From drug research and development to the production phase, strict adherence to regulations and various quality requirements is essential; the drug supply chain must also be rigorously managed. This includes the sourcing of raw materials, manufacturing, filling, drug packaging, transportation, and ensuring safety up to the stage of patient use. All these aspects are critical issues that we prioritize.

3.1 New Drug Research and Development and Innovation Management

Materiality Assessment

GRI3-3

Materiality Assessment

New Drug Research and Development and Innovation Management

Impact Assessment

PharmaEssentia's PEGylation technology platform is a core of its R&D, prolonging time of the effective concentration of protein drugs in human blood. Besremi, a new generation long-acting PEGylated α-interferon, treats multiple indications and is under development for more to benefit additional patients.

Management Policies and Commitments

In addition to the breakthrough indication approval for MPN, PharmaEssentia focuses on addressing unmet mln addition to the breakthrough indication approval for MPN, edical needs, especially in hematological diseases and solid tumors, guided by the Access to Medicine Index. Commitment to animal welfare in preclinical testing during new drug research and development.

Responsible Departments

- New Drug R&D Division: Manages new drug discovery, with decisions made by the "Project Evaluation Team ," including cross-functional members and senior management, and "Project Review Meeting."
- Clinical Operations Department: Manages clinical trials.
- Sustainable Significant Theme: Managed by the Sustainability Development Center - Access To Health care Team.

Resource Allocation

- Global R&D Clinical Staff: 142 personnel, up 15.4% from last year.
- R&D Investment: NT$2.22 billion in 2023, a 56% increase from 2022.
- Key R&D Items: PEG-IL-2 technology for inflam- matory and immune diseases, clinical trials of other various drugs from Phase I to III, post-marketing research, and IIT.
- Collaboration: Development of TCR-T cell therapy through external partnerships.

Measures

- Number of drugs in development: 13
- The headquarters completed 2 IND applications and conducted 4 new clinical trials

Practices to ensure that actions are effective

- Through the combination of AI and machine learning, we will expand the capacity of R&D
- Continue to recruit scientific professionals with experience in drug development, and combine AI/ML technology to improve efficiency in the early stage of drug development, design and optimization

2023 Performance

- The PharmaEssentia Innovation Research Center Corporation (PIRC) was established to combine AI and machine learning to further expand the capacity of R&D innovation, effectively identify research objectives in the early research stage, reduce development time and cost, and accelerate the process from R&D to market.
- Clinical trials: In 2023, 4 new plans including CML, HDV, PMF, and HCC will be added, bringing the total number of 9 clinical trial plans currently underway. In 2023, there will be 453 new patients, bringing the total number of clinical trial patients to 1,332.
- In 2023, PharmaEssentia completed the application for the IND of the Phase 1 TFDA clinical trial in Taiwan for the treatment of solid tumors with anti-PD-1 antibody (P1801). and the multi-national and multi-center Phase III clinical trial of essential thrombocythemia (ET), which also received a government grant of NT$5,435K.

Continuous Growth Trend in R&D Costs Over the Past Five Years (2019-2023)

Year	2019	2020	2021	2022	2023
Global R&D Expenditure (NT$ '000)	639,575	922,380	1,272,944	1,425,964	2,224,054
Increase in Expenditure from Previous Period (NT$ '000)	-	282,805	350,564	153,020	798,090
Growth Rate of Expenditure	-	44.2%	38.0%	12.0%	56.0%
Global R&D Personnel (number)	56	74	83	123	142
Increase in Personnel from Previous Period (number)	-	18	9	40	19
Growth Rate of Personnel	-	**32.1%**	**12.2%**	**48.2%**	**15.4%**

Innovative R&D Focus

SASB HC-BP-000.B

Apart from continued investment in MPN (Myeloproliferative Neoplasms), PharmaEssentia is also investing in PEG-IL-2 technology for the treatment of inflammatory and immune diseases. Additionally, it is engaged in joint development of TCR-T cell therapy through external collaborations.

PharmaEssentia plans to initiate two IND (Investigational New Drug) research projects:

- This includes starting clinical trials for an anti-PD-1 antibody (P1801) and a long-acting G-CSF
- clinical trials for new indications of P1101 in early PMF (Primary Myelofibrosis) and low-risk PV (Polycythemia Vera).
- the company aims to complete
  - at least one project up to the development candidate stage
  - at least one project up to the preclinical candidate development stage
  - Additionally, 1-2 external technology platform assets will be introduced. The development of an AI/ML (Artificial Intelligence/Machine Learning) platform is also planned.

Key Development Focus for the Next Five Years (2024-2029):

Continuous Growth in Besremi Operations

- Market Expansion:
  Patient usage and numbers continue to increase in existing markets.
- PV Indication:
  Expected to obtain drug approvals in China and Singapore-Malaysia in 2024.
- ET Indication:
  Plans to apply for U.S. drug approval in 2025, with approval anticipated by early 2026.

Expansion of indications for P1101

- Early PMF Clinical Trials:
  A global Phase III pivotal clinical trial for Early PMF (Primary Myelofibrosis) is currently underway, with plans to submit an FDA drug application by the end of 2026.
- Research in Other Blood Disorders:
  Ongoing research into the application of P1101 for other hematologic diseases, including ATL (Adult T-cell Leukemia/Lymphoma) and CTCL (Cutaneous T-cell Lymphoma).

