# Oncolys BioPharma Inc.

(4588 Mothers) Date issued 6/Mar./2019

## Company Enthusiastic About Licensing

### Interest rising in the joint application of Telomelysin and immunity checkpoint inhibitors

Oncolys BioPharma's main development product is Telomelysin, an oncolytic virus that has been genetically modified. Telomelysin (OBP-301) infects both normal cells and cancer cells but the telomerase enzyme which is highly active in cancer cells throws the switch on virus proliferation, effecting lysis on cancer cells. Infected cancer cells after lysing release the proliferating oncolytic virus which infects other cancer cells, and also releases cancer antigens, thereby promoting cancer immunity activity. It is thought likely that Telomelysin, in combination with immunity checkpoint inhibitors such as the well-known Opdivo and Keytruda, could provide added anti-cancer efficacy. It seems that Oncolys BioPharma is receiving numerous approaches from inside the country and out offering to try out various combination therapies.

### Product strategy subject to selective concentration

In Japanese Phase 1 clinical trials of a combination therapy with radiation targeting esophageal cancer, the registration of patients has been delayed, meaning that completion of the trials has now been deferred until the first half of 2019. However, the company is already discussing with the authorities the development policy for Phase 2 clinical trials. If a similarly high response rate as achieved in Phase 1 is repeated in Phase 2, the company will be able to move forward with an application for approval. Furthermore, trials targeting various solid cancers combining Telomelysin with immunity checkpoint inhibitors have moved up a gear: in Japan, drug administrations in physician-led trials are already proceeding, and this will be repeated in US physician-led trials this year. On the other hand, trials targeting a melanoma therapy whose development has been delayed, and an HIV therapy whose development has been at a standstill for some time, could be cancelled. Investors are likely to appreciate this policy of "selective concentration".

### Company getting keener on further licensing-out

At its results meeting on February 8, the company made comments suggesting it was going to increase its efforts to license out Telomelysin. Certainly, the major pharmaceutical companies which have developed immunity checkpoint inhibitors should be interested in therapies combining them with Telomelysin. New licensing agreements with the major pharmaceutical companies would be a big boost to Oncolys BioPharma. In passing, it should be noted that the company has refrained from producing an earnings forecast for 2019, for the first time since it was listed. The reason for this is that such results will depend significantly on the receipt or otherwise of lump sum contract payments and on progress made in product development, which would determine the size of milestone payments.

**<Note : This report is the English version of the original report which is made in Japanese on 6th March 2019. For the precise description, please refer the original report.>**

### Follow-up Report

Fair Research Inc.
Tsuyoshi Suzuki

| Company Information | |
|---|---|
| Location | Minato-ku, Tokyo |
| President | Yasuo Urata |
| Established | March 2004 |
| Capital | JPY6,402 mil. |
| Listed | December 2013 |
| URL | www.oncolys.com |
| Industry | Pharmaceuticals |
| No. of employees | 35 |
| **Key Indicators (Mar 5 2019)** | |
| Share Price | 2,310 yen |
| Year High | 2,379 yen |
| Year Low | 491 yen |
| Shares Outstanding | 13,356 thous. |
| Trading Unit | 100 shares |
| Market Cap | 30,854 million yen |
| Dividend (est) | 0 yen |
| EPS (est) | NA |
| Forecast PER | NA |
| Actual BPS | 216.61 yen |
| Actual PBR | 10.66X |

Note: EPS、PER、BPS、PBR are based on shares outstanding, excluding treasury shares

| Results | Revenues JPY mil | YoY % | Op Income JPY mil | YoY % | RP JPY mil | YoY % | Net Income JPY mil | YoY % | EPS JPY | Share Price (JPY) High | Share Price (JPY) Low |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 2015/12 Actual | 121 | 321.2 | -952 | NA | -855 | NA | -857 | NA | -93.4 | 900 | 562 |
| 2016/12 Actual | 178 | 47.0 | -861 | NA | -864 | NA | -931 | NA | -101.2 | 1,850 | 403 |
| 2017/6 1H Actual | 19 | -55.5 | -510 | NA | -517 | NA | -519 | NA | -53.9 | 1,092 | 770 |
| 2017/12 Actual | 229 | 28.5 | -1,078 | NA | -1,087 | NA | -1,091 | NA | -106.2 | 1,092 | 616 |
| 2018/6 1H Actual | 90 | 354.4 | -643 | NA | -639 | NA | -641 | NA | -57.9 | 1,161 | 656 |
| 2018/12 Actual | 168 | -26.4 | -1,247 | NA | -1,230 | NA | -1,233 | NA | -104.5 | 1,161 | 491 |

