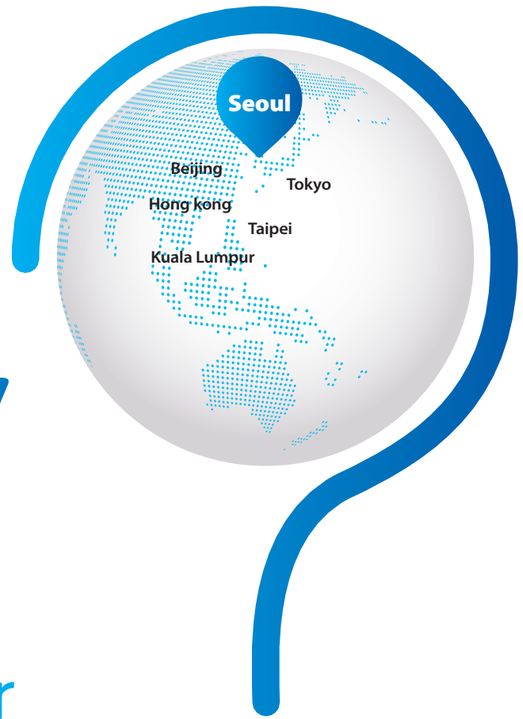
Government Initiative

KOREA DRUG DEVELOPMENT FUND

KDDF
Korea Drug Development Fund

Why

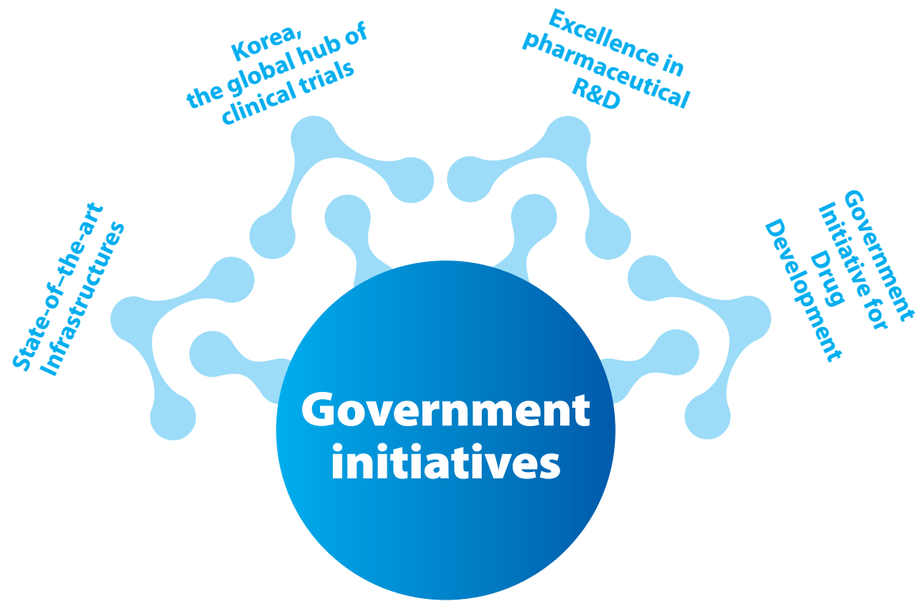


"KOREA" is the perfect place for new drug development

Geographical Advantage

Korea is strategically located at the center for transportation in Northeast Asia

- 61 cities with a population of more than 1 million within a 3-hour flight from Seoul
- Korea, Japan and China boast a combined GDP of about $14 trillion
- Total population of Korea, Japan and China exceeds 1.52 billion, or 22% of the global population, and total trade volume is $5.32 trillion, or 17.6% of total world trade.
- Established the APEC Harmonization Center for regulatory harmonization within ICH guideline.
- Efforts for Regulatory Harmonization across Korea, China, Japan – Established AHC (APEC Harmonization Center, www.apec-ahc.org) and holds tripartite forum to elicit the right policy environment for life sciences innovation.



Government initiatives

The government selected the bio industry as a new growth engine and launched various initiatives to support pharmaceutical industries

- **Government Initiative for Drug Development** : The government of the Republic of Korea launched the **Korea Drug Development Fund (KDDF)** in 2011 to transform Korea into the global leader for new drug development with a budget of US$1 billion.
- **State-of–the-art Infrastructures** : Korea National Enterprise for Clinical Trials(KoNECT), Korea Research Institute of Bioscience & Biotechnology(KRIBB), Korea Institute of Technology(KIT), Korea Research Institute of Chemical Technology (KRICT), Two high-tech medical clusters (Osong, Daegu)

Excellence in pharmaceutical R&D

Korea has strong human capital & research capability

- **Large pool of R&D experts** : 22,817 workers in the bio industry (36.7% of them having master's or doctor's degrees)
- **Strong Competitiveness in Basic Research**

▶ 28 Korean researchers' papers related to biotechnology published in the top 3 global science magazines (Nature, Science, Cell)
▶ Ranked 5th for number of patents (9,689 patents Statistics from the World Intellectual Property Organization in 2010)
▶ Registered 520 patents in the bio sector of the United States between 2006 and 2010, and recorded 166 in technology strength, ranking 14th.

Korea Drug Development Fund (KDDF)

We openly welcome foreign investment and partnerships with international organizations who seek to gain a competitive edge in the next ten years!

