

# Teaser Memorandum

**JW CHOONGWAE PHARMA CORPORATION**

**Global development of CWP232291,  
a novel cancer drug targeting Wnt/beta-catenin signaling**

## Executive Summary

- For the last 60 years ever since its foundation in 1945, on the basis of its founding spirit of "respect for life" and "pioneering spirit".
- Based on leading competitiveness in the prescription drug market, Choongwae has built up strong sales network across the country and superior pipelines in I.V- solutions, antibiotic, cardiovascular, gastrointestinal, nephrology/antianaemic, anticancer and neuropsychiatry. And now, it is pioneering the rapidly growing new field such as diabetes and so on.
- Moreover, Choongwae is making efforts to provide medical equipments, various self modification products and OTC products satisfying the requirements for prevention and diagnosis of diseases.
- Also, Choongwae has diligently opened up itself to the overseas market with competitive APIs (Active Pharmaceutical Ingredients) and finished products developed on a basis of our creative technologies. Especially, the anti-fungal agents such as Ketoconazole and Itraconazole are lively being exported to developed countries such as EU, Japan with their acquisition of EU CoS.
- Choongwae successfully developed the next generation antibiotics Imipenem in 2004. it is expected to substitute 20 billion won worth of imported antibiotics, and, along with antifungals and cephalosporins, it will be one of the core products in opening the era of 100 million dollar exportation.
- Choongwae's global business is expanding not only to the export of bulk pharmaceuticals and finished products, but also to licensing-out of technical know- hows and patents.

### Industry Sector :

medicine and medical supplies

### Therapeutic Target :

cancer, acute myeloid leukemia

### State of Development :

Stage for entry of clinical trial

## Key Technology Highlights

- The development importance of CWP232291
  - First-in-Class Wnt targeted anticancer
  - The the world's first drug CWP232291 (CWP231A), low molecular weight composition anti-cancer drug, blocking Wnt / beta catenin signal transduction path.
- The therapeutics of the acute myelocytic leukemia
  - Presently, all non-clinical toxicities, pharmacological potency, drugstuff movement (ADME), preparation, and biomarker test about the CWP232291 were successfully completed. And for clinical trial drug production is completed in the overseas GMP CMO.
  - Pre-IND meeting with US FDA, that was successfully terminated in the early November, 2010. And FDA IND approval in U.S. against the blood cancer patient in October 2011.



## IP Owner Summary

- CEO: Kyung Ha, Lee
- Foundation: August 8, 1945
- Number of Employees: 1,343
- Paid-in capital: 23.7 Billion Won
- Office address:  
698, Shindaebang-dong, Dongjak-gu,  
Seoul, Rep of KOREA

## Market Feasibility

- Domestic and global market size :  
Targeted cancer therapies market  
(ref. Datamonitor)
  - Domestic market: \$ 450M in 2015(1.5% of global market size)
  - Global market: \$ 30,000M in 2015
- Domestic and global market opportunity (competitors and competing product) :  
Competitors who are manufacturing acute myeloid leukemia are as follows.
  - Global competitors : J&J(Mylotarg), pfizer(farnesyl), Novartis(Gleevec)

## Trend & Partnership

- Future outlook and trends related to technology :  
The acute myelocytic leukemia therapeutics
- Technology Transfer and commercialization conditions :  
The global pharmaceutical company and strategic alliance. It contracts in order to secure the right to the goods production in the licensing out.  
The termination of the successful clinical test is needed.
- Type of business relationship sought (including licensing availability) :  
Technology transactions, licensing, technical cooperation and joint research

