patient recruitment for Japan ALT Phase 2 clinical trial

Targets

Short-Term Targets (1-2 Years):

- Expand into new indications and become a global leader in the MPN domain

Mid-Term Targets (3-5 Years):

- Develop PEG platform: Utilize independently developed PEC PEG platform to develop long-acting cytokines
- Develop other technologies such as BiC/FiC PEGylated cytokines (GCSF, IL-2, IFN-g, and others)
- Target solid tumors with low response rates such as renal cancer, pancreatic cancer, or immune-mediated diseases

Long-Term Goals (More Than 5 Years):

- Develop top-tier R&D platform: Develop best-in-class/first-in-class treatments
- Utilize novel BiC/FiC immune checkpoint molecules for treatment of solid tumors and hematologic diseases
- Cell therapies: TCR-T targets cancer antigens on the cell membrane as well as intracellular cancer antigens

R&D Focus

The global biopharmaceutical industry is flourishing due to advances in medical technologies and aging populations, and therefore continuous innovation and development is an important mission for pharmaceutical companies. PharmaEssentia is a new drug developer and biologics manufacturer that is actively developing drugs for MPN. The four main types of MPN are :

- Polycythemia Vera, PV
- Essential Thrombocythemia, ET
- Chronic Myeloid Leukemia, CML
- Primary Myelofibrosis, PMF

As MPN is a rare condition with many patients worldwide, there are many new drug developers working to develop associated drugs. We used our independently developed PEGylation technology platform to improve upon existing drugs, and successfully developed new-generation PEG long-acting α-interferon alfa-2b (Ropeg), a drug with multiple indications which breaks through limitations in traditional interferon drugs and treatments. We have currently obtained marketing authorizations for PV treatment and are working to obtain marketing authorizations for other indications. We have also extended use of the PEGylation technology platform to tumors, immune diseases, and cell therapies, expanding into other treatment indications and applications to provide innovative solutions for other diseases.

Even though development of new drugs requires large amounts of R&D technologies, time costs, and capital investments, we have spared no effort in utilizing our drug manufacturing and industry expertise to create innovations that enhance patient quality of life and contribute to society as we strive to become a benchmark enterprise in the biopharmaceutical industry.

Governance

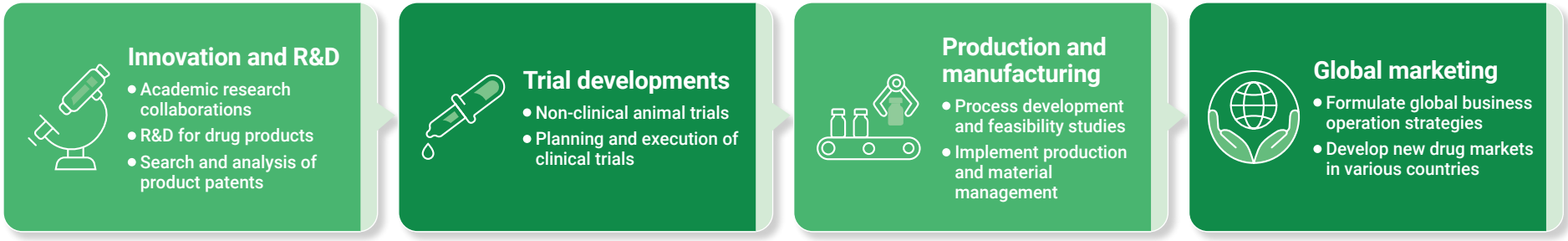
New drugs have to pass rigorous quality, safety, efficacy, and regulatory controls over a long period of time that spans from drug discovery, feasibility studies, preclinical animal trials, clinical trials, product manufacturing, and market authorization reviews before launch. PharmaEssentia has established complete drug R&D governance organizations to ensure that all responsible units implement efficient management and progress at all stages of new drug development.

Our Research and Development of New Drugs Center reports directly to the chief executive officer and is responsible for R&D of drug technologies. We have also established the “Project Evaluation Team” to make decisions regarding R&D; team members mainly include R&D team members, personnel from intellectual property departments, and senior executives from our headquarters and US subsidiary. Personnel from other departments such as the corporate planning/market development department, finance department, and legal department attend meetings based on their respective functions and R&D needs. All stages from pre-initiation analyses on project feasibility and potential values; compilation of data associated with proofs of concept, literature, market potential, competitive environments, and experiment data; and fundamental research for project initiation adhere to internal controls. Associated meeting minutes are compiled and revised on a rolling basis as necessary.