## Company outline and philosophy

| | |
|---|---|
| Oncolys BioPharma is an R&D focused drug discovery company. It uses technology based on virology to create new drugs to treat cancer and super-infections, and at the same time uses viral genetic modification technology as a platform for the provision of new diagnostic services | Oncolys Biopharma Inc. is mainly involved in using genetically modified viruses to research and develop oncolytic agents to generate lysis in cancers (tumours), and for that reason is considered unique among drug discovery companies.<br><br>The company's guiding philosophy is "To contribute to medical treatment worldwide by bringing innovation to the treatment of cancer and super-infections, making full use of virology-based drug discovery techniques". The company's business consists of two segments, the pharmaceuticals segment and the diagnostics segment. In its pharmaceuticals business model the company creates oncolytic agents and other new drugs to treat cancer, super-infections and refractory diseases, and later generates income from licensing out drug candidates and from royalties on sales after going to market. In its diagnostics business it uses the new technology of genetically modified viruses, which is one of the main planks in its pharmaceuticals business, and which has a higher detection rate than conventional diagnostic methods. The company's business model in this segment involves developing agents and services for the detection of cancer metastasis and cancer relapse, and later collects revenues from licensees (lump sum contract payments, milestone payments and royalties) in addition to revenues from sales of diagnostic agents. |
| The company began life as the developer of the oncolytic drug, Telomelysin | The company got the idea of oncolytic therapy from research produced by two academics at Okayama University, Professor Kochi Tanaka and his assistant, Professor Toshiyoshi Fujiwara. That led to a plan to commercialise Telomelysin, an oncolytic agent based on the adenovirus, and an application, the cancer diagnostic agent, TelomeScan. The company was set up and, in July 2006, the company's Investigational New Drug (IND) filing was accepted by the FDA, with US Phase 1clinical tests (on solid cancers) beginning at the end of the same year. They were completed at the end of 2008 and showed promising results. |
| Currently, several development projects are in progress simultaneously, including those covering hepatocellular carcinoma in Asia, esophageal cancer in Japan, and melanoma in the United States | For the time being, there was a switch in emphasis to developing candidate drugs for the treatment of HIV, but subsequently Telomelysin again became central to the company's development strategy. From 2013 physician-led clinical research on esophageal cancer began at Okayama University. In addition, from 2014 the company began Phases 1/2 clinical trials (South Korea and Taiwan) on hepatocellular carcinoma with the Taiwanese company Medigen Biotechnology Corp., with whom the company has a strategic tie-up. In November 2016, the company concluded an exclusive license agreement (China, Macao and Hong Kong) with the Chinese company, Jiangsu Hengrui Medicine Co. In July 2017, Phase 1 clinical trials in Japan began for use in combination with radiation treatment on patients with esophageal cancer, and in the United States Phase 2 clinical trials on malignant melanoma began. The company is now starting combination tests with immunity checkpoint inhibitors. In December 2017 physician-led trials combining Telomelysin with Pembrolizumab started in Japan, while the same trials are planned for the US. The current status is this multiplicity of projects is simultaneously ongoing, while the company announced in July 2015 it is undertaking research and development on a second-generation version of Telomelysin.<br><br>Separately, Oncolys BioPharma has invested in a US bio-venture owning some of the world's top technologies for modifying the adenovirus. In so doing it is filling out its platform of viral therapies which use the genetically modified adenovirus, thereby broadening its business reach. In March 2017, the company invested in Precision Virologics Inc., a US venture specialising in research and development work on vaccines for emerging infectious diseases, such as the dicavirus-based adenovirus, and in February 2018 announced it was investing in Unleash Immuno Oncolytics Inc., a US bio-venture. Further, in May 2018 it concluded a licensing-in agreement on formulation improvement with the UK company, Stabilitech Biopharma Ltd. to make Telomelysin easier to administer. This had the effect of |

The company is developing TelomeScan, an application of Telomelysin, to provide early cancer and relapse/metastasis detection

extending the patent protection on the Telomelysin formulation to, perhaps, as far off as March 2031.

The development of the TelomeScan diagnostic agent is also proceeding smoothly. In November 2017 the company concluded a cooperative research and development agreement with Juntendo University on the development of diagnostic methods and systems design for blood circulation tumour cells (CTC's). Overseas, the company concluded an exclusive South Korea-only licence agreement in December 2014 with South Korea's WONIK CUBE Corp. with respect to an improved TelomeScan (F35), and in November 2015 signed a licensing and, with respect to North America, a business development tie-up agreement with Liquid Biotech USA, Inc. The company is considering clinical applications centered on lung cancer.