## Technology Overview

### ■ Technology Platform

#### □ The generation of the acute myelocytic leukemia and treatment

- The generation situation of the acute myelocytic leukemia
  - As to the leukemia onset frequency of the major countries in the world, the ratio which the onset frequency of the acute myelocytic leukemia occupies is 30% or greater. About two times extent generation rate is higher than the chronic myelogenous leukemia, that is the indication of the gleevec.
  - In the case of the Domestic of a country, 1,541 leukemia patient died in 2008. And, In 2000, showing the increasing rate of 12% in comparison to 1,371 people for as much as 8 years.
- The therapeutics of the acute myelocytic leukemia
  - The primary aim of the leukemia treatment reaches utterly the complete remission.
  - Presently, there is the Ara-C(Cytarabine), daunorubicin or idarubicin as the cell toxic anti-cancer medicine, much used leukemia treatment drug. However, as to these, even when accompanying the serious side effect, the five-year survival rate of the patients is about 30-40%. Therefore, the necessity of the development of new medicine in which the side effect is small and which increases the survival rate is urgently needed.
  - In the case of the gleevec, that is the representative drug of the mark anti-cancer drug, it is the drug suppressing the activated kinase activity due to the mutation of the Bcr / Abl protein. Particularly, the effect in the acute myelocytic leukemia, at all, the none there is nearly no effect in the other indication the remarkable anticancer effect is shown in the chronic myelogenous leukemia (CML) patient and basal cell carcinoma (GIST).

### ■ Background and unmet needs

#### □ Wnt/beta-catenin signaling and pathological physiology of cancer

- In the mid 1980's, in the research of the Wnt protein discovered for the first time, it was clarified that over activation of the Wnt signal transmission is very important in the birth of the various cancer, including the colorectal cancer.
- As to the onset of the various cancers, it is reported that abnormal activation of the Wnt signal transduction system is related with and the cyclin D1, cMyc, survivin as Wnt associated gene, and It is reported to play the role of being important in the outbreak of cancer(fig. 1).

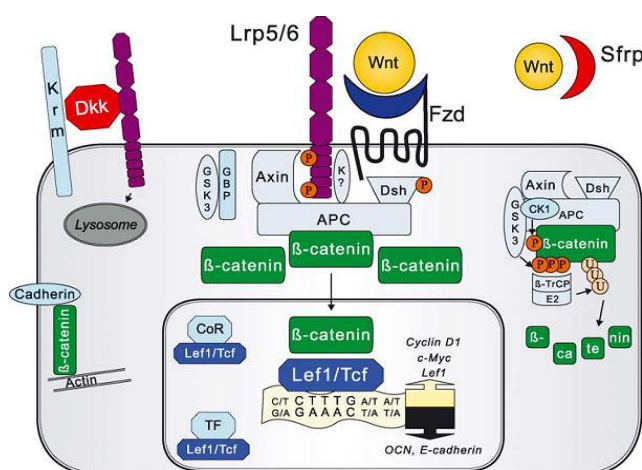


Fig. 1. Wnt signaling system

□ **Diseases for which medicine is efficacious of cancer drug targeting Wnt/beta-catenin signaling**

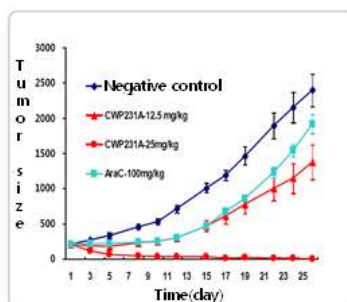
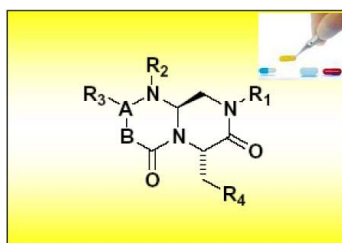
- Wnt/beta-catenin signaling and acute myeloid leukemia
  - In 61% of the acute myelocytic leukemia patient, over of the Wnt signal transmission and activation were discovered(Leukemia, 2006, 20, 1211).
- Wnt/beta-catenin signaling and other cancer