About the KDDF

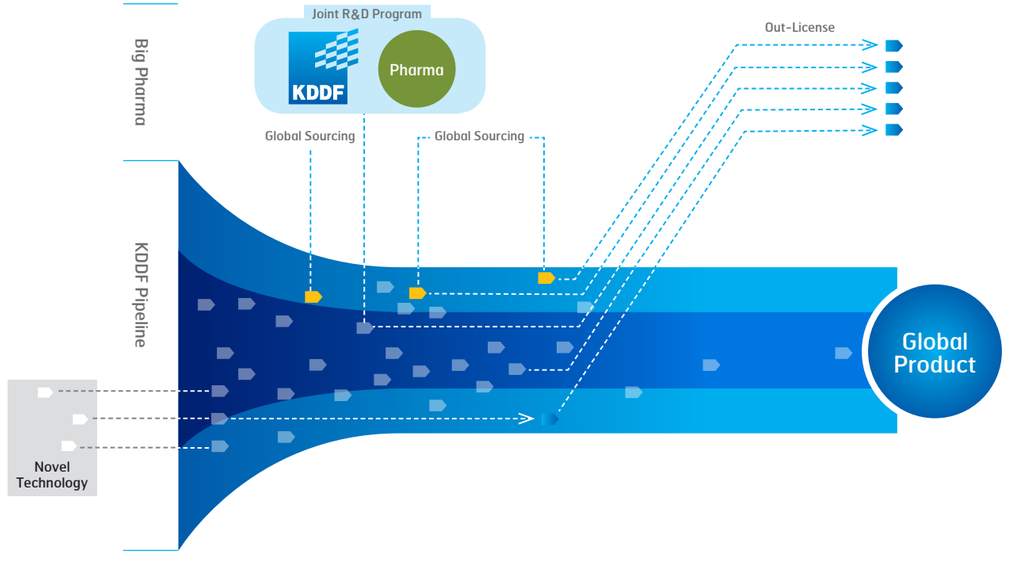
Korea Drug Development Fund (KDDF) is a government-initiated drug development program that manages a total budget of US $1 billion, backed by a collaborative effort of healthcare related Korean ministries. KDDF supports new drug development projects across discovery to clinical stage and actively builds local and global networks that will drive innovation in biopharmaceutical industry.

Acting as a neutral third party in reviewing proposals from local companies and academia, KDDF selects projects and operates through close project management linking with monetary support for developing its pipelines to be global products. KDDF currently manages over 90 selected projects (Pipeline information on http://eng.kddf.org/).

KDDF actively focuses on business development activities to commercialize its pipelines through R&D partnerships & collaborations with international organizations who seek to gain a competitive edge in the next ten years.

- Government Fund / Non-profit organization
- Global New Drug Development support
- Develop experts human resources for new drug R&D
- International networking of experts from Industry-Academia-Institute
- Business Development activities across the portfolio

KDDF Business Models



Novel & Innovative Track

Novel & Innovative Track is designed to accelerate novel and innovative technologies into pharmaceutical pipelines. Projects are guided through one of KDDF's experienced Project Manager to develop viable research-stage technologies into innovative medicines.

Big Pharma Customized Model

KDDF selects and manages pipelines aligned with in-license demand of Global Pharmaceutical Companies who can distribute and sell products globally.

Connect & Development Model

Adapting Open Innovation Strategy, KDDF seeks promising drug candidates outside Korea to co-develop with well-known Korean pharmaceutical companies and research institutes. Submit your Pipeline to KDDF and become part of Connect & Development Program. (http://cnd.kddf.org/)

Selection process

Proposal

1st — Applicant Presentation

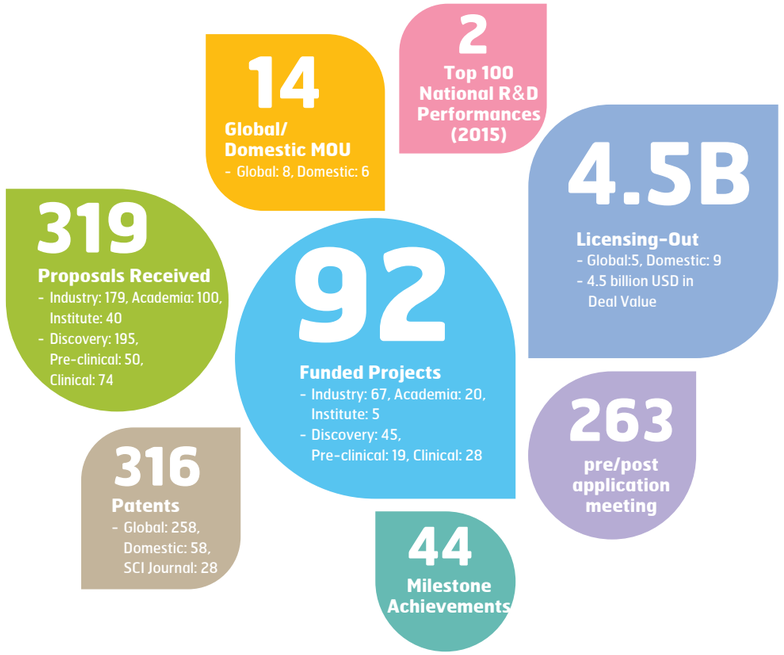
2nd — Due diligence

3rd — Investment Decision via KDDF Evaluation Committee.
- Technical Feasibility, Commercial Viability, IP, etc

