Solasia

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To: All Concerned Parties

Company Name: Solasia Pharma K.K.
Representative: Yoshihiro Arai, President & CEO
(Code number: 4597, TSE Growth)
Contact: Toshio Miyashita, CFO
Tel: 81-3-5843-8046
URL: https://solasia.co.jp/en/

# Business Overview of Pipeline Products
# (The Fiscal Year Ending December 31, 2022)

Solasia Pharma K.K. (hereinafter "the Company") today announced its Consolidated Financial Results for the Fiscal Year Ending December 31, 2022. The Company hereby supplements this information by providing notice of the status of its major pipeline products and business overview.

【Commercial Products】

| Product (Development code) | Indication | Area | Pre-clinical | Clinical study PI | Clinical study PII | Clinical study PIII | NDA | Approval / Launch | Progress | Partner |
|---|---|---|---|---|---|---|---|---|---|---|
| **Sancuso®** (SP-01) | Chemotherapy induced nausea and vomiting (CINV) | China | | | | | | | Launched in 2019<br>Preparing to apply for change of manufacturing facility | Lee's Pharm |
| **DARVIAS®** (SP-02) | Peripheral T-cell lymphoma (PTCL) | Japan | | | | | | | Launched in August 2022<br>Began searching for additional indications | Nippon Kayaku (Japan)<br>HB Human BioScience (South America) |
| | | South Korea, Taiwan, Hong Kong | | | | | | | Phase II (pivotal) study completed<br>Out-licensing activities ongoing | |
| | | South America | | | | | | | Preparations to file for approval underway in each country based on approval granted in Japan | |
| | | China, US, Europe | | | | | | | Development strategy being drafted based on US study data and approval in Japan; out-licensing activity ongoing | |
| | | Europe, India | | | | | | | NPP strategy being evaluated based on approval in Japan | WEP(Europe)<br>Sayre (India) |
| **episil® oral liquid** (SP-03) | Pain associated oral mucositis (medical device) | Japan | | | | | | | Launched in 2018 | Meiji Seika Pharma |
| | | China | | | | | | | Launched in 2019 | Lee's Pharm |
| | | South Korea | | | | | | | Launched in 2020 | Synex |

Note: For the development status of DARVIAS® in South America, China, US and Europe, are based on past US trials and Japanese approval status.

【Under Development】

| Pipeline Code | Indication | Area | Pre-clinical | Clinical study PI | Clinical study PII | Clinical study PIII | NDA | Approval / Launch | Progress | Partner |
|---|---|---|---|---|---|---|---|---|---|---|
| **SP-04** | Chemotherapy induced peripheral neuropathy (CIPN) | Japan, etc. | | | | | | | Pre-clinical study in taxane-induced peripheral neuropathy ongoing*<br>*PIII study of oxaliplatin-induced peripheral neuropathy completed; results not achieved | Maruho (Japan) |

Note: SP-05 has been removed from the above table based on Phase III trial results

【New Drug and Technology Candidates】

**GeneCare Project:** Aims to treat peritoneal metastasis (peritoneal dissemination) associated with various gastrointestinal cancers, ovarian cancer, etc. and accompanying ascites with the novel nucleic acid drug RECQL1-siRNA.

**EditForce Project:** Aims to discover gene therapies for cancer using RNA editing that uses the PPR (pentatricopeptide repeat) protein platform technology.

**HikariQ Project:** Aims to develop innovative immunoassays and discover the next-generation antibody-drug conjugates (ADC), using the novel Q-body technology that embeds fluorescent dyes and drugs inside antibodies.

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1. **Commercial Products:**

➢ **Sancuso® (SP-01): Granisetron transdermal delivery system (Indication: Chemotherapy-induced nausea and vomiting)**

- The Company holds rights in China, etc. In China, the Company pursues sales through its partner Lee's Pharmaceutical (HK) Limited ("Lee's").

China - Current status

- The Company launched in 2019.
- The Company dissolved its own sales structure covering Beijing, Shanghai, and Guangzhou, China (hereafter the "three cities") as of July 31, 2022, and on August 1 of the same year, transferred its sales functions to sales partner Lee's Pharmaceutical.