Table 1. The abnormal activation ratio of Wnt/beta-catenin signaling in cancer patient organization

| Cancer                   | Wnt abnormal activation ratio | Assay                | Reference                     |
|--------------------------|-------------------------------|----------------------|-------------------------------|
| colorectal cancer        | 80-85%                        | APC Mutation         | Science (1997) 275:1784       |
| acute myelocyte leukemia | 61-100%                       | WB                   | Leukemia (2006), 20, 1211     |
| lung cancer              | 75%                           | WB(Dvl3)             | Oncogene (2003)22:7218        |
| stomach[gastric] cancer  | 40-60%                        | APC Mutation         | (in differentiated types)     |
| liver cancer             | 78%                           | Immunohistochemistry | World J Gastr. (2005) 11:2398 |
| pancreatic cancer        | 39%                           | Immunohistochemistry | Human Path. (2006), 37:212    |
| prostate cancer          | 36%                           | Immunohistochemistry | Int J Can (2005)113:415       |
| cancer of the esophagus  | 59%                           | Immunohistochemistry | Int J Can (2005)113:981       |
| breast cancer            | 13%                           | WB                   | EJC (2000) 242:248            |
| multiple myeloma         | 75-100%                       | PCR                  | Ai Zheng (2007) 26:1010       |
| ovarian cancer           | 27%                           | Immunohistochemistry | J Path (2004) 204:268         |

■ **Discovery and Achievements**

- The the world's first drug CWP232291 (CWP231A), low molecular weight composition anti-cancer drug, blocking Wnt / beta catenin signal transduction path.



The anticancer effect which tenfold is high than AraC

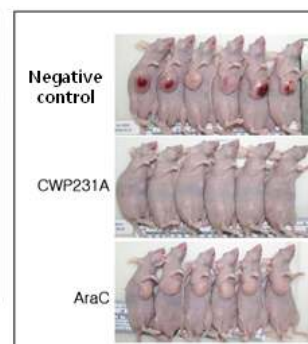


Fig2. The core framework of the CWP232291 drug      Fig. 3. The Ara-C and CWP231A (CWP232291) anticancer effect in the leucosis model

- Presently, all non-clinical toxicities, pharmacological potency, drugstuff movement (ADME), preparation, and biomarker test about the CWP232291 were successfully completed. And for clinical trial drug production is completed in the overseas GMP CMO.
- Pre-IND meeting with US FDA, that was successfully terminated in the early November, 2010. And FDA IND approval in U.S. against the blood cancer patient in October 2011.
- The development importance of CWP232291
  - First-in-Class Wnt targeted anticancer

Table 2. A representative kind of predetermined molecular target anti-cancer drug and indication

| Division                      | Pharmacophore target | Product                                     | Indication                        |
|-------------------------------|----------------------|---|-----------------------------------|
| Signal transduction inhibitor | BCR-ABL              | Gleevec                                     | leukemia                          |
|                               | HER@                 | Herceptin                                   | breast cancer                     |
|                               | EGFR                 | Iressa, Erbitux                             | lung cancer, colorectal cancer    |
|                               | Wnt                  | nothing                                     | colorectal cancer, leukemia, etc. |
| Angiogenesis Inhibitor        | VEGFR, PDGFR         | Avastin, Sutene, Nexavar, Greenstatin, etc. | colorectal cancer, kidney cancer  |
| Immunotherapy                 | CD20                 | Rituxan                                     | lymphoma                          |
| apoptosis derivative s        | 26S protease         | Velcade                                     | multiple myeloma                  |