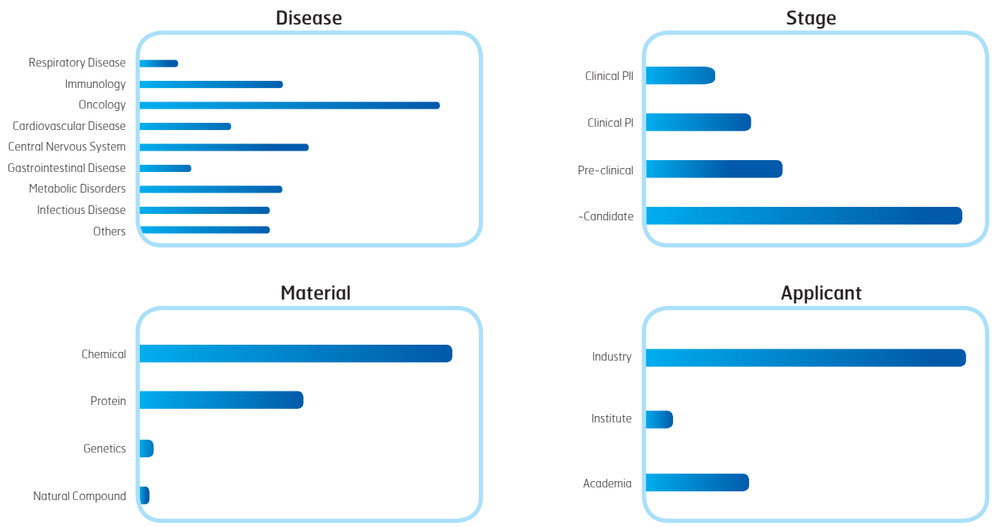
4th — Milestone/Budget Adjustment

Contract (Agreement)

KDDF Performance (As of May 2016)



Statistics of the Funded Projects (As of May 2016)



KDDF Pipeline (As of May 2016)

Government Initiative

Korea Drug Development Fund

Contents

Dinona Inc.

Phase I study of a novel therapeutic antibody, DNP001 in acute leukemia

Code Number : KDDF-201406-09

Development and Market Objectives

- Our goal is to complete phase I testing for DNP001, an antibody therapeutic targeting an acute leukemia-specific antigen called JL1 and to obtain IND approval for phase 2, followed by scale-up production. An additional global clinical phase 2 trial is expected to be undertaken in the future.

Unmet Medical Need & Target Patients

Target patients

- JL1-positive acute leukemia patients and myelodysplastic syndrome (MDS) patients

Unmet Medical Needs

- Adult patients with ALL and AML have a long term disease-free survival rate of only 30-40%, and 20-30%, respectively, even with chemotherapy and bone-marrow transplantation. Of particular note, the 5-year survival rate for patients over 65 years of age in the AML patient group remains below 10%, and has not improved for decades (Lancet 2013;381:484-495).
- The primary reasons for the prevailing unsuccessful treatment of acute leukemia are due to recurrence of the disease, and the side effects of chemotherapy and bone-marrow transplantation, which contribute to a high mortality. Bone-marrow transplantation in particular is only attempted for leukemia patients that cannot be treated with chemotherapy. However, for high-risk AML and ALL, patients only survive long term and disease-free at rates of 20-30% and 30-40%, respectively, even after bone-marrow transplantation (Bone Marrow Transplant. 2005, 36_1021).
- To increase the long term survival rate and number of effective treatments for acute leukemia, we need to develop a curative alternative to bone-marrow transplantation and develop therapeutics that can reduce toxicity and retain remission. Novel therapies to overcome multidrug resistance without increasing toxicity are also needed, as well as techniques that can effectively destroy minimal residual disease with a high risk of recurrence and effective medicines for relapsed patients.

Status

- Clinical phase 1 testing for DNP001, a new antibody treatment for acute leukemia, is currently in progress at Seoul Asan Hospital in KOREA and is expected to be completed by the end of 2016.

Intellectual Property

- 28 patent registrations approved, 4 applications under examination
- Registered Countries: South Korea, United States of America, Japan, Australia, Mexico, Singapore, Canada, Europe, Germany, Indonesia, Philippines, India
- Countries where application has been lodged and is under examination: Brazil, Israel, Vietnam
- Title of Patent: Acute leukemia and lymphoma-specific CD43 epitope and use thereof.
- Patent Registration Number/ Registration Date

- USA, 7,622,560 / 2005.12.20
- USA, 8,426,555 / 2009.10.09
- USA, 8,753,636 / 2013.03.15
- KOREA, 10-0738401 / 2005.08.24

Competitive Advantages

- Epitope-specific antibody that selectively binds to leukemia cells, while leaving other cells unaffected.
- FIH (First-in-Human) trial antibody with a novel target for acute leukemia
- An ADCC-reinforced antibody via defucosylation
- There is a market with high unmet needs and potential for sustainable growth

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AbClon Inc.

Novel HER2 targeted therapeutic antibody against Gastric Cancer

Code Number : KDDF-201408-02

Development and Market Objectives

- By successfully completing optimization studies for efficacy, pharmacokinetics and single-dose toxicity studies of an innovative antibody drug targeting HER2 for the treatment of patient with gastric cancer, our final objective is to enter preclinical development.