**Main Development Pipeline Products**

| | Pipeline/Project | Indications | Explore | Preclinical | Phase1 | Phase2 | Phase3 |
|---|---|---|---|---|---|---|---|
| **Virus** | Telomelysin（OBP-301） | Esophageal cancer<br>Melanoma<br>Hepatocellular cancer | | | | | |
| **Low molecular weight** | OBP-801 (HDAC inhibitor) | Solid cancers<br>Opthalmological | | | | | |
| **Anti-Virus** | OBP-601 | HIV | | | | | |
| | OBP-AI-004 | Hepatis B | | | | | |

| Area | Pipeline/Project | Indications | Basic Research | Clinical research |
|---|---|---|---|---|
| **Cancer diagnostic agents** | TelomeScan<br>OBP-401/1101 | All camcers | | |

Source: Company briefing materials

**Follow-up on Product development**

Below we provide a follow-up on product development at Oncolys BioPharma since our last report (dated August 27 2018).

**1. Telomelysin**

In Japan the company has achieved promising results in clinical trials on inoperative and chemotherapy maladaptive cases of esophageal cancer. Phase 1 will be completed in the first half of 2019, with Phase 2 starting in the second half

① Japan: esophageal cancer (inoperable, chemotherapy maladaptive, in combination with radiation)

With the conclusion of physician-led clinical research (13 cases) by Okayama University since 2013, Phase 1 of the company clinical trials (6 cases scheduled) was due for completion by around the end of 2018. However, delays in registering patients (as of February 2019, 4 cases) has pushed this date out to the first half of 2019. This delay is probably due to the limited number of patients local to the main therapy location of Okayama University, and the limitations imposed by the inoperable and chemotherapy maladaptive constraints.

Nevertheless, the company is in receipt of data on radiation-only therapy from the Japan Esophageal Society. Data so far shows a local complete response rate of around 40% for all stages, and for Stages II and III of around 30%. This compares with a local complete response rate for a combined Telomelysin+radiation therapy of around 70% for all stages and above 60% for Stages II and III. The company has already completed consultation with the PMDA on how to proceed and is steadily making preparations for Phase 2 trials. If all goes according to plan, it will start Phase 2 in the second half of 2019, targeting some 35 cases at more than 10 institutions. If the results exceed those of Phase 1 it can omit Phase 3 and estimates an application date in 2020-2021. Parallel results would suggest aiming for early approval under the pioneering review designation system or as an orphan drug.

The company is also planning a tie-up or licensing-out in 2019 or later. Rather than licensing out a drug candidate for individual illnesses it is more normal to license out the commercialisation rights of the platform without limitation as to illnesses. Candidate licensees (pharmaceutical companies) would then estimate the size of the Telomelysin market, and that would affect the lump-sum contract payment and milestones.

The company initiated clinical trials on solid tumours, such as advanced esophageal cancer and metastatic esophageal cancer, in combination with an immunity checkpoint inhibitor. Escalating repeat dose studies (Phase 1a) have been completed and multiple repeat dose studies (Phase 1b) are now scheduled

② Japan: solid tumours (in combination with immunity checkpoint inhibitors – physician led trials)

As noted above, while there has been progress in therapies combining Telomelysin and radiation treatment, Oncolys BioPharma is targeting a combination of Telomelysin with a checkpoint inhibitor (Pembrolizumab) as a second and third-line therapy to treat advanced/metastatic esophageal cancer.

Pembrolizumab has a 15-20% response rate in the case of esophageal cancer, but if the response rate rose to 25% in combination with Telomelysin then, so goes the company's thinking, there is a greater possibility of approval. Since December 2017, Phase 1 trials have been ongoing at the National Cancer Center Hospital East and Okayama University targeting progressive and metastatic solid, mainly esophageal, cancers (stages III and IV). The therapy being trialled is a combination of Pembrolizumab, an anti-PD-1 antibody immunity checkpoint inhibitor, and Telomelysin.

The aim is to move on to Phase 2 in 2020 and, if the coming announcement of intermediate Phase 1 data is supportive, switch early on to company clinical trials (Phases 2/3), allowing the possibility of filing an application for approval in or around 2022.