➢ **DARVIAS® Injection 135mg (development code: SP-02, generic name: darinaparsin): organic arsenic compound (indication: relapsed or refractory peripheral T-cell lymphoma)**

- The Company holds worldwide rights.

Japan - Current status

- The Company out-licensed for marketing and other rights in Japan to Nippon Kayaku, and the company will conduct sales activities in the future.
- In June 2022, the Company obtained marketing approval from the Ministry of Health, Labour and Welfare for DARVIAS® Injection 135mg for the treatment of relapsed or refractory peripheral T-cell lymphoma. Nippon Kayaku began selling the product in August 2022, and its MRs are promoting the product to medical institutions.

Other regions- Current status

- In 2018, the Company out-licensed marketing rights to DARVIAS® in South America to HB Human BioScience SAS. HB Human Bioscience began preparing to apply for regulatory approval in South America based on the approval status in Japan.

Named Patient Program (NPP) and other

- The Company is preparing to provide DARVIAS® in countries and regions where it does not yet have a sales partner or where the drug has yet to be approved or covered by medical insurance (i.e., no reimbursement price has been set) through the Named Patient Program (NPP). The NPP allows the marketing authorization holder to provide physicians access to drugs that are not available to them in their own country after completing the necessary procedures. The Company is preparing the NPP covering for in Europe, India, and South America.
- Currently, the Company is conducting non-clinical studies targeting hematologic cancers other than peripheral T-cell lymphoma with an eye to expanding the drug's indications.

- **episil® oral liquid (development code: SP-03): The protection and relief of oral pain associated with oral mucositis/stomatitis caused by chemotherapy and radiotherapy for cancer.**

  - In July 2022, the Company acquired worldwide rights, including manufacturing rights, to episil® oral liquid from Camurus AB. The Company will continue supplying the product in Japan, China, and Korea. The business transfer from Camurus AB, primarily manufacturing and regulatory procedures for the product, is expected to be completed by 2024.

Japan - Current status

- Meiji Seika Pharma Co., Ltd. launched in 2018, based on a license and collaboration agreement for episil®.

China - Current status

- Sales of episil® oral liquid began in 2019. The Company dissolved its own sales structure covering Beijing, Shanghai, and Guangzhou, China, as of July 31, 2022, and on August 1 of the same year transferred its sales functions to sales partner Lee's Pharm. Currently, Lee's Pharm is conducting sales activities for the product throughout China.
- The Company dissolved its own sales structure covering Beijing, Shanghai, and Guangzhou, China, as of July 31, 2022, and on August 1 of the same year transferred its sales functions to sales partner Lee's Pharm. Currently, Lee's Pharm is conducting sales activities for the product throughout China.

South Korea - Current status

- Synex Consulting Ltd. launched episil® in 2020, based on a license and collaboration agreement with the Company.

## 2. Pipelines Under Development:

- **SP-04 (PledOx®): Intracellular superoxide removing agent**
  **(Target Indication: Chemotherapy-induced peripheral neuropathy)**

  - The Company holds rights in Japan, China (including Hong Kong and Macau), South Korea and Taiwan.
  - The Company out-licensed marketing and other rights of PledOx® in Japan to Maruho Co., Ltd.

Current status

- The Company halted the development of SP-04 as a treatment for peripheral neuropathy caused by multidrug chemotherapy containing oxaliplatin, based on the results of the global Phase III study of the drug for the said indication. We are currently conducting animal studies, using rat models of taxane-induced peripheral neuropathy, in collaboration with licensor Egetis Therapeutics (formerly PledPharma) to investigate the possibility of developing the drug for the treatment of taxane-induced peripheral neuropathy. Results of animal studies conducted thus far suggest potential efficacy of the drug in suppressing the onset of peripheral neuropathy, but the effect was not clearly demonstrated enough. Going forward, the Company plans to conduct new animal studies with an eye to resuming clinical development of SP-04.