Unmet Medical Need & Target Patients

- Gastric cancer is third leading cause of cancer deaths worldwide, and the fifth most common cancer, with a 5-year survival rate for progressive gastric cancer patients at diagnosis of only 7%. HER2 is overexpressed in 22% of gastric cancer patients and is known to be involved in the development and progress of malignant growth. The blockbuster breast cancer treatment Herceptin was approved as a targeted treatment for HER2 overexpression in gastric cancer patients but compared to existing chemotherapy, the average survival rate is only extended for 2.7 months and the response rate is 47%, indicative of a limited effect. Therefore, new drugs that can increase the survival and response rates of gastric cancer patients with HER2 overexpression are urgently needed.

Status

- Confirmation of correlation between anti-proliferation activity of antibody and HER2 expression level and anti-proliferative activity in Herceptin-resistant cancer cells by in vitro profiling.
- Confirmation of synergistic anti-tumor activity of novel antibody in combination with Herceptin in human gastric cancer xenograft and patient-derived xenograft (PDX) models.
- Establishment of CHO-based production cell lines.
- Conduction of pharmacokinetics (PK) and dose-range finding (DRF) in cynomolgus monkey.
- Studies for mechanism of action and biomarker development

Intellectual Property

- National patent registered (10-1453462, HER2 specific-binding antibody): Specific CDR listed antibody and/or antigen binding fragment and pharmaceutical composition which includes use for preventing or treating breast cancer or gastric cancer.
- National patent registered (10-2014-0109642, HER2 specific-binding antibody): CDR listing, antibody with specificity for the CDR3 area in light and heavy chains and/or its antigen binding fragment and pharmaceutical composition which includes its use for preventing or treating breast cancer or gastric cancer.
- PCT application (PCT/KR2014/004317, HER2 specific-binding antibody): Combined antibody with a specific CDR listing and/or antigen binding fragment and pharmaceutical composition which includes its use for preventing or treating breast cancer or gastric cancer.
- The patent has been applied in 10 national phases (HER2 specific-binding antibody): Combined antibody with a specific CDR listing and/or antigen binding fragment and pharmaceutical composition which includes its use for preventing or treating breast cancer or gastric cancer.

Competitive Advantages

- Limited therapeutic options are available for the treatment of patients with gastric cancer, so there is a big potential for clinical development and a large market size.
- Novel anticancer activity based on distinct mechanism of action compared to the existing antibody therapeutics.
- Shows superior anticancer efficacy in combination with Herceptin compared to Herceptin single treatment and combination treatment of Herceptin and Perjeta.
- Shows anticancer activity in some HER2-positive and Herceptin-resistant cancer cells.

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JW Pharmaceutical Corporation

Clinical phase 1 Study of CWP291 in Relapsed Patients with Multiple Myeloma

Code Number : KDDF-201408-09

Development and Market Objectives

- To receive fast-track FDA approval for CWP291, a potent β-catenin inhibitor that has shown excellent antitumor activity in multiple myeloma models, as a therapeutic agent and conduct multinational clinical trial research in patients suffering from relapsed and refractory multiple myeloma in Korea and the US.
- Future commercialization through licensing and developmental collaboration with a multinational pharmaceutical company.

Unmet Medical Need & Target Patients

Target patients

- Relapsed or refractory multiple myeloma patients who have failed standard therapies.

Unmet Medical Needs

- Poor prognosis for many multiple myeloma patients, with high rates of relapse after receiving standard of care.
- Targeted therapies with lowered toxicity are needed, particularly because the majority of multiple myeloma patients are seniors.
- Novel approaches that can synergize with standard therapies are needed to increase the therapeutic options available to physicians.

Status

- Preclinical studies have revealed that CWP291 demonstrates outstanding in vitro, and in vivo anti-tumor effects through the inhibition of β-catenin, a major factor implicated in relapsed and refractory multiple myeloma cases. CWP291 also demonstrated synergism when treated in combination with standard therapies.
- In order to increase translational relevance, we conducted and confirmed CWP291's antitumor activity in additional preclinical models including mesenchymal stem cell co-culture system, patient-derived (PD) xenografts and standard treatment resistant cells.
- A phase 1 study to assess the safety, tolerability, pharmacokinetics and efficacy of CWP291 in subjects with relapsed or refractory myeloma patients has been filed and received FDA IND approval in July 2014. MFDS IND approval in Feb 2015. Patient enrollment is ongoing.

Intellectual Property

- CWP291 compound-patents are granted in major markets valid until 2028.

Competitive Advantages

- First-in-class drug with potent β-catenin inhibitory effects at an early development stage in comparison to competing candidates
- Exhibits outstanding in vitro/in vivo anti-cancer effects in resistant multiple myeloma models and demonstrates synergism in co-administration with standard therapy
- Lower toxicity profile when compared to standard therapy and existing cytotoxic drugs
- Indications may be expanded to various solid tumor types that display drug tolerance due to β-catenin overexpression
- Strong patent position and guaranteed monopoly period

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Eutilex Co., LTD.

Anti-cancer antibody therapeutics, anti-AITR

Code Number : KDDF-201408-11

Development and Market Objectives

- Anti-AITR has been characterized in human PBMC and humanized mouse model. It polarized Teff to Th1 and converted Treg to Th1, and suppressed human cancers in HLA-match humanized mice. We plan to develop the antibody as an anti-cancer drug by taking steps of nonclinical and clinical trials.

Unmet Medical Need & Target Patients

- Our newly developed anti-AITR converts Treg to Teff cells, and then activates effector T cells, which enables to trigger potent and comprehensive anti-tumor activities, and thus provide therapeutic effects for all types of hematologic and solid cancers.

Status

- The antibodies are being validated and optimized.