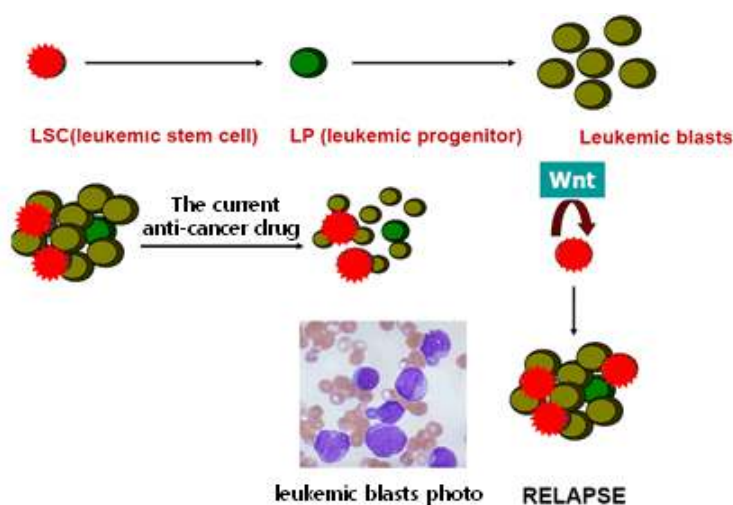


Fig. 4. The role of the Wnt in the playback of the leukemia stem cell which is important in the leukemia recurrence

- The Wnt restraint drugs development current state

Table 3. The Wnt signal transmission suppression anticancer drug development current state

|                           | Target                         | Development, Inc.               | Indication  | Note  |
|---------------------------|--------------------------------|---------------------------------|---|---|
| Antibody drug             | Wnt Receptor, Fzd              | Genentech                       | Cancer  | acts on the upper signal                                  |
|                           | Fzd Receptor                   | OncoMed                         | Cancer  | acts on the upper signal(cooperation research with Bayer) |
| Low molecular weight drug | $\beta$ -catenin               | JW CHOONGWAE PHARMA CORPORATION | leukemia, multiple myeloma, lymphoma, colorectal cancer, etc. | acts on the sub-signal                                    |
|                           | Tcf/ $\beta$ -cat Interaction  | novartis, pfizer                | Cancer  | bad medicamentosa   |
|                           | $\beta$ -catenin degradation   | Avalon                          | colorectal cancer, multiple myeloma, CML                      | research initial step                                     |
|                           | Fzd-Dvl Interaction            | Genentech, St. Jude hospital    | lung cancer, colorectal cancer                                | acts on the upper signal, low activity                    |
|                           | BLC9/ $\beta$ -cat Interaction | Genetics                        | colorectal cancer   | research initial step                                     |

- the leukemia treatment trend of research (the other target drug excluded Wnt)
  - . IY5511 is undergoing research for the treatment of chronic myeloid leukemia, develop by Ilyang Pharm.
  - . Zamyli is undergoing research for the treatment of acute myeloid leukemia, develop by Protein Design Labs Inc.
  - . CEP-701 is undergoing research for the treatment of acute myeloid leukemia, develop by Cephalon.

## Patents and Publications

| Country | Appln. No.      | Status  | Description  |
|---------|-----------------|---------|--|
| Europe  | EP14442350      | Granted | Reverse-turn mimetics and method relating thereto  |
| Korea   | KR10-0910307    | Granted | Reverse-turn mimetics and method relating thereto  |
| US      | US12/682,881    | pending | Novel compounds of reverse turn mimetics and the use thereof (2)                             |
| Korea   | KR2010-7010576  | pending | Novel compounds of reverse turn mimetics and the use thereof (2)                             |
| US      | US12/738,066    | pending | Novel compounds of reverse turn mimetics and the use thereof (3)                             |
| Korea   | KR2010-7010575  | pending | Novel compounds of reverse turn mimetics and the use thereof (3)                             |
| US      | US7671054       | Granted | Reverse-turn mimetics and method relating thereto  |
| WIPO    | PCT/KR10/002306 | pending | Novel compounds of reverse -turn mimetics, method for manufacturing the same and use thereof |
| US      | US12/759,854    | pending | Novel compounds of reverse -turn mimetics, method for manufacturing the same and use thereof |

## Contact Point

KHIDI (Korea Health Industry Development Institute) is currently receiving inquiries from interested parties in this transaction. If you are interested, please contact any of the KHIDI professionals below :

| Name       | Title                        | Tel. number    | E-mail address   |
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|            |                              |                |                  |