

Biotechnology-related Business



The SBI Group considers the Biotechnology-related Business to be one of its three core businesses, and is conducting business operations through SBI Biotech, SBI Pharmaceuticals and SBI ALApromo. Particularly important is the 5-aminolevulinic acid (5-ALA)-related business, which is based on the development and sale of pharmaceuticals, health foods and cosmetics containing 5-ALA, which is expected to become the most significant growth area for the Group, and for which the pace of global expansion has been accelerated.

Financial Results for FY2014

Operating revenue for the Biotechnology-related Business declined by 0.6% year-on-year to ¥2.2 billion in FY2014, with a ¥7.3 billion loss before income tax expense recorded, versus a ¥2.4 billion loss in FY2013. The increased loss was mainly attributable to the fact that the results for FY2014 no longer benefited from a special factor relating to the sale of pharmaceutical development seeds to another company by the U.S. bio-venture company Quark Pharmaceuticals, Inc., a wholly owned subsidiary of SBI Biotech, in FY2013. Another factor was an error in the trial population secured by the contract research organization (CRO) in the clinical trial on a product in Quark's pharmaceutical development pipeline, which was subsequently determined to be statistically insignificant. This necessitated the revaluation of assets, resulting in a one-time loss of approximately ¥3.8 billion.

Selling, general and administrative expenses for the 5-ALA-related business increased owing to SBI ALApromo's extensive marketing campaigns for the ALAPlus series of health foods. However, the campaigns were successful, resulting in a steady growth in shipment volumes and the number of consulting pharmacies, drugstores and other outlets handling products containing 5-ALA.

Principal Companies

Intermediate Holding Company: SBI ALA Hong Kong

SBI Biotech

SBI Pharmaceuticals

SBI ALApromo

Full-year Profit before Income Tax Expense of the Biotechnology-related Business (based on IFRSs)

(Millions of yen)

	FY2013	FY2014
Biotechnology-related Business	(2,432)	(7,310)
SBI Biotech	(611)	(637)
Quark Pharmaceuticals	(721)	(1,436)
Partial write-down of Quark's pipeline	—	(3,793)
SBI Pharmaceuticals	(1,083)	(1,220)
SBI ALApromo	(176)	(426)



Attains Multiple Drug Pipeline, and the IPO Preparations are Resumed

Takeshi Irie

SBI Biotech Co., Ltd.
Representative Director and
President



Development and Sales Rights Granted to the U.S. Company MedImmune

SBI Biotech has focused primarily on R&D relating to drugs for the treatment of cancer and autoimmune disease, in partnership with bio-ventures and research organizations in Japan and abroad, but it is now reviewing its portfolio through the application of the selection and concentration strategy to its drug development projects, and currently, the company is developing revolutionary new drugs with a particular focus on antibodies used to control plascytoid dendritic cells (pDC), and functional RNA.

One of the products to result from this research is the Anti-ILT7 antibody, a molecular targeted drug developed for use in the treatment of autoimmune disease. A development and sales license has been granted to MedImmune LLC, a member of the AstraZeneca Group, which has already gained an international reputation as a developer of antibody drugs.

Progress on Drug Pipelines through Quark Pharmaceuticals

Quark Pharmaceuticals, a wholly owned subsidiary of SBI Biotech, has advanced technology relating to short-interfering RNA (siRNA), which is attracting intense interest at a time when progress in low-molecular drug discovery is waning.

Quark Pharmaceuticals has several promising candidate drugs, and has already concluded licensing and other agreements with Pfizer Inc. and Novartis International AG.

Quark Pharmaceuticals has agreed with Novartis to grant an option to obtain license covering QPI-1002, which is currently undergoing Phase II and Phase III trials as a candidate for use in the treatment of acute kidney failure, and delayed graft function after kidney transplant surgery for which there is still no promising therapeutic agent. Phase II trials as a candidate drug for the treatment of delayed graft function have been completed, and comments have been obtained from the U.S. Food and Drug Administration (FDA) concerning the design for Phase III trials, including the primary endpoint and the number of subjects. Based on the results, the option agreement with Novartis will be renewed, allowing Phase III trials to begin by the autumn of 2015 at the latest.

The terms of a licensing agreement concluded with Pfizer concerning PF-655 include milestone payments and royalty payments. Also, a valuation loss was incurred on a pipeline asset, a drug for use in the treatment of diabetic macular edema, due to an error by the CRO. However, Phase IIa clinical trials have been completed, and R&D work is continuing. PF-655 could also be developed as a candidate drug for the treatment of glaucoma, and preparations for developments are already in progress.