| | |
|---|---|
| Very soon, Phase 2 physician-led trials on combination therapies with immunity checkpoint inhibitor agents will begin in the US also | ③ United States: Stomach cancer /gastroesophageal junctional cancer<br>(Trials planned for combination therapy using immunity checkpoint inhibitor: physician-led)<br><br>Planning is now underway for Phase 2 physician-led trials on a combination therapy using Pembrolizumab targeting advanced and metastatic stomach cancer/gastroesophageal junctional cancer to be conducted at 3-4 institutions in the US centred on Cornell University. As early as August 2018 an application for approval of the trials was submitted to the FDA, which so approved in December. An agreement governing the physician-led trials was concluded with Cornell University in January.<br><br>In Japan, a high proportion of esophageal cancer is squamous cell carcinoma, while in the United States the proportion of adenocarcinoma is high, and for this reason it is necessary to conduct clinical trials in both Japan and the United States. Trials are due to begin in the near future with a maximum of 37 cases. If the physician-led trials achieve the same results as in Japan then, like Japan, there will be a switch to company trials (Phases 2/3) with a view to submitting an application for approval in or around 2022. An application for orphan drug status has already been submitted. |
| In trials targeting melanoma, patient registrations have been delayed, and this may lead the company to concentrate on targeting esophageal cancer | ④ United States: Melanoma (single agent => in combination with immune checkpoint inhibitor planned)<br><br>Phase 2 trials (50 patients) on inoperable and metastatic Stages III and IV malignant melanoma began in July 2017. Currently, immune checkpoint inhibitor combination trials targeting melanoma are underway using various drugs because of the ease with which reactions can be analyzed. However, securing melanoma patients has been problematic. Oncolys BioPharma's trials are also falling behind the original schedule with the fourth patient only recently receiving a single dose. At a company briefing session held on February 8 the company mentioned that, after considering whether an evaluation can or cannot be made on the basis of a small number of examples, they might, depending on circumstances, concentrate on trials of checkpoint inhibitor combinations in the area of esophageal cancer and the like. |
| In Asia, a collaborator is now developing an agent targeting hepatocellular carcinoma. Phase 2 trials in combination with an immune checkpoint inhibitor may be undertaken | ⑤ Asia: Hepatocellular cancer (single agent: company trials phase1)<br>Since 2014, in collaboration with its Taiwanese affiliate, Medigen Biotechnology Corp, the company has been going ahead with Phase 1 tests targeting stage III and IV hepatocellular carcinoma in Taiwan and South Korea. The development status now is that Phase 1a (single dose administration: 4 cohorts 12 cases) has been completed and a report has been prepared. Further, in the repeat dose test administration 5 out of 6 cases have been completed (at the time of our last report it was 4 cases completed). Looking ahead, the major Chinese pharmaceuticals company, Hengrui, is planning to promote development in combination with its own anti-PD-antibody "SHR-1210" in combination trials. Preparations are underway to apply for authorisation to undertake Chinese Phase 2 tests during 2018. Oncolys BioPharma is expected to receive milestone income commensurate with the stage of development achieved. |

Because of the paradigm shift in cancer therapies several proposals have surfaced suggesting new Telomelysin combination therapies

**Best Case Outlook for Telomelysin (OBP-301) Development**

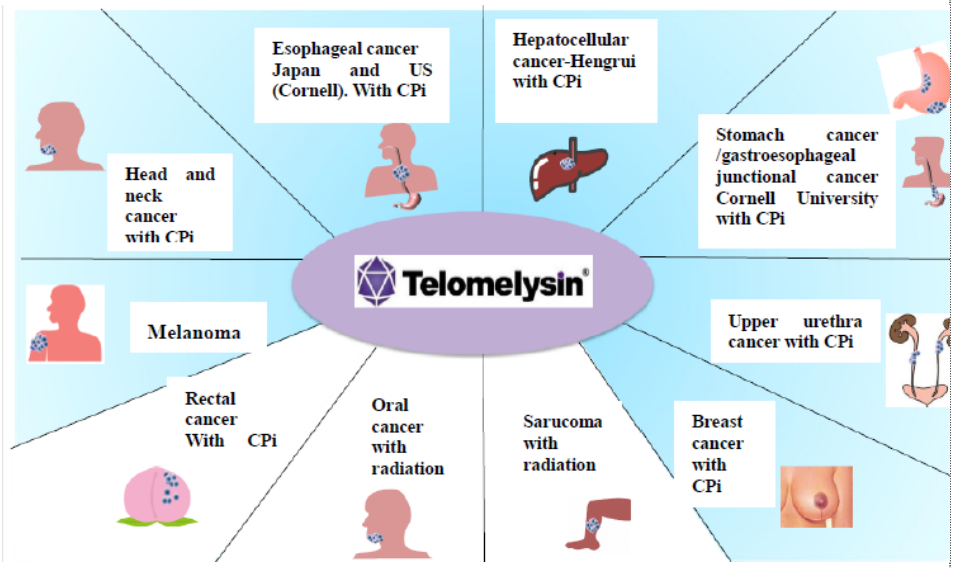
| Cancer type | Therapy | Region | Status | 2019 | 2020 | 2021 | 2022 | 2023 | 2024~ |
|---|---|---|---|---|---|---|---|---|---|
| Esophageal | With radiation Physician-led trials | Japan | Ph1Results for all 13 cases published | | | | | | |
| | With radiation Physician-led trials | | Ph1 completed 4 out of 6 cases | First half Ph1 finishes, then licensing-out considered From second half, Ph2 Pivotal starts==>Broader range of conditions | | | Application | Launch | |
| | Anti-PD-1 antigen physician-led trials | | Ph1a completed 9 out of 19 cases | Ph1b starts | Proceed to Ph2 Pivotal, during which may license out | | Application | Launch | |
| | Anti-PD-1 antigen Physician-led trials | USA | Plans to start Ph2. If results support, will move to Pivotal company trials. May license out during trials | | | | Application | Launch | |
| | With radiation | | Now at the idea stage | Orphan designation sought in Ph2 trials expanding indications to surgery eligible cases | | | | | |
| Skin cancer (melanoma) | Single agent Company trials | USA | Ph2, 4 out of 50 cases registered | Switch to anti-PD- antigen Ph2 trials; may focus on esophageal cancer | | | Undecided | | |
| Hepatocellular carcinoma | Single agent | Taiwan, Korea (Medigen) | Ph1 repeat dose trials | First half Ph1 finish ▼ | | | Future moves undecided | | |
| | With anti-PD-1 antigen | China (Hengrui) | GMP manuf. completed Preps for CFDA application | Hengrui to take over Ph2 | | | | | |
| Others | Currently pre-clinical (Japan: radiation combined) head and neck squamous cell carcinoma (HNSCC) Next generation Telomelysin (USA lung cancer, colorectal cancer, etc.) to enter PH1 by 2020 | | | | | | | | |