Intellectual Property

- Patents are being applied

Competitive Advantages

- Polarization of Treg to Th1 and activation of $CD8^+$ T cells

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Green Cross Corporation

Development of a novel EGFR-targeted antibody

Code Number : KDDF-201412-08

Development and Market Objectives

- The objective of this study is to determine the safety, tolerability, and the recommended phase II dose, and to investigate the potential efficacy of the recommended phase II dose in target disease indication through expansion study. A rationale for development strategy and competitiveness compared with other drugs will be established through translation study.

Unmet Medical Need & Target Patients

- Current EGFR-targeted antibodies have low response rate and recurrence problem and it is highly in need for therapeutics with higher response rate and prolonged efficacy. In phase 1 clinical study GC1118 is open for the stage IV patients with solid tumors who failed in standard therapy or other EGFR-targeted therapeutics. The ultimate target patients are stage IV colorectal cancer patients including those refractory to other EGFR-targeted antibodies and stage IV gastric cancer who failed in standard therapy.

Status

- An underlying mechanism for superior tumor inhibitory effect of GC1118 to other EGFR-targeted antibodies was provided by efficacy and mechanism study. Furthermore potential use of GC1118 for Erbitux-failed patients was also implicated in Erbitux-resistant animal model. We're planning to have a proof of concept data through phase 1 clinical trial including expansion study.
- A Dose escalation study has been completed and indicated that GC1118 is tolerable and safe. Recommended phase II dose has been determined. An overall response rate was encouraging where partial responses were observed at the RP2D level. An expansion study has begun to further determine the safety as well as efficacy in the specific subsets of target patients. The expansion study is expected to be completed on Aug. 2017.

Intellectual Property

- Antibodies specifically binding to the epidermal growth factor receptor, patent registered in KR, US, others (11 nations) including BR, CA are under review
- Epitopes of epidermal growth factor receptor surface antigen and use thereof, patented in PCT/KR and under review in 15 other nations

Competitive Advantages

- Potent inhibition on a broad range of EGFR ligands including high affinity ligands implicated in Erbitux resistance, invasion, and metastasis
- Strong tumor suppression in Erbitux-resistant model
- Superior growth inhibitory activity on tumor xenografts with K-Ras mutation compared with other EGFR-targeted antibodies

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ST PHARM, Co., Ltd.

Tankyrase inhibitors as anti-cancer therapeutic reagents

Code Number : KDDF-201504-01

Development and Market Objectives

- Almost 80% of colorectal cancers (CRC) are driven by aberrantly-activated Wnt signaling, mainly through APC mutations. The activation of the Wnt pathway allows ?-catenin levels to increase, leading to the expression of multiple tumorigenic gene products. The enzyme, tankyrase parsylates Axin which leads to dissociation of the "destruction complex" (APC, Axin, GSK3?, and CK1?), resulting in the increase of ?-catenin levels. Blocking of enzyme activity of the tankyrase will restore the destruction complex and maintain homeostasis of the level of ?-catenin.
- The project goal is to identify selective Tankyrase 1&2 inhibitors that are suitable for oral administration (once daily) and to profile for tumor growth inhibition in a variety of models of colorectal and breast cancers.

Unmet Medical Need & Target Patients

- According to the worldwide statistics, colorectal cancer is the 3rd most common cancer in men and the 2nd in women, and 1.2 million incidences and 609,000 mortalities by the CRC were reported in 2010. The incidence rates in several Asian and Eastern European countries are still increasing. The sales amount of colorectal cancer therapeutics reached $2.5 billion in seven global markets (US, Japan, France, Germany, Italy, Spain, UK) in 2012.
- While Erbitux (Cetuximab) is well-known anti-cancer therapeutics for colorectal cancers, its application is limited to the patients with wild-type KRas and there are no remarkable medicines developed for the patients with mutant KRas, approximately 40% of the total CRC patient population.
- ST Pharm's STP06-1002 aims to target the patient population with mutant KRas (750,000 patients in 2014) and also the Erbitux non-responders (210,000 patients in 2014) with strong predictive biomarker strategies.

Status

(1) On-going studies

- Pre-formulation study, process development and manufacture
- Pharmacokinetics study
- Preclinical toxicology study (non-GLP toxicity in rodent and non-rodent)
- In vivo efficacy study (pharmacodynamics)

(2) Existing study results

- Excellent in vitro potency and PARP selectivity
- Excellent stability (xML, plasma, CYPs)
- Good solubility (FaSSGF, FaSSIF, FeSSIF)
- No toxicity issues observed (hERG, cytotoxicity, Ames)
- Excellent PK profiles in mouse & rat
- PD POC in Xenograft DLD-1 model study
- No abnormalities detected in vivo toxicity study and ileum histology
- No toxicity issues in single acute, 10-day DRF, and Toxicokinetic studies
- No activity in pan-kinase and off-target binding assay

Intellectual Property

- Strong IP positions

Competitive Advantages

(1) Partial responses were

- STP06-1002 is a small molecule tankyrase inhibitor targeting CRC with novel MOA and has been developed as first-in-class anti-cancer therapeutics with predictive biomarker strategies.

(2) Internal capability of ST Pharm

- ST Pharm is a "Top-Tier GMP Chemical Service Provider" with outstanding cGMP compliance based on ICH Q7.
- ST Pharm has been audited by numerous domestic and foreign regulatory agencies (MFDS, US FDA, EDQM, PMDA, TGA, and etc.) and approved successfully its cGMP quality system. The non- and clinical-samples will be manufactured using the internal capacities.