Main Drug Pipeline Research and Development by SBI Biotech

Pipeline (Licensing partner)	Adaptation disease	Pre-clinical	Phase I	Phase II	Phase III
① QPI-1002 (Novartis International AG)	Kidney transplantation (DGF)				Planning to start at the latest by the autumn of 2015
	Acute kidney injury (AKI)			Planning to start Phase II in this year	
② PF-655 (Pfizer Inc.)	Diabetic macular edema (DME)	Compensation for damages sought from the CRO, and partial damages already collected. R&D to continue		Completed Phase IIa	
	Glaucoma			Start of Phase IIa protocol finalization	
③ Anti-ILT7 antibody (MedImmune, Inc.*)	Autoimmune diseases	Pre-clinical			

* Subsidiary of AstraZeneca



Progress on Commercialization of Pharmaceuticals, as well as Health Foods and Cosmetics Containing 5-ALA Continues

Satofumi Kawata

SBI Pharmaceuticals Co., Ltd.
Representative Director and
COO



5-Aminolevulinic Acid (5-ALA) that is Essential to Human Life

The existence of 5-ALA as a natural amino acid has been known for many years. In recent years, however, it has become the focus of intense interest as an extremely important substance needed to support life functions, such as respiration and energy production. Scientists have also discovered that 5-ALA production within the body declines with age, and that supplementation is important to maintain good health.

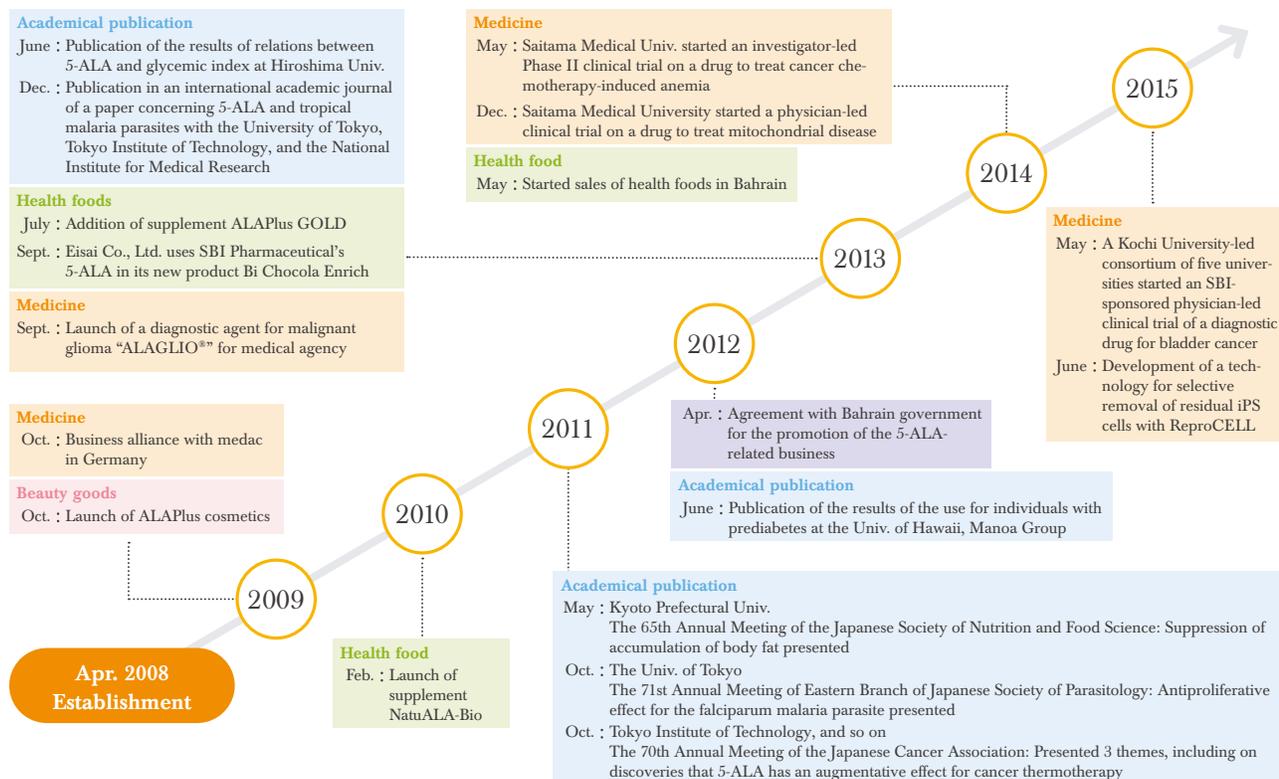
Collaboration with Global Research Institutions

SBI Pharmaceuticals has commercialized health foods and

cosmetics containing 5-ALA in Japan, and is now also actively researching 5-ALA in pharmaceuticals. In September 2013, it launched its first 5-ALA pharmaceutical products, ALAGLIO®. ALAGLIO® as Japan’s first orally administered intraoperative diagnostic agent, is for use during surgery to remove malignant gliomas, which is a form of brain tumor.