Source: Fair Research Inc.
Note: The above is not a forecast but an estimate based on the most optimistic product development assumptions. There is always the possibility of delays or termination

⑥ Expanded indications for immunity checkpoint inhibitor combination therapies

It used to be the case that indications for Telomelysin were concentrated in cancer of the digestive system, particularly esophageal cancer. Recently, however, there has been a paradigm shift (notably with the arrival of immunity checkpoint inhibitors) leading to a much expanded number of cancer indications. In addition to hepatocellular cancer (China's Hengrui) and stomach cancer /gastroesophageal junctional cancer in the US (Cornell University), both of which were mentioned earlier, Oncolys BioPharma has received applications to use Telomelysin to develop a number of combination therapies. Most involve physician-led trials at universities and the like, which tend to proceed faster than trials carried out by companies, in addition to which the high costs of the immunity checkpoint inhibitors are not borne directly by Oncolys BioPharma. The company is now planning to carefully examine the progress and results of these trials, select the most promising and subject those to company trials.

**Expansion in range of combination therapies**




Note: CPi =immunity checkpoint inhibitors
Source: Company briefing materials

The company has explained that it plans to intensify its licensing-out activities to major pharmaceutical

companies which have immunity checkpoint inhibiting agents

⑦ Increased licensing activity

At a corporate briefing held on February 8, 2019 the company commented on its intention to intensify its Telomelysin licensing activities. The company president noted that the company's policy was to seek licensing agreements with those pharmaceutical makers who had immunity checkpoint inhibitors. The achievement of such arrangements would certainly be a big boost for Oncolys BioPharma. However, key to this is the results of checkpoint inhibitor combination tests conducted by the National Cancer Center Hospital East (mentioned in ② above), and by Cornell University (③ above).

**Immunity Checkpoint Inhibitor Combinations Extend the Possibilities**

| Target | Generic name/Trade name | Sales Company |
|---|---|---|
| Anti-PD-1 antibody | Nivolumab (Opdivo)<br>Pembrolizumab (Keytruda) | Ono Pharm./BMS<br>MSD |
| Anti-PD-L1 antibody | Abelumab (Bavencio)<br>Atezolizumab (Tecentriq)<br>Durvalumab (Imfinzi) | Merck/Pfizer<br>Chugai Pharm.<br>Astrazeneca |
| Anti-CTLA-4 antibody | Ipilimumab (Yervoy)<br>Toremerimumab (under development) | BMS/Ono Pharm.<br>Astrazeneca |
| GITR antibody<br>4-1BB antibody<br>OX-40L antibody<br>ICOS antibody | Phase 1<br>Phase 1<br>Phase II<br>Preclinical trials | Amgen<br>Pfizer<br>Daichi Sankyo<br>Ono Pharm. |

Source: Oncolys BioPharma

**2. TelomeScan (OBP401)**

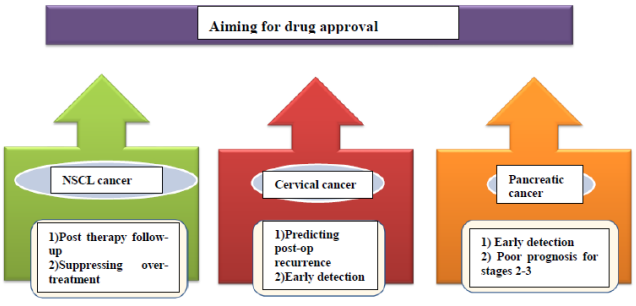
TelomeScan incorporates a light-emitting site in Telomelysin. It detects blood circulating cancer cells involved in cancer metastasis