Project achievements must be reported at "Project Review Meetings" during specific stages of progress. Review meeting attendees assess the competitive potential and infringement risks of projects based on their unique characteristics and associated experiment data, and project directions are ultimately determined by the "Project Evaluation Committee," which is composed of senior executives. After project launch, project supervisors coordinate project progress and ask internal patent lawyers to conduct assessments or provide recommendations as appropriate based on innovativeness, progressiveness, free operation, and other project characteristics to ensure the value of developed project technologies.

Apart from the Research and Development of New Drugs Center and intellectual property department, we have also established a medical research center to formulate medical strategies for products and clinical trial plans. Our Taichung Plant plans manufacturing processes and implements material management, and our global operations division is responsible for formulating global strategies and market development plans.

▶ PharmaEssentia drug R&D to marketing process



Strategy

▶ Innovation and R&D Focuses

SASB HC-BP-000.B

In 2024, PharmaEssentia completed Phase 3 ET clinical trials (LPLV) for Ropeg. We expect to apply for ET marketing authorizations in Taiwan, the US, Korea, and China in 2025 to bring more medical value to the MPN field and strengthen PharmaEssentia's leadership in this domain.

Preparations for ET marketing authorization applications and market launch

- Estimate drug permit application and acquisition schedules based on clinical trial report completion times
- Implement Good Clinical Practice (GCP) simulation inspections
- Formulate drug pricing and drug listing strategies and schedules
- Conduct national market surveys of ET in Taiwan, the US, Japan, Korea, and China to understand current drug treatments

Benefits of obtaining ET marketing authorization

- Our PV indication physician team has several years of experience in MPN market deployments; we therefore used the same team on the ET indication. PharmaEssentia was able to achieve global reach by surveying patient distributions, without the need to build a new team or spend excess marketing and preparation costs, achieving better depth and breadth with minimal effort
- At present, very few drugs have been approved for ET treatment, and these have severe side effects and poor patient adherence. These Phase 3 clinical trial results indicate that Ropeg has good efficacy, few side effects, and good patient adherence
- Enhance academic medical developments and patient well-being while strengthening Ropeg's leadership position in the MPN field

Apart from MPN, PharmaEssentia also used the patented PEGylation technology to develop the new drug PEG-IL-2 for treatment of inflammatory or immune diseases. We plan to submit Phase 1 clinical trial applications at the end of 2025. We are also working with external partners to jointly develop TCR-T cell therapies and will begin recruiting Phase 1 clinical trial patients in Taiwan at the end of 2025.

The following is a summary of R&D progress made on our drugs in 2024:

R&D Product Pipelines SASB HC-BP-210a.1

Therapeutic Area	Drug Candidate	Indication	Markets	Pre-IND	Phase I/II	Phase III	Registration	Marketed
Hematology	Ropeginterferon alfa 2b (P1101)	PV	Europe					
			US, Taiwan, Korea, Japan, China, Malaysia, Singapore					
			Hong Kong, Brazil, Argentina, Mexico, Columbia					
		ET	Global					
		Pre-PMF	Global					
		Adult T-cell leukemia/lymphoma	Japan, Taiwan, China					
		Chronic myeloid leukemia	Korea					
Oncology	TCRT	Solid tumors	US, Taiwan					
	P1101 + Anti PD-1	Hepatocellular carcinoma	Global					
	Anti PD-1 (P1801)	Solid tumors	Global					
	PEG-GCSF	Neutropenia	Global					
	PEG-Cytokine X,Y	Solid tumors	Global					
	Novel Checkpoint Abs	Solid tumors	Global					

Note: For the latest information on our R&D product pipelines, please refer to our official website: https://hq.pharmaessentia.com/en/pipeline

PharmaEssentia Innovation Research Center (PIRC)

PharmaEssentia established the PharmaEssentia Innovation Research Center in 2023 to work with headquarters on breaking into new research fields. We hope to further expand our R&D and innovation capacity by combining AI (artificial intelligence) and ML (machine learning) to accelerate the process from new drug development to market launch. In 2024, we worked with Qiagen to utilize data analytics and AI in finding new indications for Ropeg, and presented the results at the ASH Annual Meeting. We also worked with DeepSeq.AI in using AI to design new-generation smart cytokines that could be used in cancer treatments. We continue to build AI platforms and introduce relevant tools to accelerate the development of new drugs, continue to recruit professional scientific talents with expertise in drug development, and utilize AI/ML technologies to enhance the efficiency of early drug development, design, and optimization stages.

Intellectual Property Strategies to Protect Innovative R&D Technologies

During the early stages, PharmaEssentia focused on increasing production and reducing costs, using blanket collection of R&D results combined with dedicated analysis by a team of medical patent lawyers to gradually develop patent strategies against potential future biosimilars. PharmaEssentia's core product BESREMi is listed in the US and other international markets. Our intellectual property department works with existing research achievements from the R&D department to actively respond to the US biosimilars patent dance process and to conduct in-depth considerations of technical research.

