

# BIOTECHNOLOGY-RELATED



## BIOTECHNOLOGY-RELATED BUSINESS

With Each Company in a Full-scale Monetization Phase, Two Companies have Achieved Their First Single-year Profitability since Their Establishments

### Principal Companies

Intermediate Holding Company: SBI ALA Hong Kong

SBI Biotech	photonamic
Quark Pharmaceuticals	Suzhou Yan Biotech
SBI Pharmaceuticals	SBI Neopharma
SBI ALApromo	

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

	(Millions of yen)	
	FY2015	FY2016
SBI Biotech	(297)	737
Quark Pharmaceuticals	(2,572)	(8,270)
5-ALA-related business	(3,471)	(298)
SBI Pharmaceuticals	(1,425)	91
SBI ALApromo	(587)	(233)
photonamic (consolidated in Jan. 2016)	38	(41)
SBI ALA Hong Kong	(65)	(69)
Suzhou Yan Biotech	(1,432)	(46)

### 5-ALA-related Products

#### Ethical drug



ALAGLIO® Granule 1.5g

#### Health foods and cosmetics



ALAplus / ALAplus Gold



ALAplus Sports High-performance



ALAplus Tou (Sugar) Down



ALAplus Cosmetic Series

### Principal Initiatives in FY2016 and Future Priority Measures

#### SBI Biotech, Quark Pharmaceuticals

- SBI Biotech achieved its first single-year profitability on a non-consolidated basis, owing to the receipt of milestone payments from its multiple drug pipeline, and an upfront payment for out-licensing to Kyowa Hakko Kirin Co., Ltd.
- On the other hand, Quark Pharmaceuticals, a wholly owned subsidiary of SBI Biotech, experienced a sharp increase in R&D expenses as a result of steady progress in multiple clinical trials, including two Phase III trials. However, R&D expenses are expected to decline after peaking in the fiscal year ending December 2017
- SBI Biotech and Quark Pharmaceuticals are planning their respective stock exchange listings

#### SBI Pharmaceuticals

- SBI Pharmaceuticals received upfront payments for the out-licensing of its multiple R&D pipeline, and accordingly recorded its first single-year profitability
- There has been steady progress in the R&D pipeline for clinical trials for an orally administered diagnostic reagent for photodynamic diagnosis ("PDD") utilizing 5-ALA, for peritoneal dissemination of gastric cancer, and a therapeutic drug for mitochondrial diseases, as well as for other diseases
- Revenue contributions are expected from a joint business with Neopharma LLC, a global pharmaceutical company based in the United Arab Emirates

#### SBI ALApromo

- A steady increase in the number of stores offering health foods utilizing 5-ALA, centering on "ALAplus Tou (Sugar) Down," Japan's first food with function claims containing 5-ALA
- Owing to an increase in the number of subscribers for direct sales, sales increased by approximately 2.3 times from the previous year
- Endeavoring to achieve profitability in FY2017, by promoting the development of new foods with function claims containing 5-ALA, as well as new products and cosmetics containing ingredients other than 5-ALA

# SBI BIOTECH

## Achieved First-time Profitability from Successful Monetization Initiatives, with Steady Progress in the Drug Pipeline

Takeshi Irie

SBI Biotech Co., Ltd.  
Representative Director  
and President



### SBI Biotech Achieved Its First-time Profitability on a Single-year Non-consolidated Basis

SBI Biotech is a bio-venture engaged in the development of medical treatments and innovative new drugs for intractable diseases, such as cancer and autoimmune disorders. In FY2016, the company achieved its first full-year profitability since its founding, recording profit before income tax expense (IFRSs) of approximately ¥0.7 billion on a non-consolidated basis. Factors contributing significantly to the achievement of profitability were the strengthening of the business base through drug pipeline restructuring, coupled with substantial cost-cutting, and a receipt of a portion of milestone payments accompanying the initiation of a Phase I clinical trial for an Anti-ILT7 antibody (MEDI7734) out-licensed to U.S.-based MedImmune, LLC, a subsidiary of a major pharmaceutical company AstraZeneca PLC, and the receipt of an upfront payment upon conclusion of an exclusive license agreement concerning SBI-9674 with Kyowa Hakko Kirin Co., Ltd.