TelomeScan is a genetically modified virus that introduces a jellyfish luciferase gene into Telomelysin. It is able to detect blood circulating tumour cells (CTC's) involved in cancer metastasis by promoting fluorescence emission specifically in telomerase positive cells, such as cancer cells and inflammatory cells. Early detection of cancer cells with a diameter of 5 mm or less, which was difficult to achieve with conventional tumor marker tests or PET examination, and early detection of metastasis/recurrence is possible. There are already about 20-30 companies developing CTC detection services, but the company boasts of the fact that only TelomeScan can capture living mesenchymal cancer cells.

With TelomeScan and Telomelysin Oncolys BioPharma believes it can cover the whole cycle from early detection to therapy, and from prognosis of recurrent metastasis to therapy.

The illustration below depicts three cancers for which the use of TelomeScan is expected to be promising.

**TelomeScan Development**




Source: Company briefing materials

Development as a detection agent for non-small cell lung cancer - possible approval application in 2021

Of the three conditions noted above, development work on non-small cell lung cancer is the most advanced. Oncolys BioPharma initiated discussions with the PMDA in 2019 and implemented their findings so as to submit an application for approval in 2021. In joint research with Juntendo University results showed that TelomeScan had a detection rate in excess of 90%, versus 20-30% for existing CEA markers. The difference in detection rates was particularly notable for Stages 0-I

In addition, examination of cervical cancer is under development, mainly to predict postoperative recurrence. Trials are now underway on a target of 30 cases at a hospital connected with Shimane University. Interim data now available points to a detection rate of 60%, well above the 30% detection rate of existing CEA markers. It is also superior to the existing SCC marker detection rate of 50%. In addition, collaborative research on the early detection of pancreatic cancer is also continuing with Osaka University.

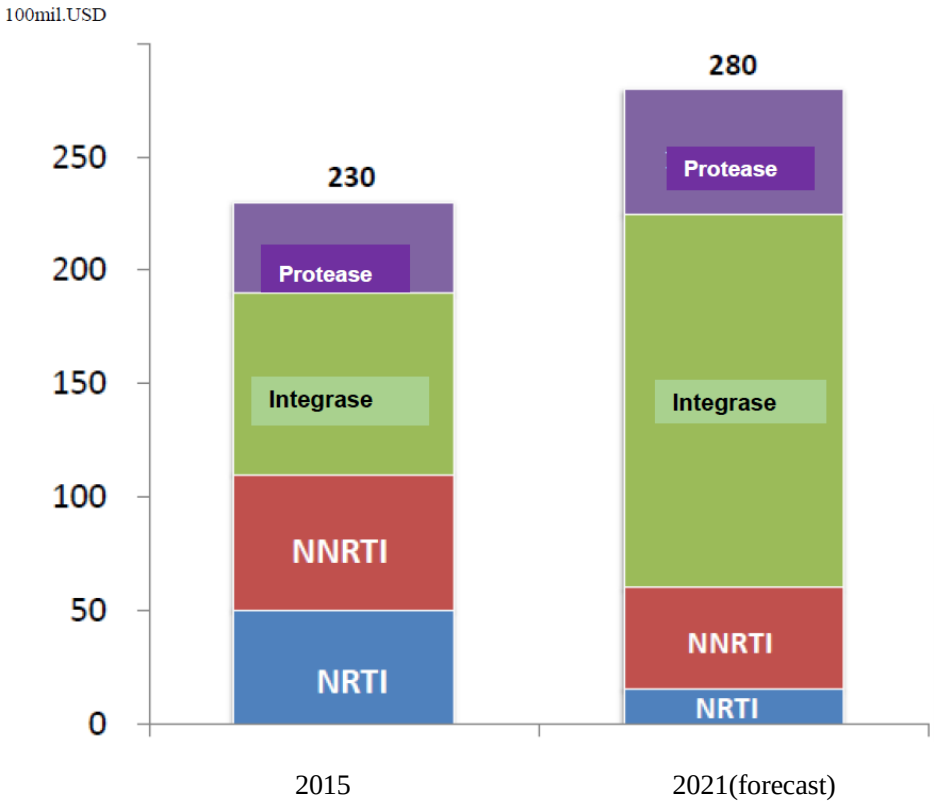
**3. Other examples of "selective concentration"**

Development work on OBP-601 is increasingly likely to be terminated

① OBP-601

OBP-601 is a therapy candidate indicated for HIV infection introduced from Yale University in the United States in June 2006 to enhance the company's pipeline. In December 2010, it was licensed out to Bristol-Myers Squibb Co. (hereinafter, "BMS") in the United States, but in April 2014 this licensing agreement was cancelled because of a change in BMS's product portfolio strategy, and a consequent decline in development priority. In the HIV drug market, there is increasing use of integrase-type and protease-type drugs, so that the NRTI-type drugs to which OBP-601 belongs have receded. At the company briefing session on February 8, 2019, it was suggested that the company might return the development rights to Yale unless a company to take over development could be found.