SBI Pharmaceuticals has built a global research network of over 90 research organizations in Japan and abroad, to carry out basic research and clinical trials involving the use of 5-ALA to treat a number of diseases. In Japan, for example, there is an R&D project relating to an intraoperative diagnostic agent for use during bladder cancer surgery. The product has been classified as an “orphan drug,” which is a drug used to treat rare diseases. For this drug, physician-led clinical trials have been carried out at Kochi University and four other universities, and

The 5-ALA-related Business is Progressing Steadily, Boosted by a Tailwind from Academic Papers



in May 2015 SBI Pharmaceuticals commenced a company-led Phase III clinical trial.

An investigational new drug (IND) supplied by SBI Pharmaceuticals is being used in a physician-led clinical trial that commenced in December 2014 by a nationwide pediatric network centering on Saitama Medical University, for clinical trials relating to mitochondrial disease. In addition, SBI Pharmaceuticals is working with Oxford University in the United Kingdom on the development of a 5-ALA drug to prevent post-operative ischemia-reperfusion injury, which can cause a reduction in the amount of blood flow per heartbeat in coronary bypass patients. Physician-led Phase II clinical trials will be carried out at multiple universities in the United Kingdom.

Patent Held by SBI Pharmaceuticals Increases to 21 in Japan

SBI Pharmaceuticals currently holds 21 patents in Japan, covering drugs developed for use in the prevention or alleviation of cancer and adult diseases with 5-ALA as their main constituent, and ten of these patents have also been patented overseas. SBI Pharmaceuticals will continue to obtain patents domestically and abroad for products using 5-ALA. Recently, it has obtained patents for a number of products, including drugs used to prevent or alleviate adult diseases, as well as for the treatment of malaria. Moreover, SBI Pharmaceuticals and ReproCELL Inc. have jointly applied for a patent covering technology for the use of 5-ALA in the selective removal technique on residual iPS cells, which can cause tumors, from iPS-derived differentiated cells.

5-ALA-related Business in the Middle East

SBI Pharmaceuticals is working closely with the government of Bahrain to build the 5-ALA-related business in Bahrain and the Gulf Cooperation Council (GCC) region. Bahrain has become a key center for the 5-ALA-related business in the Middle East, and clinical trials and other activities are being implemented with a variety of partner organizations.

With the approval of Bahrain's National Health Regulatory Authority (NHRA), clinical research relating to diabetes is being carried out at the Bahrain Defense Force Medical Service Hospital. Clinical research has been initiated concerning the use of 5-ALA to treat type-2 diabetes, and a food intervention trial is in progress. Diabetes-related research is also being carried out in collaboration with Arabian Gulf University (AGU) Hospital and the RCSI-Bahrain School of Medicine.

Clinical research concerning the use of 5-ALA in photodynamic diagnosis is being carried out at AGU Hospital. This work resulted in the world's first successful surgery to remove bladder cancer using 5-ALA as an intraoperative diagnostic agent in conjunction with a newly developed medical light source. To date, 11 successful operations have been completed, including that carried out at King Hamad University Hospital. Preparations are now being made at AGU Hospital for clinical research concerning surgery for the removal of prostate cancer.

Permission has been obtained for the sale of 5-ALA health foods in the United Arab Emirates, as well as Bahrain, and SBI Pharmaceuticals also expects to receive similar approval from the government of Jordan. This expansion of sales areas in the Middle East will further strengthen the health food business.

R&D Pipeline Sponsored by SBI Pharmaceuticals

	Phase I	Phase II	Phase III	Marketing
① Diagnostic Agent for Cancer Treatment (Brain tumor)				ALAGLIO* (from Sept. 2013)
② Diagnostic Agent for Cancer Treatment (Carcinoma vesicae) *Designated as an orphan drug			SBI corporate trial at the same five universities that conducted the physician-led trial (Started in May 2015)	Endeavor to increase the indications
③ A Drug to Treat Cancer Chemotherapy-induced Anemia (Saitama Medical Univ.) ARO: Kitasato Academic Research Organization		Investigator-led trial by Saitama Medical University, as the medical institution conducting the clinical trial (Providing drugs and funds)		
④ Preventing Cardiac Ischemia-reperfusion Injury (The Univ. of Oxford) Planning to jointly submit a test plan to the Medicines and Healthcare Products Regulatory Agency (MHRA) soon		Investigator-led trial by Professor Houman, the Univ. of Oxford, (Providing drugs and funds) (Phase II clinical trial will be implemented in several university hospitals in the U.K.)		
⑤ A Drug to Treat Mitochondrial Diseases (Saitama Medical Univ.)		Investigator-led trial led by Saitama Medical University (Providing funds) (Started in December 2014)		