The immunotherapy drugs the company seeks to discover and develop are drugs for the treatment of diseases through action on the human immune system. The field of autoimmune

disorders represents the fourth largest market after cancer, diabetes and pain, and in light of the attention focused on immunotherapy drugs following the success of the immunotherapy drug OPDIVO in the field of cancer therapy, further development is considered certain. To take advantage of the current momentum, SBI Biotech has selected a lead managing underwriter, and began discussions in preparation for an individual IPO.

### Quark Pharmaceuticals is Preparing for its Own Exchange Listing

Quark Pharmaceuticals, a wholly owned subsidiary of SBI Biotech, possesses superior technology in the field of small interfering RNA (siRNA), and is making steady progress with clinical trials for multiple drugs in its development pipeline. These include two drugs in Phase III of development, a preventive agent for the failure of kidney function following an organ transplant (QPI-1002, licensed to Novartis International AG of Switzerland), and a drug indicated for non-arteritic anterior ischemic optic neuropathy (QPI-1007, licensed to Biocon Ltd. of India). Since Quark has two drug discovery pipeline in Phase III development, it fully satisfies the requirements for an IPO on the NASDAQ market in the U.S., and is currently making preparations for an exchange listing.

### R&D Pipeline Sponsored by SBI Biotech

	Licensing partner (timing)	Adaptation disease	Progress	
MEDI7734 (Anti-ILT7 antibody)	MedImmune, LLC.* (Sept. 2008)	Autoimmune disorders (Systemic Lupus Erythematosus (SLE), Sjogren's Syndrome, Dermatomyositis, etc.) (Systemic Lupus)	Phase I	MedImmune, LLC. is conducting Phase I clinical trial. SBI Biotech recorded an allotted milestone payment in 2Q FY2016 (undisclosed amount)
SBI-9674	Kyowa Hakko Kirin Co., Ltd (Dec. 2016)	Autoimmune disorders	Pre-clinical (Kyowa Hakko Kirin promoting development)	Conducted license agreements at the end of 2016 SBI Biotech received an upfront payment and recorded it in 3Q FY2016 (undisclosed amount) *Further receipt of milestone payments due to development progress is also expected
Cdc7 inhibitor	Carna Biosciences, Inc. (May 2014)	Cancers	Pre-clinical (plan to apply for clinical trial in 2017)	Carna Biosciences, Inc. entered into an out-licensing agreement with Sierra Oncology, Inc. ●SBI Biotech received a partial milestone payment in June 2016 *Further receipt of milestone payments due to development progress is also expected
GNKS356	Independently	Psoriasis / Systemic Lupus Erythematosus (SLE)	Pre-clinical	Selected as Japan Agency for Medical Research and Development's (AMED) project of promoting support for drug discovery on orphan drugs (from FY2015 to FY2017) ●Received subsidies (up to ¥200 million per fiscal year) and promoting R&D
SBI-3150	Independently	Various diseases caused by pDC / activated B cells	Pre-clinical	Using the advantages of the development concept, we are actively engaged in out-licensing activities

\*Subsidiary of AstraZeneca PLC

## 5-ALA-RELATED BUSINESS

### Pursuing the Potential of 5-ALA in Ethical Pharmaceuticals, and Expanding the Product Offering of Foods with Function Claims Containing 5-ALA

#### Achieved Out-licensing of Three 5-ALA-related Drugs

SBI Pharmaceuticals has focused on the utility of 5-Amino-levulinic Acid (5-ALA), a natural amino acid, and since its establishment in 2008 has conducted research and development for the utilization of 5-ALA in a broad range of fields, including pharmaceuticals, health foods and cosmetics, in collaboration with more than 90 research organizations in Japan and abroad.