Global supply capacity expansion

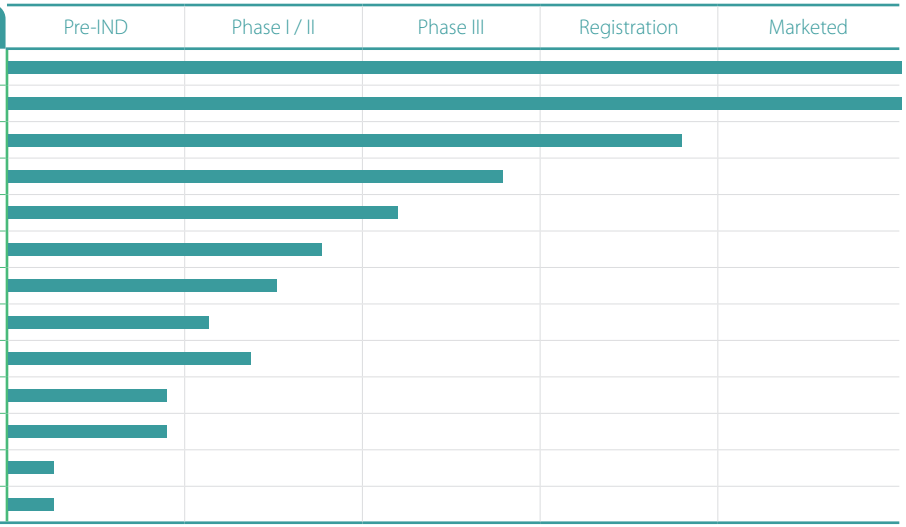
- Global Production Capacity :
  Expected to supply over 10,000 people
- Zhubei Plant Construction:
  In response to market demand, construction has begun on the Zhubei plant, with completion projected for 2026.

Top-tier R&D platform

- Innovative Immune Checkpoint Molecules and Cytokines:
  New types of immune checkpoint molecules and cytokines are being developed for the treatment of solid tumors, blood disorders, and immune diseases.
- Cell Therapy with TCR-T:
  This advanced therapy targets cancer antigens on the cell membrane for the treatment of solid tumors.

Source: March 2024 Analyst Presentation Documents

Therapeutic Area	Candidate	Indication	Market
Hematology	Ropeginterferon alfa 2b (P1101)	PV	EU
			US, TW, KR, JP
			CN, MY, HK, SG
		ET	Global
		Early myelofibrosis	Global
		Aduit T-cell Leukemia	JP, TW, CN
		CML	KR
Oncology	TCRT	Solid tumors	US, TW
	P1101 + anti PD-1	HCC	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 updates on our R&D product line, please refer to the official PharmaEssentia website at https://hq.pharmaessentia.com/index.php?/en/pipeline

Commitment to Animal Welfare in Preclinical Animal Experiments

To ensure adherence to animal welfare, the company selects domestic and international contract research organizations (CROs) that are GLP-certified. These organizations are required to comply with the regulations of the Institutional Animal Care and Use Committee (IACUC) and adhere to the 3Rs principle (Refinement, Reduction, Replacement). This approach aligns with the directives of the Animal Welfare Committee to conduct experiments humanely. Currently, the company has entrusted three qualified domestic and international institutions to carry out preclinical animal experiments.

Participant Safety in Clinical Trials SASB HC-BP-210a.1

To ensure the safety of participants in clinical trials, PharmaEssentia has developed about 20 Standard for clinical operations management. Audit and verification mechanisms are implemented at each phase to maintain trial quality. All clinical trials, including Phases I, II, and III, are conducted in accordance with approved study protocols and comply with local national regulations. Currently, there are no clinical trials that have been terminated due to violations of Good Clinical Practice (GCP) standards.

Clinical Trial Quality Maintenance and Risk Management

Before Clinical Trials	Based on the characteristics of the drug and the differences in the trial design, the risks and extent that may be encountered during the trial process are evaluated.	
Risk Assessment	Develop "Monitoring Plan" and "Auditing Plan" through contracted CRO based on risk level to ensure QA and QC. Ensure participant rights and welfare protection and compliance with trial protocols, GCP, and regulations regarding trial execution and data generation、recording and reporting.	
Execution Process	**Quality Assurance (QA):** Independent auditing system, issue assessment and tracking, formulation of corrective and preventive actions (CAPA)	**Quality Control (QC):** Execute monitoring and co-monitoring activities.

Phase I Clinical Trial — Safety Exploration

Phase II Clinical Trial — Preliminary Efficacy Study

Phase III Clinical Trial — Large-Scale Confirmatory Efficacy Study

Trial Planning

Risk Assessment: Evaluate risks based on the services provided by the Contract Research Organization (CRO) and the characteristics of the clinical trial.
Monitoring and Auditing Plans: Develop monitoring and auditing plans based on the level of assessed risks.
Quality Management and Assurance: Establish plans for quality management and assurance to maintain high standards throughout the trial based on the level of assessed risks.

Before the Trial

Regulatory and Ethics Approval: The trial protocol and related documents must be reviewed and approved by health regulatory authorities and the Institutional Review Board Committee.
Investigator Meeting: Conduct training related to the trial.
Informed Consent from Participants: Participants must be fully informed and give written consent after careful consideration before screening can commence.
Participant Screening: Strictly screen participants based on the inclusion and exclusion criteria outlined in the trial protocol.

During the Trial

Co-Monitoring by Clinical Operations: The clinical operations department conducts co-monitoring with the CRO handling monitoring duties.
Auditing: Carry out audits according to the audit plan to ensure that the CRO's services meet quality standards.

After the Trial

Data Compilation and Review: Compile data on efficacy and safety for review and onsite verification by health regulatory authorities. Only after assessing benefits and risks can approval for marketing be granted.