- **SP-05 (arfolitixorin): Increase in antitumor efficacy, folic acid compound**
  - Global Phase III clinical trials in patients with advanced colorectal cancer were conducted in multiple countries including Japan, to compare the outcomes of patients in the arfolitixorin group (administered 5-FU + oxaliplatin + bevacizumab combination therapy + SP-05 [arfolitixorin]), with those of the standard therapy group (received 5-FU + oxaliplatin + bevacizumab combination therapy + leucovorin). In November 2022, the Company confirmed through the final topline results of the study that no statistically significant difference was found in the primary and key secondary endpoints between the outcomes of the arfolitixorin (SP-05) group and the standard therapy group.

## 3. New Drug /Technology Candidates:

Development candidates and technologies below are early-stage projects in the research or pre-clinical development stages. They have potential to become our next pipeline products, and we are working on research and development together with each partner company.

- **Nucleic acid drug candidate for peritoneal metastases**
  - In 2020, the Company entered into an agreement with Japan-based GeneCare Research Institute Co., Ltd. ("GC") for exclusive negotiating rights (option rights) to in-license the latter's nucleic acid drug candidate RECQL1-siRNA and related technologies. We are currently engaged in joint development with GC, and will decide whether to practice the option rights to in-license the drug candidate, taking into consideration progress in non-clinical studies and new formulation development going forward.
  - RECQL1-siRNA is an siRNA (small interfering, double-stranded RNA) and a nucleic acid drug discovered by GC based on technologies in-licensed from US-based Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), a world leader in RNA inference (RNAi) technologies. The drug is believed to have a novel mechanism of action to induce cell death by selectively suppressing the expression of the DNA repair enzyme helicase RECQL1, which is found to be overexpressed in cancer cells. In multiple pharmacological studies, the drug was shown to suppress the growth of various types of cancer and prolong survival in animal models of peritoneal dissemination associated with advanced-stage ovarian or gastric cancer.
  - Currently, the Company is examining various conditions necessary for the expression of the effects of new, potentially more effective siRNA sequences discovered in collaboration with Ui-Tei Laboratory of the Graduate School of Science, the University of Tokyo, with a view to product development. The Company and GC began for pharmacological studies and the development of new formulations to advance the novel siRNA sequences to the clinical development stage.

    *Peritoneal dissemination is a type of metastasis observed in ovarian or gastric cancer patients, where cancer cells migrate to the peritoneal cavity and spread like seeds scattered and sown in the soil. As the condition progresses, it may be accompanied by malignant ascites, and the prognosis is said to be poor. Systemic chemotherapy has not been sufficiently effective in treating peritoneal dissemination, and novel local treatments, such as intraperitoneal administration of drugs, are also being tried.

➢ **Drug discovery utilizing RNA editing technology (gene therapy)**

- In 2019, the Company concluded a joint research and development agreement with EditForce, Inc., a biotech company originating from Kyushu University. For the Company, the initiative is a means of acquiring candidate products for long-term development. Specifically, it furthers the Company's plans to develop new gene therapy drugs in the field of oncology based on its core RNA editing technology.
- The Company has selected a potential target disease and gene mutations causing the disease, and is preparing and examining various matters necessary to conduct non-clinical studies to confirm the efficacy of the pentatricopeptide repeat (PPR) candidate discovered using the RNA editing technology of EditForce.

➢ **Drug discovery using novel antibody modification technology**

- In April 2022, the Company entered into a capital and business alliance agreement with HikariQ, Inc., a startup with roots in Tokyo Institute of Technology. The agreement mainly outlines the Company's investment in HikariQ.
- The fundamental technology of HikariQ's Q-body involves attaching a fluorescent dye to the Q-body, an antibody, and quenching the fluorescence of the dye so the Q-body does not emit fluorescence when it is not bound to the target antigen. However, when the antibody binds to the target antigen, the fluorescent dye is ejected and emits fluorescence. In this way, the Q-body acts as a biosensor whose fluorescence intensity changes according to the target antigen concentration. Immunoassays utilizing this technology are expected to be much simpler and less costly than existing immunoassays that rely on immune reactions. Further, a preliminary review regarding the discovery and development of the next-generation antibody-drug conjugates (ADC) using the Q-body technology is also underway.
- HikariQ is conducting research on immunoassays, and the Company, jointly with HikariQ, has commenced a preliminary review of the discovery and development of the next-generation ADCs using the Q-body technology.

