Japan’s Bioventures Today —

CanBas Co., Ltd.

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Background of CanBas

CanBas Co., Ltd. (“CanBas”) is a venture company that develops innovative cancer drugs and diagnostic products with a focus on G2 checkpoint of a cell cycle. In order to commercialize their research accomplishment, Dr. Takumi Kawabe, former associate professor from the Nagoya City Medical School and current president & chief executive officer of CanBas; and Dr. Masashi Suganuma, a former lecturer from the Fujita Health Medical School and current executive vice president & chief operating officer of CanBas founded CanBas in January 2000. The company aims to develop cancer therapeutics with minimal adverse effects as well as diagnostic products in order to identify optimum cancer treatments for each patient.

G1 and G2 Checkpoints

A cell division cycle consists of several phases. These are namely G1 phase, preparation for DNA replication; S phase, replication of DNA; G2 phase, preparation for cell division; and M phase, division of chromosomes. Within the cell cycle, there is a mechanism to check and repair damages in deoxyribonucleic acid (DNA) at the end of G1 phase and G2 phase. In a normal cell, G1 checkpoint at the end of the G1 phase is generally activated and pause the cell cycle to repair damaged DNA. When DNA is damaged beyond repair, a safety mechanism is induced to trigger apoptosis, or cell death.

In cancer cells, on the other hand, it is known that the G1 checkpoint is often impaired, causing the DNA to replicate itself with damages unrepaired, inducing further mutations. Early studies revealed that as much as 80% of cancer cells are said to be proliferated with damaged DNA. However, even cancer cells cannot survive if DNA is severely damaged. So those cells with impaired G1 checkpoint generally rely on the G2 checkpoint, which is not extensively used by normal cells to check and repair the damaged DNA.
Fig. 2 Checkpoints used in normal cells and cancer cells.

Technology of CanBas
As cancer cells rely on G2 checkpoint to check the damaged DNA, but normal cells utilizes G1 checkpoint as a primary checking function, abrogating G2 checkpoint is found to be effective in facilitating damages to DNA in cancer cells with minimal disruption in normal cells. Having identified the G2 checkpoint as the promising target for development of novel cancer drugs and screening systems, CanBas has developed a technology to screen potential compounds that inhibits signaling system of G2 checkpoint.

This screening system enables us to observe the distribution of cell cycles when compounds are added. This system had led CanBas to discover a G2 checkpoint inhibitory peptide which was further modified and optimized to become a compound called CBP501. CBP501 selectively abrogates the G2 checkpoint and facilitates the DNA damages, thus triggering cancer cell apoptosis. With further studies, the company also discovered additional two small molecule compounds that inhibit different G2 checkpoint signaling system from the one that CBP501 inhibits.

The research on G2 checkpoint inhibitor as a potential cancer drug has been conducted by various scientists in the world since mid 1990s. However, compounds that selectively inhibit G2 checkpoint could not be readily found. In 1999, Dr Kawabe and Dr Suganuma discovered that a peptide they created during their research on G2 checkpoint signaling system could selectively kills cancer cells. When phase I clinical trials commenced in May 2005, CBP501 became the first G2 checkpoint inhibitor in the world to be tested in clinical trials as a potential cancer drug.

Business of CanBas
One of the CanBas’ business strategies is to develop its potential products in the U.S. The company has already obtained patents for its proprietary screening system in the U.S. and E.U., and for development of CBP501 in the U.S. In addition to its expertise in cancer research, the technologies
\[ \text{Industry Watch} \]

and the pipelines; the company’s strengths include its scientific advisory board consisting preeminent scientists in the cancer research field in the U.S. CanBas’ scientific advisory board consists of Professor Daniel D. Von Hoff, M.D., F.A.C.P., Arizona Cancer Center; Professor Donald W. Kufe, M.D., Harvard Medical School; and Professor William G. Dunphy, Ph.D., California Institute of Technology.

The company’s wide network with professionals and companies with extensive expertise in cancer research in the U.S. and in Japan is an additional advantage for successful development of its pipelines.

**Product Pipelines**

CanBas has been conducting phase I clinical trials for CBP501 in the U.S. So far, the result is highly promising as little adverse effect is confirmed even exceeded dosage is administered. The company also started the phase I clinical trials for CBP501 for a combined usage with another anticancer agent, cisplatin, in late 2006. Cisplatin is one of the most widely used anticancer agents that act by facilitating DNA damage and hindering cancer cell division, which then triggers apoptosis.

One of the causes for developing resistance to anti-cancer agents is believed to be the DNA repair function at G2 checkpoint in cancer cells. CBP501 is expected to increase the efficacy of cisplatin for even drug tolerant patients, by inhibiting the DNA repair process and increasing sensitivity to the drug. In addition, as the increased sensitivity to the drug can contribute in reducing the drug dosage, CBP501 is expected to reduce the possible adverse effects.

The additional two small molecule compounds that inhibit different G2 checkpoint signaling system from the one that CBP501 inhibits are currently being optimized for future clinical trials.

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Fig. 3 Product pipelines.
Future of CanBas

On March 30, 2007, CanBas signed a collaborative research and marketing agreement with a Japan’s leading pharmaceutical company, Takeda Pharmaceutical Company Limited (“Takeda”). Under the agreement, Takeda acquired the worldwide exclusive rights for the development, manufacturing and marketing of CBP501 and its backup compounds discovered by CanBas. CanBas and Takeda will jointly develop and market the above compounds in the U.S. With this collaboration and funds raised from venture capitals and other companies, the company aims to accelerate the commercialization of CBP501. Also on the anvil is the development of the above pipelines in Japan. CanBas intends to go public within a few years.