(3) Business development strategy

- ST Pharm maintains long-term relationships with lots of global pharmaceuticals and biotechs from discovery to commercial stage.

ST PHARM, Co., Ltd.

- A broad range of collaborations by virtual R&D strategy is being developed to facilitate the new drug development process in an efficient and effective manner.

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PharmAbcine, Inc.

PharmAbcine
Antibody Therapeutics for Life

Clinical Phase IIa Trial with Tanibirumab, a Novel Anti-Cancer Antibody Therapeutics, in Recurrent Glioblastoma Patients

Code Number : KDDF-201509-07

Development and Market Objectives

- Phase I clinical study of tanibirumab, a fully human monoclonal antibody, for advanced and metastatic cancer patients were completed and it showed its strong tolerability and safety profile. With those results, phase 2a clinical study of tanibirumab for recurrent glioblastoma (GBM) will be done at Australia to evaluate safety and preliminary efficacy. Phase 2b clinical study will be followed for efficacy evaluation and predictive biomarker finding on tanibirumab for recurrent glioblastoma.

Unmet Medical Need & Target Patients

- Glioblastoma covers 15 % of all brain tumors and 45 % of malignant brain tumors. New cases of glioblastoma occur in approximately 2~3 persons per each 100,000 every year and it is the third leading cause of youth (age of 15-35) death by cancer. The incidence rate of glioblastoma has been increased 1.5 % annually.
- The current standard therapy for glioblastoma is surgery, radiation and chemotherapy with temodal (temozolomide). It showed about 14 months of median overall survival, but most of patients are recurred within two years. The 5 year survival rate of glioblastoma is less than 3 %. Currently, there is little option for the recurrent glioblastoma patient. Avastin which gave benefit of edema relief to patient was approved at 2009 as an orphan drug for recurrent glioblastoma but was failed at phase 3 clinical study in patients with newly diagnosed glioblastoma recently.
- Tanibirumab blocks Vascular endothelial growth factor/ Vascular endothelial growth factor receptor-2 (VEGF/VEGFR-2) signal pathway similar to avastin, but it can also block VEGF-C and VEGF-D binding to VEGFR-2 in addition to VEGF-A. Thus, it is expected to give more benefit to recurrent glioblastoma patient. It is also expect that this study will give a clue about predictive biomarker for the target grouping of patients who will get benefit by tanibirumab.

Status

- The phase I clinical study of tanibirumab, an anti-cancer antibody therapeutic agent, was completed for advanced and metastatic tumor patients during 2011-2013. It showed no DLT(dose-limiting toxicity) up to 24 mg/kg and no neutralization positive subject. The pharmacodynamics biomarker also showed expected trends. By the results of phase I clinical study, phase 2a clinical trial for recurrent glioblastoma patients has been approved at Australia recently.

Intellectual Property

Patent registered

- The patent has been registered for 22 countries (Registered Countries: South Korea, Japan, Singapore, China, Australia, Canada, EU(15 Countries), United States of America)
- Title of Patent: Human Monoclonal Antibody Neutralizing Vascular Endothelial Growth Receptor and Use Thereof.

Patent Roll

No.	Registration No.	Registration Date	Country
1	10-883430	2009.02.05	Korea
2	5086430	2012.09.14	Japan
3	157597	2013.04.30	Singapore
4	101802003	2013.02.13	China
5	2007354976	2014.06.26	Australia
6	2691159	2014.07.29	Canada
7	2158217	2014.01.15	EU(15 Countries)
8	9150650	2015.10.06	USA

Patent registered

- ScFv and IgG molecules neutralizing vascular endothelial cell growth factor receptor (VEGFR) with combinations of 19 species in the light chain variable region, including the light chain of Tanibirumab as well as the heavy chain variable region
- Composition of the molecule for the inhibition of angiogenesis in paragraph 1
- Composition of the molecule for cancer treatment containing molecule in paragraph 1

PharmAbcine, Inc.

Competitive Advantages

- A strong market cap exists in the field of angiogenesis inhibitors.
- Tanibirumab is a fully human antibody therapeutic agent, the most suitable antibody type for therapeutic application in humans.
- Tanibirumab showed minor side-effects and lower toxicity than competitors, which is due to the high level of specificity with high binding affinity to the vascular endothelial growth factor receptor-2 (VEGFR-2), a primary regulator of angiogenesis.
- Tanibirumab is expected to show the efficacy in several indications such as Her2-negative breast cancer, in which competitors have not showed the significant efficacy.
- Tanibirumab showed the efficacy in an avastin-resistant tumor model and is anticipated that it gives a solution to overcome the avastin-resistance.
- Tanibirumab is the only therapeutic antibody containing cross-species reactivity for VEGFR-2 in rodents which is available in translational research opportunities and in selection of optimal indications. As a result, it is expected to increase the success rate in clinical trials.

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Graduate School of Cancer Science and Policy

NATIONAL CANCER CENTER

Development of novel anti-cancer reagent targeting glioma stem cells

Code Number : KDDF-201509-13

Development and Market Objectives

- Glioblastoma(GBM) is the most aggressive type of malignant brain tumors. Despite multimodal treatment with surgery, radiotherapy, and chemotherapy, the prognosis of GBM is poor, with a median survival of 15 months.
- Failure of GBM treatment is largely attributed to its highly recurrent characteristic as well as easily obtained resistance against standard therapeutics. Emerging evidence suggests that glioma stem cells, only a small portion of GBM, might contribute to tumor recurrence and resistance, making the current treatment frustrating.
- Here, this project is aiming to develop First-In-Class drugs for targeting glioma stem cells.

