



Japan Biotech Forum: London 2010

9 September 2010, London, UK

Reported by Asma Al-Shamahi, Thomson Reuters, London, UK

Email: asma.al-shamahi@thomsonreuters.com

Introduction

The second annual Japan Biotech Forum was held at the Royal Society in London with pharmaceutical industry delegates from over 70 companies in attendance to discuss licensing and investment opportunities emerging from Japan. transB, a consulting firm focused on Japanese biotech and pharma, organized the forum, which began with sessions providing insights into the investment strategies adopted by Japanese companies, and presentations from five biotech companies from the region. The afternoon included a seminar giving an overview of the current biotech industry and investment outlook, as well as one-to-one partnering sessions. This report will focus on four of company presentations, with particular emphasis on programs available for outlicensing.

CanBas seeks partners for phase III development of CBP-501

Takumi Kawabe, President and CEO of CanBas, began the morning's company presentations with an insightful overview of the company and its pipeline. CanBas, founded in 2000, is a clinical stage biopharmaceutical company focused on discovering and developing oncology therapeutics.

The company is seeking codevelopment partners for phase III development and to expand the indications of its most advanced program CBP-501, a cisplatin potentiator currently in US phase II trials for NSCLC and malignant pleural mesothelioma, which are expected to complete in 2011. The drug was reported to leverage cisplatin's success by enhancing its efficacy without exacerbating toxicity. Results from a phase I study found no potentiation of adverse events from the therapy. A release of histamine was the only other adverse event observed and could be easily managed with antihistamine pretreatment. Although limited antitumor activity was seen with the drug as a single agent, combination dosing with cisplatin in a number of tumor types was promising. Furthermore, CBP-501 has potential for reversing cisplatin resistance. In tumor cell lines, CBP-501 selectively increased the formation of adducts. Responders to cisplatin therapy also had an increased levels of adduct formation in comparison to non-responders. CanBas holds over 65 issued and pending patents for CBP-501, including those for composition of matter, with exclusivity through to 2023.

The company's second pipeline program is the preclinical, small-molecule therapeutic CBS-9106. Data from xenograft tumor models demonstrated a wide therapeutic index. Dr Kawabe expected phase I trials for the program to begin in 2011.

LivTech details LIV-2008 program

A presentation from LivTech, delivered by Koji Nakamura, the company's President and CEO, focused primarily on LIV-2008. LivTech, founded in 2004, is a privately owned biotech company that develops anticancer therapeutic antibodies based on stem cell research. Its lead pipeline product, LIV-1205, is a humanized anti-Delta-like homolog-1 (Dlk-1) mAb in preclinical development and licensed to Kyowa Hakko Kirin in February 2008.

LIV-2008 is a humanized anti-hepatic oval cell-derived factor-1 (OCDF-1) mAb in preclinical development for solid tumors, including pancreatic and colorectal cancer. Dr Nakamura presented

data confirming the expression of OCDF-1 in various cancer types by immunostaining cancer tissues and flow cytometric analysis of cancer cell lines. In vitro, the antitumor activity of LIV-2008 was demonstrated in a soft agar colony formation assay using human colon cell line HCT-116. In vivo data from mice also indicated that the antibody suppressed cancer cell growth. Patents covering the antibody's use for cancer have been filed and humanization of a lead is scheduled for completion. Worldwide or regional development and marketing rights to LIV-2008 are available in exchange for upfront, milestone, R&D and royalty payments. A long-term partner could also acquire first evaluation right on future pipelines and make an equity investment in LivTech.

Licensing opportunities from REGiMMUNE

Haru Morita, President and CEO of REGiMMUNE, gave an overview of the company which was established to discover and develop immunoregulatory drugs developed using the company's reverse vaccination (reVax) technology. The reVax technology, which was licensed from the Japanese research institute RIKEN from which REGiMMUNE spun-out in 2006, enables target-specific immune suppression by the induction of tolerance. Mr Morita explained that, unlike current immunosuppressants which non-specifically suppress T-cells, reVax increases specific regulatory T-cells (Treg), restoring the balance of effector and regulatory cells disrupted in immune disorders. REGiMMUNE has received over \$12 million in funding from the Japanese government to support its drug development programs.

The company's current pipeline includes RGI-2001 (ToleroVax) for the prevention of GvHD in allogeneic stem cell transplantation, for which an IND was filed in early 2010. In mouse models of GvHD, RGI-2001 significantly prolonged survival. Mr Morita reported that GMP production has been completed, a stability study was ongoing, and that GLP toxicology and drug metabolism and pharmacokinetics in mouse and monkey had also been completed with no outstanding issues. The company is seeking a licensing partner outside Japan for the therapeutic.