**Evolution of the HIV Drug Market**



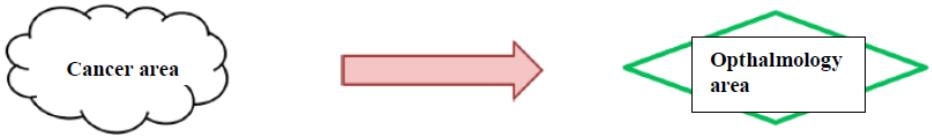

Source: Company briefing materials

OBP-801 produced side effects at Phase 1 and the development strategy is now being reconsidered. Switch to ophthalmological indications underway

② OBP-801 (HDAC inhibitor)

OBP-801, an HDAC inhibitor (histone deacetylase inhibitor) was licensed in from Astellas Pharma Inc. in October 2009. The company is pursuing research and development to determine its status as an epigenetic cancer therapeutic agent that promotes the expression of cancer supressing genes by inhibiting HDAC activity. Three homologous formulations, notably Vorinostat (Merck's Zolinza) are already on the market for T-cell lymphoma, and POC in this area has been confirmed. There has been no significant change in OBP-801's development status since the time of our last report. In US Phase 1 trials on solid cancers, two out of the six cases have developed side-effects, new patient starts have been halted and thought is being given to revising protocols. At present, the focus is shifting to possibilities in the ophthalmological field. The company has been collaborating with the Kyoto Prefectural University of Medicine since August 2016 with the aim of suppressing scar formation after glaucoma surgery, and developing applications for age-related macular degeneration. The company filed a joint patent application with the University in July 2018 and is now considering the possibility of licensing out at the pre-clinical stage.

**OBP-801 Development Strategy**




Source: Company briefing materials

In 2018 there was a fall in revenues due to the delay, until 2019, in concluding an agreement on US trials in combination with an immunity checkpoint inhibitor

For 2019, the company is going to boost licensing activities but cannot logically forecast the income from licensing and has therefore refrained from issuing an earnings forecast

Greater R&D activity means that R&D costs will more or less double in 2019. Cash on the balance sheet is sufficient for a year but the company is urgently looking for opportunities to license out to one or more of the pharmaceuticals majors

**Trend in Revenues and Balance Sheet**

Revenues in the pharmaceuticals segment in the period ending December 2018 came mainly from Medigen development collaboration payments, and in the diagnostics segment from TelomeScan sales in the United States. The reason why revenues were down year-on-year and fell so far short of the original forecast of JPY230 million was the postponed conclusion of an agreement, mentioned earlier, with Cornell University on pembrolizumab combination trials. As noted earlier, this was put off until early 2019. Another important reason was the lag in receipt of second-half development collaboration payments from Medigen, now due in 2019. A secondary reason was the decline in sales related to TelomeScan.

R&D and like costs in the period ending December 2018 stood at JPY720 million, exceeding the JPY700 million expected at the beginning of the period, mainly because of expenditures not anticipated at the beginning of the year and delays to melanoma-related clinical trials. In addition, SG&A costs excluding R&D contracted from a forecast JPY700 million to JPY640 million. As a result, operating profits for the period ending December 2018 recorded a loss of JPY1,247 million.

For the first time since listing the company is foregoing the issue of a results forecast. This is because it is putting a lot of effort into licensing activities and, if successful, the consequent receipt of lump-sum contractual payments and milestone income in line with development progress on the part of licensees will have a major impact on results. Worthy of note is the fact that cash on the balance sheet at the end of December 2018 stood at JPY2.46 billion, only JPY400 million less than at the end of the previous year. This was because, despite the JPY1.23 billion net profit loss in 2018, options on new shares issued in July 2018 had all been exercised.

R&D costs in 2019 are likely to come in at JPY1.39 billion, approximately double the level of the previous year, due to the start of Japanese Phase 2 company trials on Telomelysin. With other SG&A costs standing at approximately JPY700 million, this is not a level which threatens the imminent exhaustion of funds.

Nevertheless, in order to establish Telomelysin as a standard initial treatment the company will need to expand the development of radiation therapy combinations, and at the same time combination therapies using immunity checkpoint inhibitors. For Oncolys BioPharma on its own this would be problematic in terms of the funds and resources required. For that reason, its plan is to license out to a major pharmaceuticals company as a matter of urgency.