The company launched “ALAGLIO® Oral 1.5g,” the first drug containing 5-ALA, in September 2013 for use in surgery to remove malignant glioma, a type of brain tumor. “ALAGLIO® Oral 1.5g” is Japan’s first orally administered intraoperative diagnostic agent for use with these tumors, and sales in the domestic market are steadily increasing. In October 2016, SBI Pharmaceuticals out-licensed its R&D pipeline for the first time, by concluding two exclusive license agreements with Neopharma LLC, a global pharmaceutical company based in the United Arab Emirates. One license is for a drug for the treatment of diabetes for which Phase II and Phase III clinical trials are planned to be conducted by overseas medical institutions. The other license is for a drug for the treatment of malaria that SBI Pharmaceuticals is developing at the National Institute of Malaria Research in India, in cooperation with Neopharma LLC. The protocol for a Phase II clinical trial for this drug is expected to be approved soon. SBI Pharmaceuticals also plans to out-license an intraoperative diagnostic agent for brain tumors to Neopharma LLC as well. SBI Neopharma, which was established in Dubai of the Middle East, in March 2017 as a joint venture between the SBI Group and Neopharma LLC, is progressing toward the overseas sales of drugs for diabetes and malaria infection, which was out-licensed to and developed by Neopharma LLC using 5-ALA, along with health foods, cosmetics, feeds and fertilizers, developed by SBI Pharmaceuticals and Neopharma LLC.

Furthermore, in March 2017, SBI Pharmaceuticals concluded the third out-licensing agreement with Chugai Pharmaceutical Co., Ltd., granting exclusive marketing rights in Japan for “ALAGLIO® Granule 1.5g,” for the purpose of visualizing tumor tissues during resection of bladder cancer, for which a manufacture and sales approval is under application. Owing to the strict selection of the R&D pipeline and rigorous cost-cutting, as well as the contribution of these upfront payments from out-licensing, SBI Pharmaceuticals achieved profitability in FY2016 for the first time



since its founding, recording profit before income tax expense of ¥0.1 billion (IFRSs).

Other R&D pipeline projects are also progressing favorably. SBI Pharmaceuticals is preparing for Phase III physician-led clinical trials for a diagnostic reagent for peritoneal dissemination of gastric cancer and a therapeutic drug for mitochondrial diseases, and expects completion of Phase III development and an out-licensing within three years. It has completed a Phase II physician-led clinical trial for a therapeutic drug cisplatin nephropathy protection, and is preparing for a Phase II corporate-initiated trial. It also plans to conduct a Phase II physician-led clinical trial of 5-ALA for preventing cardiac ischemia-reperfusion injury, at Oxford University and University Hospitals Birmingham in the U.K.

#### Business Expansion Leveraging the Momentum of the Major Hit Product “ALAplus Tou (Sugar) Down”

SBI ALApromo, which plans, manufactures, and sells cosmetics and health foods containing 5-ALA, sells its products through more than 14,000 drugstores and pharmacies nationwide, on an official online shop, as well as through other channels. Since its establishment in 2012, the company has steadily expanded its product offering and distribution network. In particular, “ALAplus Tou (Sugar) Down,” a food with function claims launched in December 2015, has become a major hit, and SBI ALApromo’s revenue in FY2016 surged 2.3 times compared to FY2015.

“ALAplus Tou (Sugar) Down” has attracted a great deal of attention, winning the “Excellence Award for the Hit Item Awards (in the category of health foods and supplements category)” in the 29th Hit Products and Spotlight Products Awards, sponsored by DRUG Magazine and the Yachiyo-kai, as well as the “Award for the Shining Name” in the 1st Foods with Function Claims/Market Contribution Grand Prize, sponsored by Monthly H&B Retail. In the April 2017 foods with function claims sales rankings (Monthly H&B Retail June 2017 edition), “ALAplus Tou (Sugar) Down 30 Capsules” ranked 15th among 952 foods with function claims, making the rankings for fourteen consecutive months since March 2016. The popularity of “ALAplus Tou (Sugar) Down” contributed to an expansion of the number of stores offering SBI ALApromo’s health foods containing 5-ALA, increasing sharply from 603 in January 2014 to more than 14,000 in June 2017.

SBI ALApromo will endeavor to further increase sales through sales promotion measures that are adapted to the needs of individual drugstores, as well as the provision of POP materials.