**4. <u>Organizational structure and capital relationship:</u>**

➢ **Dissolution of the China Own Sales Organization**

- Solasia began operating its own sales structure for Sancuso® and episil® in the three cities in China in 2019. Shipment volumes of Sancuso® to hospitals and pharmacies in the three cities expanded from 10,000 units in FY2019 to 15,000 units in FY2020 and 30,000 units in FY2021 supported by the Company's own sales activities. However, prolonged impacts of the COVID-19 pandemic and the lockdown of Shanghai and other regions since Mach 2022 have depressed sales volumes, which together with other factors, resulted in the sales volumes lagging the necessary amount to reach the breakeven point. Further, maintaining the Company's own sales structure requires about 1 billion yen each year, primarily for marketing activities and personnel expenses. As a result, profitability of China operations continued to suffer, and costs for maintaining the sales structure had become a key factor behind the Group's losses.
- In light of these factors, the Company dissolved its own sales organization in China as of July 31, 2022, curtailing personnel expenses for sales staff and suspending expenditures on marketing activities. As a result, the number of employees on a consolidated basis (including Chinese nationals)

fell from 77 at the end of March 2022 to 27 at the end of December the same year, and the Company anticipates this to contribute to annual cost reductions of approximately 1 billion yen from FY2023 onward.

- **Change in principal shareholders.**
  - In June 2022, Solasia entered into a capital and business alliance agreement with Nippon Kayaku Co., Ltd., a pharmaceutical company with an extensive track record and sales experience in the oncology field. Based on the terms of the agreement, in July 2022, the Company issued 12,000,000 shares of its common stock to Nippon Kayaku and raised funds of 1.02 billion yen.
  - In September, November, and December 2022, Itochu Corp., the Company's previous largest shareholder, sold all of its shareholding in the Company to Japanese securities companies, Mr. Yoshihiro Arai, president and CEO of the Company, and Mr. Toshio Miyashita, board director and CFO of the Company, due to the termination of its business relationship with the Company following the dissolution of the Company's own sales infrastructure in China.
  - The largest shareholder of the Company as recorded in the Shareholder Registry as of December 31, 2022 was Nippon Kayaku Co., Ltd. (7.1% stake in the Company; partner for DARVIAS® in Japan), followed by Maruho Co., Ltd. (6.7% stake; partner for SP-04 in Japan). The Company concluded an agreement with Nippon Kayaku, requiring the latter to obtain prior written consent from the Company if it is to sell the Company's shares during the two-year period from July 14, 2022.

**Impact of the COVID-19 pandemic on the Company's business activities and efforts to prevent the spread of infection:**

Japanese business

- The Company adopted a telework system for all employees of the Tokyo office as of today.

Chinese business

- Medical treatments were restricted at hospitals the Company's sales teams had targeted due to the city-wide lockdowns imposed since March 2022, mainly in Shanghai. However, such restrictions have largely been relaxed, and medical opportunities for cancer patients, the target users of the Company's products, are recovering.

Product supply

- The Company's products are manufactured in Europe and the United States. At present, provision almost continues uninterrupted.

Clinical development

- The spreading pandemic is having a limited impact on clinical development activities. To ensure the safety of subjects and lessen the burden on the medical systems, visits to medical institutions by subjects and employees handling clinical studies have been curtailed to some extent, and we are utilizing online methods of communication instead.

Business alliances

- Overseas travel resumed, and the Company is proceeding with negotiations with licensing partner candidates.

The Company is a specialty pharma company, specializing in the development and commercialization of products in the oncology field. In the United States, which is home to numerous successful biopharma venture companies, the majority of those companies post losses on a single-year basis. (According to research by Solasia Pharma, of the companies that make up the NASDAQ Biotechnology Index, 150 companies have market capitalization of more than ¥100 billion. Of those, 109 are posting operating losses as of January 31, 2023.) We believe that this situation exists because the marketplaces more importance on making proactive upfront investments in promising drug development than on assessing such companies on the basis of their single-year gains and losses. At present, the Company is operating in accordance with this sort of business strategy. In addition to the operating results and other financial information in our earnings reports, we believe in the importance of disclosing to investors information about our key pipeline products to a certain level of detail. We have disclosed such our business information on this report.