Apart from formulating innovative intellectual property strategies during the life cycles of core products, our internal patent lawyers also invite experienced research teams to conduct "invention mining" processes on R&D results to explore patent opportunities hidden within technical details, uncover and refine results previously missed by researchers, and transform these into new patents that bring greater value to technical innovations, thereby enhancing the value and life cycle of good products. For example, we inventoried, refined, and tested Ropeg, and uncovered detailed patent technologies and values in the technology which we used to apply for new patents, thereby continually extend our patent protection period through accumulation of Ropeg patents. In 2024, PharmaEssentia used this technology-mining approach to build upon and integrate multiple ongoing achievements from the R&D department. We spare no effort in exploring and protecting our innovative medical technologies. In the US, we secured provisional patents to provide protection for emerging technologies and several future product pipelines that are still in the R&D stage, using these as a foundation for strengthening future product patent landscapes in accordance with R&D progress.

Risk Management

Commitment to Animal Welfare in Preclinical Animal Experiments

We first determine whether institutes conducting trials adhere to our requirements and standards, such as whether they hold GLP (Good Laboratory Practice), ISO 17025 (Laboratory Quality Management System), and AAALAC (American Association for Accreditation of Laboratory Animal Care) certification, and then conduct online or on-site visits/audits to better understand the expertise of the CRO (Contract Research Organization) and expert team, trial schedule coordination, and market price rationales. We also review contracts and technical agreements with legal personnel, supervise trials and review data during trial periods, and compile reports for review once trials have concluded. We use this process to confirm that our CROs comply with regulatory requirements, and to ensure the reliability and compliance of data from animal trials. In 2024, we commissioned 5 domestic and overseas reputable and qualified institutes to conduct preclinical animal trials.

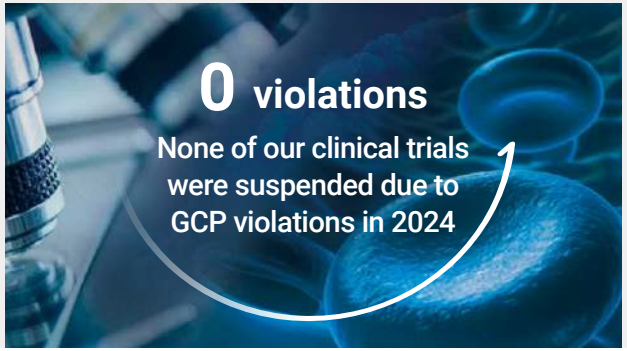
The pharmaceutical industry requires large amounts of horseshoe crabs for experimental use, so these crabs are now a borderline endangered species. The Pharmaceutical Supply Chain Initiative (PSCI), which was formed by multiple international pharmaceutical brands, has called on the biopharmaceutical industry and supply chain partners to cease capturing these crabs and use innovative alternative solutions such as microfluidic technologies and recombinant reagents to reduce reliance on limulus amebocyte lysate (LAL). Where there is still need to use LAL, initiative members are encouraged to actively enhance their understanding of raw material sources and associated animal welfare and biodiversity issues while also sharing information on horseshoe crab traceability, population numbers, and conservation conditions with other members.

PharmaEssentia only procures necessary amounts of reagents in LAL kits (the substances remaining after vendors have extracted horseshoe crab blood) to test whether drugs or medical equipment have been polluted by endotoxins. This significantly maintains survival rates of horseshoe crabs and prevents them from being endangered. Our collaborating vendors also adopt the 3R (Replacement, Reduction, Refinement) measures to protect horseshoe crabs by seeking out replacement reagents to test for endotoxins, using microfluidic technologies to reduce 95% of raw materials extracted from horseshoe crabs, and actively refining current LAL formulations. We have never used other endangered species during trial processes and we work to fulfill our responsibilities to protect endangered species.

Clinical Trial Quality Maintenance and Participant Safety in Clinical Trials

SASB HC-BP-210a.1

PharmaEssentia has developed a 20-step standard operating procedure for clinical operations to ensure the safety of clinical trial participants. We have established audit and inspection mechanisms at all stages to maintain trial quality, and conduct Phase 1, 2, and 3 clinical trials in accordance with approved trial protocols and local regulations. None of our clinical trials were suspended due to GCP violations in 2024.



Trial Planning

Evaluate potential risks of trial procedures based on preclinical data, drug characteristics, and clinical trial designs; require CROs to formulate a case-specific “Monitoring Plan” and “Audit Plan” based on risk levels to implement QC (quality control) and QA (quality assurance) items, ensuring that clinical trial processes, data records, and reports all adhere to trial protocols and GCP regulations, thereby protecting the rights and well-being of trial participants.