Going forward, SBI ALApromo will undertake to further boost sales of “ALApplus Tou (Sugar) Down” by increasing the number of customers who regularly purchase from direct sales, and further increase the number of offering stores. At the same time, it has begun offering new products containing 5-ALA for specific needs, launching in May 2017 “ALApplus Meno. STOP,” a supplement focused on the particular hormone balance of women, and in July 2017, launched “ALApplus Body Shape,” which focuses on the metabolism of sugar and fat through the combination of 5-ALA and carnitine. Furthermore, the company is implementing clinical trials with Hiroshima University, Juntendo University and other institutions, for the purpose of offering new foods with function claims each fiscal year to follow “ALApplus Tou (Sugar) Down,” and is also planning to offer supplements and ordinary food products made with ingredients other than 5-ALA. It has begun research on a food with function claims containing ginkgo biloba, and on germinated brown rice as its first products that do not contain 5-ALA, which it plans to commercialize by FY2018. In addition, SBI ALApromo has set its sights on achieving full-year profitability in FY2017, by also aggressively engaging in an OEM business for health foods and cosmetics.

### Further Acceleration of Global Business Expansion through SBI ALA Hong Kong, which is Planning a Public Listing

The SBI Group has begun considering an IPO for SBI ALA Hong Kong, an intermediate holding company that supervises the Group’s principal 5-ALA-related subsidiaries. The holding company manages SBI Pharmaceuticals and SBI ALApromo, as well as photonamic of Germany, a company that engages in the development of drugs that use 5-ALA in Europe, the U.S. and Australia, that became a wholly owned subsidiary in January 2016, and Suzhou Yian Biotech of China. SBI ALA Hong Kong has now added SBI Neopharma under its aegis, enhancing its business portfolio in preparation for the IPO. SBI Neopharma was jointly established to strengthen overseas sales of 5-ALA-related products with Neopharma LLC, a company based in the United Arab Emirates, to which SBI Pharmaceuticals has out-licensed two R&D pipeline projects. In addition, an intraoperative imaging agent for malignant glioma developed by photonamic was approved by the U.S. Food and Drug Administration (FDA) in June 2017, and preparations are being made to expand the sales area.

#### Drug Pipeline Including Ethical Pharmaceuticals Utilizing 5-ALA

Fields	Pipeline projects	Current status				Prospects for the next three years
		Phase I	Phase II	Phase III	Application	
Diagnostic agents (PDD)	① Carcinoma vesicae	Under application for production approval				Launch
	② Peritoneal dissemination of gastric cancer	Preparing for Phase III*				Completed Phase III / Out-licensing
Therapeutic drugs	③ Cisplatin nephropathy protection	Completed Phase I*		Preparing for a corporate trial (Phase II)		Completed Phase II
	④ Mitochondrial diseases*	Preparing for Phase III*				Completed Phase III / Out-licensing
	⑤ Cardiac ischemia-reperfusion injury	Preparing for Phase II*		Scheduled by Oxford University and Birmingham University Hospital in the U.K.		
Photodynamic therapy (PDT)	⑥ Brain tumors* (by photonamic, a wholly owned subsidiary)	Phase II is underway*				Conducting Phase II

\* Investigator-led trial

#### Out-licensing:

- Therapeutic drugs for diabetes and malaria infection (to Neopharma LLC, UAE pharmaceutical company, in October 2016)
- “ALAGLIO® Granule 1.5g,” diagnostic agent for cancer treatment (carcinoma vesicae) (to Chugai Pharmaceutical Co., Ltd. in March 2017)