Unmet Medical Need & Target Patients

- Most GBM patients treated with concurrent therapies experience relapse within a year. In the case of recurrent glioblastoma, they no longer show any response to the therapy, followed by poor prognosis. Drugs for treating the recurrent patient, however, haven't been developed, yet. We need novel approach to treat the cases.
- Cancer stem cells have been identified from many cancers, and its functional significance was well elucidated. Especially, glioma stem cell has been reported to contribute to multiple aspects of GBM tumor biology, including the initiation, progression, diffusive infiltration, recurrence and drug resistance of glioma. Although many biotech companies have tried to develop targeted therapy for cancer stem cells, most of the drugs were poor in therapeutic efficacy and had significant side effects. Therefore, we need to develop new drugs, targeting cancer stem cells with exceptional therapeutic efficacy and specificity.

Status

- Developed one hit in glioma stem cell model
- Confirmed therapeutic efficacy to the compound in PDX model
- We are trying to validate clinical importance of our targets.
- We are preparing new compounds with different scaffolds.

Intellectual Property

- Patents are under preparation.

Competitive Advantages

- Since there has been no specific inhibitor for cancer stem cells in the market, our attempt to develop the drugs will be easier to open up a new market space, compared to other target agents.
- It is the first targeted agent for recurrent glioblastoma. We don't have other competitors for the glioma stem cell targeting agents.
- Combination with current therapeutic agents will demonstrate synergistic effects, boosting market economy.

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Cancer Biology Laboratory, Department of Biological Sciences, UNIST

Development of Cancer Therapeutics Targeting Mitochondrial TRAP1

Code Number : **KDDF-201512-02**

Development and Market Objectives

- Development of mitochondria TRAP1 inhibitor as cancer therapeutics

Unmet Medical Need & Target Patients

Target patients:

- Cancer patients with malignancies exhibiting a TRAP1 overexpression phenotype

Unmet medical needs:

- Despite increases in cancer incidence due to an aging population, effective anti-cancer drugs are still lacking.
- Anticancer drugs with noble mechanism of action are required to treat patients who do not respond to conventional anticancer therapeutics and to overcome drug resistance against conventional chemotherapy
- Novel therapeutics are required to improve combination therapy with current anticancer drugs

Status

- Tumors often overexpress mitochondrial chaperone TRAP1 which is closely related to poor prognosis of cancer patients. We have developed two different classes of lead compounds (different MOA) targeting mitochondrial TRAP1: SMTINs and Panvotinibs. TRAP1 inhibitors are conjugated with the mitochondrial targeting moiety, triphenylphosphonium, to afford SMTINs which efficiently accumulate inside mitochondria. Panvotinibs are mitochondria-permeable Hsp90 inhibitors inactivating Hsp90 and Grp94 as well as TRAP1. The simultaneous inactivation of all the Hsp90 family proteins by Panvotinibs dramatically augment cancer-specific cytotoxic activity. Currently, we are optimizing SMTINs and Panvotinibs to improve DMPK properties of the drugs.

Intellectual Property

- Patent application of a SMTIN class inhibitor, SMTIN-P01, was filed. Several SMTIN inhibitors with better anticancer activity than SMTIN-P01 have been developed and patent application of the inhibitors will be filed soon. We did not disclose drug information on Panvotinib at all, and the patent application will be finished soon.

Competitive Advantages

- In addition to target inhibition, we consider "subcellular drug distribution" and whereby are able to develop novel MOA drug with much improved anticancer activity.
- In case of Panvotinib, as an example, it inactivates Hsp90 and Grp94 similar to current Hsp90 inhibitors and degrades client proteins to increase cell death. However, different from Hsp90 inhibitors, Panvotinib never triggers heat shock response such as pro-survival Hsp70 induction, a well-known adverse effect of Hsp90 inhibitors. Therefore, Panvotinib shows dramatically improved cytotoxicity against cancer cells in vitro and in vivo compared with Hsp90 inhibitors.

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Chodang Pharmaceuticals

Development of novel anti-cancer drug targeting p34, a novel modulator of NEDD4-1-mediated PTEN ubiquitination

Code Number : **KDDF-201512-06**

Development and Market Objectives

- The lead compound generation of the first-in-class novel anticancer drug through PTEN activation by inhibiting the interaction between p34 and NEDD4-1 protein

Unmet Medical Need & Target Patients

- Colon cancer is a serious disease where recurrence rate is 20~50% even after curative resection of colorectal cancer. Targeted treatments in colon cancer patients with Erbitux, which targets the EGFR but these drugs do not show potential efficacy on all patient groups
- The novel anti-cancer drugs target groups of colon cancer patients with p34 and NEDD4-1 double positives along with PTEN wild type patients exhibiting the mutant KRAS or the wild KRAS not responsive to Erbitux treatment.

Status

- Biological studies of NEDD4-1/p34 interaction for clarifying exact mechanism of PTEN activation
- Complex structure study and new hit generation using virtual screening
- Structure & modeling guided synthesis of hit derivatives
- in vitro, in vivo efficacy evaluation for hit derivatives

Intellectual Property

- Domestic and PCT Patents were published in the major countries
- Patents for the selected compounds are filed.