Phase 1 Clinical Trial: Safety Exploration

Quality Assurance (QA)	Quality Control (QC)
• Includes independent audit system and commissioning of alternate CROs or independent consultants to conduct audits during the later phases of clinical trials to ensure trial quality and consistency. Identified issues are assessed and tracked appropriately, and auditees must submit relevant corrective actions and preventive action (CAPA) to auditors for review • Data Safety Monitoring Committee (DSMC): Monitors patient safety and drug efficacy of clinical trials	Monitoring and co-monitoring

Before the Trial

Phase 2 Clinical Trial: Preliminary Efficacy Study

- The trial protocol and related documents must be reviewed and approved by health regulatory authorities and the trial institute Institutional Review Board Committee
- Investigator meeting: Conduct training related to the trial
- Informed consent from participants: Participants must be fully informed of and give written consent to join the clinical trial after careful consideration before trial screening can commence
- Participant screening: Rigorously screen participants based on the inclusion and exclusion criteria outlined in the trial protocol

During the Trial

Phase 3 Clinical Trial: Large-Scale Confirmatory Efficacy Study

- The clinical operations department conducts joint monitoring with CROs contracted for monitoring services
- Audits are carried out in accordance with audit plans to ensure that CRO services meet quality standards

After the Trial

- Compile data on efficacy and safety for review, on-site verification, and assessment of benefits and risks by health regulatory authorities to obtain marketing authorization

Metrics and Targets

R&D expenditures over past five years

Year	2020	2021	2022	2023	2024
Global R&D Expenditures (NT$ '000)	922,380	1,272,944	1,425,964	2,224,054	2,587,570
Expenditure Increases Compared to Previous Period (NT$ '000)	282,805	350,564	153,020	798,090	363,516
Expenditure Growth Rate	44%	38%	12%	56%	16%
Global R&D Personnel (Persons)	74	83	123	142	165
Personnel Increases Compared to Previous Period (Persons)	18	9	40	19	23
Personnel Growth Rate	32.1%	12.2%	48.2%	15.4%	16.2%

Continued increases in R&D expenditures brings four main benefits for PharmaEssentia:

Product innovation and technological breakthroughs

Increases in R&D expenditures indicate that PharmaEssentia is committed to development of new products and technological innovations, and is also actively seeking market breakthroughs to enhance competitiveness.

Increase future revenue potentials

Even though R&D expenditures increase costs in the short term, they also serve as a foundation for future corporate growth. Successful development of new drugs help to expand markets, increase revenues, and bring long-term returns and investment benefits.

Expand market share

PharmaEssentia is currently conducting in-depth research into specific therapeutic areas such as blood disorders and cancers, and we are also working to extend product patent protection periods to further maintain our market leadership so we can expand market shares in target markets.

Enhance corporate brand value and collaboration opportunities

We enhance our brand value through continued investment in breakthrough R&D technologies for new drugs to attract support from more collaborators and investors, and are working to become a leader in Taiwan's biopharmaceutical industry.

R&D Focuses in 2024

- Number of drugs in development: 13
- Submitting IND application for TCRT-ESO-A2-TW cell therapy
- Completed 2 IND applications (PEG-GCSF and Anti PD-1)
- Conducted 5 new clinical trials (PEG-GCSF, Anti PD-1, TCRT-ESO-A2, HOPE PMF, and ATL)
- Obtained PV marketing authorizations in China, Singapore, and Malaysia
- Future expectations:

☆ Submit IND application for PEG-IL-2 in 2025
☆ Advance at least 1 project to development candidate stage
☆ Advance at least 1 project to preclinical candidate development stage
☆ Introduce 1-2 external technology platform asset projects
☆ Build AI (artificial intelligence)/ML (machine learning) platform

Development Focuses for Next Five Years (2025-2030)

Continued growth in Ropeg operations
- Continue to increase patient numbers in existing markets
- ET indication: Apply for US marketing authorization in 2025 and obtain marketing authorization in 2026

Expansion of Ropeg indications
- Currently conducting global Phase 3 pivotal clinical trials for early PMF and plan to submit applications for FDA approval at the end of 2027
- Other blood disorders: Research into ATL, CTCL, and other application areas

Expand global production capacity
- Aim to fulfill demand for more than 100,000 patients around the world
- Initiated construction of Zhubei Plant in 2023 in response to market demand, with completion projected for year-end 2025

Top-tier platform
- Utilize novel immune checkpoint molecules and cytokines for treatment of solid tumors, blood disorders, and immune diseases
- Cell therapies: TCR-T targets cancer cell antigens and can be used for treatment of solid tumors

Source: February 2025 Analyst Presentation Documents and information from Zhubei Plant