**Trend in the Income Statement**

(JPY mil)

| | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
|---|---|---|---|---|---|---|
| **Sales** | 1 | 29 | 121 | 178 | 229 | 168 |
| Drugs segment | 0 | 0 | 0 | 119 | 197 | 152 |
| Diagnostics | 1 | 29 | 121 | 60 | 33 | 16 |
| Gross profit | 1 | 28 | 121 | 178 | 158 | 47 |
| SG&A expenses | 667 | 856 | 1,073 | 1,040 | 1,236 | 1,295 |
| of which, R&D | 232 | 391 | 553 | 361 | 571 | 606 |
| (R&D costs etc.) | | | | | 642 | 725 |
| **Operating income** | -665 | -828 | -952 | -861 | -1,078 | -1,247 |
| Non-op income | 84 | 107 | 103 | 6 | 4 | 21 |
| Subsidies | 16 | 51 | 89 | 1 | na | na |
| R&D costs borne | 21 | 47 | 10 | 0 | na | na |
| Non-op costs | 44 | 5 | 6 | 9 | 13 | 4 |
| **Recurring profit** | -625 | -726 | -855 | -864 | -1,087 | -1,230 |
| Extraord. Profit | 0 | 0 | 0 | 0 | 0 | 0 |
| Extraord. losses | 8 | 11 | 0 | 64 | 0 | 0 |
| Pre-tax net profit | -633 | -737 | -855 | -928 | -1,087 | -1,230 |
| **Net profit** | -636 | -739 | -857 | -931 | -1,091 | -1,234 |

Note: R&D costs, etc. = R&D costs plus the service costs portion of manufacturing costs

Source: Compiled by Fair Research Inc. from company's financial statements

This year will see the start of active moves on the part of the company to license out to one or more major pharmaceutical companies who have the necessary immunity checkpoint inhibitors

**Trend in Balance Sheet**

(JPYmil)

| | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
|---|---|---|---|---|---|---|
| Liquid assets | 5,631 | 4,885 | 3,674 | 2,747 | 3,072 | 2,618 |
| Cash | 5,580 | 4,727 | 3,605 | 2,564 | 2,868 | 2,463 |
| Fixed assets | 65 | 124 | 332 | 394 | 455 | 811 |
| Tangible fixed assets | 36 | 59 | 46 | 0 | 3 | 2 |
| Intangible fixed assets | 1 | 1 | 4 | 0 | 0 | 0 |
| Investments, others | 28 | 124 | 332 | 394 | 452 | 809 |
| Total assets | 5,697 | 5,009 | 4,006 | 3,140 | 3,526 | 3,430 |
| Liquid liabilities | 233 | 263 | 177 | 205 | 239 | 212 |
| Short term loans | 155 | 173 | 93 | 63 | 93 | 83 |
| Fixed liabilities | 370 | 374 | 328 | 318 | 355 | 316 |
| Long term loans | 342 | 337 | 303 | 300 | 344 | 311 |
| Total liabilities | 603 | 637 | 504 | 523 | 594 | 528 |
| Net assets | 5,094 | 4,371 | 3,501 | 2,617 | 2,932 | 2,901 |
| Shareholders equity | 5,090 | 4,356 | 3,499 | 2,605 | 2,937 | 2,903 |
| Valuation difference | 4 | 11 | -5 | -8 | -16 | -13 |
| New share subscription rigl | 0 | 4 | 8 | 21 | 10 | 10 |
| (Capital raising) | | | | | | |
| From share issues | 5,233 | 6 | 0 | 37 | 1,409 | 1,188 |
| From suscription rights | 20 | 4 | 3 | 13 | 3 | 12 |
| Share issue disbursements | -25 | -15 | 0 | 0 | 0 | 0 |

Source: Compiled by Fair Research Inc. from company's financial statements

## Conclusions

With a clearer understanding of the cancer micro-environment there has, since 2010, been a paradigm shift in the area of cancer therapy, as represented by the appearance of Opdivo, Keytruda and other immunity checkpoint inhibitors. Oncolys BioPharma's tumor lysing drug Telomelysin® and its successor candidate enhance the effectiveness of immunity checkpoint inhibitors and are set to become one of the leading therapies in the often under-researched field of esophageal cancer, and other cancer types. 2019 will be a year in which the company realises latent possibilities, moving vigorously to license out Telomelysin to major pharmaceutical companies with immunity checkpoint inhibitors.

At the same time, Oncolys BioPharma could decide to terminate tests on melanoma, which have fallen behind schedule, and could terminate its development of an HIV treatment, which has been on the backburner for some time. By so doing it would demonstrate its determination to maintain a product policy of "selective concentration".

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