RGI-1001, also in preclinical development, is a recombinant cedar antigen peptide encapsulated in GalCer liposome being developed for cedar pollinosis. In a mouse prophylactic allergy model, the drug (2 microg, ip) suppressed IgE responses, with effects being sustained long term (132 days). In a therapeutic allergy model, suppression was also demonstrated. Mr Morita reported that an IND filing is expected for the drug in 2012, and that an opportunity existed for R&D collaboration on the allergy products.

Licensing partners sought for HMN-214

Chizuko Koseki of transB delivered the presentation from D Western Therapeutics Institute (DWTI) in the absence of its President and CEO, Yuichi Hidaka. The biotech company, founded in 1999, is focused on development of protein kinase inhibitors and is named after the drug-western method for identifying target proteins of a new drug.

HMN-214 (IVX-214; Nippon Shinyaku), with the transcription factor NF-YB as its molecular target, is being developed for a share of the \$18 billion anticancer therapy market. The drug was shown in preclinical studies to possess equal or more potent antitumor activity than currently marketed anticancer drugs, and has shown efficacy in cisplatin-resistant cancers. Global exclusive development and commercialization rights to the drug were licensed out to Nippon Shinyaku in March 2001.

In cultured human TERT-RIPE 1 cells, treatment with HMN-214 resulted in multipolar spindles and thus irregular morphology during cell division. Two US phase I trials have been successfully completed. In a 5-day schedule, dose-escalation study to evaluate safety and efficacy in patients with solid tumors refractory to known therapies, the MTD was defined as 15 mg/m²/day. HMN-214 is rapidly hydrolyzed to HMN-176, with dose-proportional increases in AUC and C_{max}. In a 21-day schedule study in 33 patients, MTD was defined as 8 mg/m²/day. This has been selected

as the recommended dose for phase II studies. A dose-proportional increase was only observed at AUC and not Cmax. Seven patients had stable disease as their best tumor response. DWTI and Nippon Shinyaku are seeking licensing partners for development of HMN-214.

ADLib technology from Chiome

A presentation mainly focused on Chiome Bioscience's ADLib system was given by Masa Fujiwara, the company's President and CEO. Chiome was established in 2005 following official authorization as a RIKEN venture enterprise, and it is from RIKEN that its core technology is licensed. The ADLib system is a platform technology for rapidly generating antibodies by accelerating gene conversion in immunoglobulin loci. The technology also provides adaptability to diverse antigens from peptides to lipids and glycol chains to evolutionary conserved proteins. The ADLib-axCELL system has also been developed by the company to overcome cell surface antigens. Mr Fujiwara explained that the ADLib system did not require purification of target antigens and that unique antibodies could be generated in around 2 weeks.

The technology was used to generate an antibody to semaphorin 3A, an inhibitor of axon elongation in the nervous system, as well as a known difficult target to generate antibodies against by other methods. The company generated antibodies that demonstrated inhibitory activity, and then confirmed specificity within 9 days of antibody selection. The anti-Sema 3A antibody is currently in preclinical development for spinal cord injury.

As of August 2009, Chiome had received five Japanese government grants for its research. The company also has a multi-year research agreement with Chugai Pharmaceutical for development of therapeutic antibodies against multiple targets using the ADLib system; Chugai agreed to pay milestones and then to expand the scope of the agreement to further targets. China Novartis Institutes for BioMedical Research (CNIBR) is also another partner for use of the technology. The organizations entered a Frame Service Agreement in 2009, under which Chiome agreed to use the ADLib system to perform mAb production services for CNIBR in exchange for CNIBR paying Chiome compensations based on work load and strategy for each target. Chiome is seeking partners worldwide.

The website for this meeting can be found at
http://www.transb.co.uk/japan_biotech_forum_2010.htm

Thomson Reuters is the leading source of intelligent information for professionals around the world. Our customers are knowledge workers in key sectors of the global economy. We supply intelligent information needed to succeed in fields vital to developed and emerging economies such as law, financial services, tax and accounting, healthcare, science and media.

Our knowledge and information is essential for drug companies to discover new drugs and get them to market faster, for researchers to find relevant papers and know what's newly published in their subject, and for businesses to optimize their intellectual property and find competitive intelligence.

Reproduction and distribution of this document is prohibited unless agreed by Thomson Reuters
<http://thomsonreuters.com/copyright/>