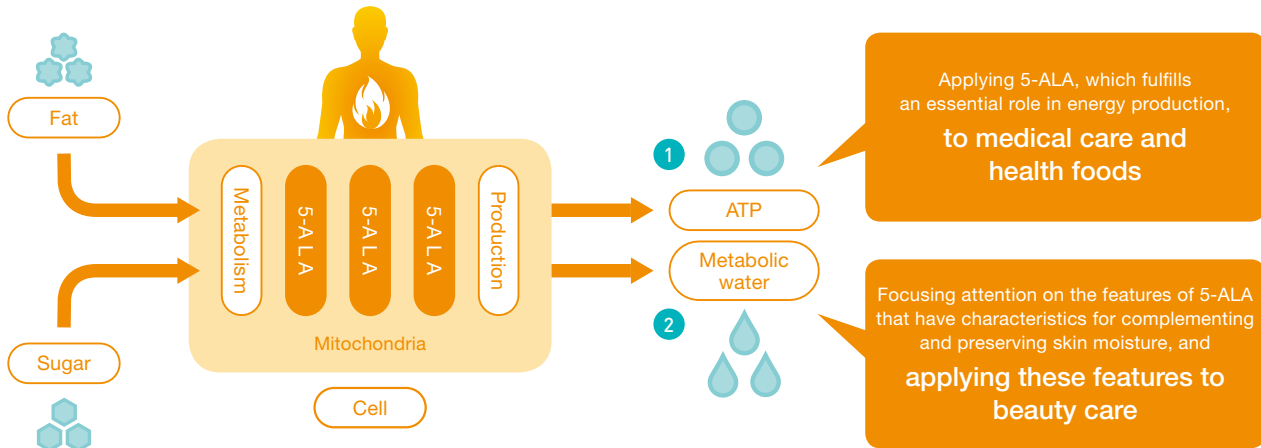
#### Already launched:

- Diagnostic agent for cancer treatment (brain tumor) “ALAGLIO® Oral 1.5g” (by SBI Pharmaceuticals)
- Same as above, “Gliolan” (by photonamic)
- Drug for treating actinic keratosis “Alacare” (by photonamic)

**What is 5-ALA  
(5-Aminolevulinic Acid)?**

5-ALA is a type of natural amino acid contained in living cells of plants and animals. 5-ALA works to aid photosynthesis in plants, as well as to preserve energy production and moisture retention in humans and animals that plays an essential role in preserving health. Recent research confirms its usefulness in a variety of fields including beauty care, health and medical care, which results from a well-balanced ingestion of 5-ALA and minerals such as iron (Fe).

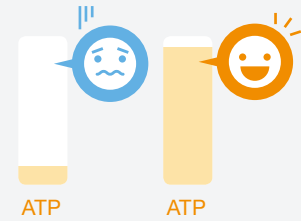
**Action of 5-ALA in Mitochondria, the “Energy Factory” of Cells**



- 1** Inside the mitochondria, sugar and fat are metabolized and energy is produced in the form of ATP, which is indispensable to maintaining good health.
- 2** As a result of ATP production, metabolic water is produced for the crucial role in retaining the body's moisture

**ATP (Adenosine Triphosphate),  
a Health Barometer**

ATP production efficiency is believed to atrophy as people age and their metabolism slows down. Fatigue and low activity will then occur as a result. In order to remain healthy, it is absolutely essential to maintain the mitochondrial function of producing ATP.



**A RESEARCHER DISCUSSES 5-ALA**



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5-ALA, which is essential for biological activities, is a substance with extremely high potential as a single substance that can be applied in various fields, including pharmaceuticals, health foods and cosmetics. "ALAGLIO® Oral 1.5g," an intraoperative diagnostic agent already on the market, is orally administered before surgery. When activated by light of a specific wavelength during surgical removal of malignant glioma, it illuminates only the malignant glioma and can improve resection accuracy. As a result, it has the potential to contribute to preventing cancer recurrence. In fact, an application has been filed for approval for its use as an intraoperative diagnostic agent for bladder cancer as well, and application in surgery for other cancers may be expected. At the same time, we are developing a therapeutic drug for mitochondrial diseases, which is an intractable disorder. No therapeutic agent for these diseases has yet been released on the market, and expectations are high for the drug currently under development at SBI Pharmaceuticals, which is the only promising candidate.



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5-ALA naturally occurs in plants and animals, and this safety makes it an excellent substance in terms of development speed. Although the probability of success in the field of drug development is generally considered to be low, I think that 5-ALA also offers high market introduction feasibility. Previously, awareness of 5-ALA was low, and we struggled to persuade researchers and physicians to participate in joint research. However, now that people have gradually become more aware of 5-ALA, we have received offers from universities and hospitals. In the future, I would like to utilize 5-ALA to contribute to the treatment of patients who suffer from diseases for which no treatment method yet exists, or for those that cures do exist, but are beyond complete recovery.