Competitive Advantages

- Due to the first-in-class target mechanism, thus, first-in-class drug, it is likely to become an effective global drug for colon cancer patients exhibiting the mutant KRAS (about 40%) or the wild KRAS not responsive to Erbitux treatment (about 30%).

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Scripps Korea Antibody Institute

Identification of candidate antibody molecules for inhibiting tumor angiogenesis

Code Number : KDDF-201210-05

Development and Market Objectives

- This project aims to develop optimized anti-angiogenic antibody lead substances through a three-step optimization process, using in vitro characterization and efficacy analysis to identify the final candidate antibodies.

Unmet Medical Need & Target Patients

Target patients

- Patients with malignant tumors (inhibition of tumor angiogenesis).

Unmet medical needs

- Bevacizumab (Avastin®) is a U.S. Food and Drug Administration-approved anti-angiogenic therapeutic antibody currently used in clinics and occupied a market share of $590 million in 2012.
- However, Bevacizumab has the following limitations:
  - No significant efficacy as a single therapeutic agent.
  - Distinct side effects, including hypertension, proteinuria, bleeding, and gastrointestinal perforation.
  - Limitations of cancer therapy due to drug resistance issues.

Status

- Target validation and selection of anti-angiogenic antibody lead substances have been completed in previous studies. A three-step optimization process is currently under development.

Intellectual Property

- U.S. provisional application: Targeted inhibition of angiogenesis by C-type lectin domain specific human antibodies against clec14a tumor endothelial cell marker 61/659,654
- PCT application: Novel antibody specific for clec14a and uses thereof PCT/KR2012/008618
- Provisional application for the patent was lodged on June 14, 2012, with conversion to a PCT patent on October 19, 2012. The broad scope of rights includes the lead substances (antibodies) and epitopes, diagnostic and therapeutic compositions, kits, and methods for cancers and angiogenesis-related diseases

Competitive Advantages

- Higher likelihood of development of a first-in-class drug through preclinical and clinical trials due to no development of therapeutic antibodies against the target molecule.
- A broad range of intellectual property rights have already been secured, including development of antibodies and epitope identification.
- Superior anti-angiogenic treatment efficacy is expected through mechanisms distinct from the existing therapeutic antibody, Bevacizumab.
- Developed antibodies are expected to have fewer side-effects because human antibodies have lower immunogenicity and exclusively target tumor blood vessel-specific antigens for specific targeted therapy.
- Because the developed antibodies will be functional domain-specific antibodies that build on existing therapeutic antibodies and surpass their limitations, the time, effort, and costs associated with development are reduced. It is therefore expected that the wide range of industrial applications for the developed antibodies will enable a ripple effect superior to existing therapeutic antibodies.
- Treatment can be applied to a variety of cancers through specific targeting of tumor blood vessels.
- Treatment can be applied to several other diseases that require inhibition of angiogenesis, such as glaucoma and macular degeneration.
- The antibodies under development can induce endocytosis through the cross-linking of antigen, underscoring an original technology for novel anti-cancer drug development that may be used as a platform technology for antibody-drug conjugates.

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Kangwon National University

Preliminary non-clinical study of a therapeutic antibody candidate for the treatment of cholangiocarcinomas

Code Number : KDDF-201212-12

Development and Market Objectives

- Our developmental goal is to analyze the pharmacokinetics, single-dose toxicity, and antitumor activities of human anti-L1CAM monoclonal antibody that cross-reacts with rodent L1CAM. We have conducted PK, single-dose toxicity in mice and efficacy studies in human cholangiocarcinoma xenograft nude mouse models. Our immediate goal is to conduct repeated-dose toxicity study in monkeys.

Unmet Medical Need & Target Patients

- Target patients include those with intrahepatic bile duct cancer, extrahepatic bile duct cancer and gallbladder cancer.
- The survival rate for bile duct cancer patients is less than 5 percent. Although bile duct cancer is not as prevalent as many other types of cancer, the 5-year overall survival rate is among the lowest, after pancreatic, lung and liver cancer.
- As of 2012, only 13 out of 144 clinical tests being conducted worldwide on bile duct cancer are EGFR/VEGFR targeted therapy tests. In order to improve bile duct cancer treatment, various targeted therapies must be further developed.

Status

- PK, single-dose toxicity and in vivo efficacy studies have been completed. We plan to perform repeated-dose toxicity study in monkeys.

Intellectual Property

- A novel monoclonal antibody specific to the L1CAM, A hybridoma producing the same and a method producing the same (licensed number 0756051, license date 2007.08.30).
- A composition for treating L1CAM-expressing cancer comprising an inhibitor of activity or expression of L1CAM and anticancer agent (application number 2008-0118921, application date: 2008.11.27 PCT/KR2009/007056).
- A pharmaceutical composition for treating cholangiocarcinoma, a method for inhibiting growth or invasion of cholangiocarcinoma and a method for treating cholangiocarcinoma.

Country of Application	Date of Application	Application Number	Date of Registration	Registration Number
Australia	2009.3.12	2007288620	2012-12-13	2007288620
Brazil	2009.2.25	0715844-0		
Canada	2009.2.23	2,661,669		
China	2009.4.21	200780039170.9	2013- 06-26	ZL200780039170.9
Europe	2009.2.27	07793649.0	2013-11-27	2054083
Indonesia	2009.2.23	W00200900471		
India	2009.3.6	474/MUMNP/2009		
Philippines	2009.2.23	1-2009-500353		
Japan	2009.2.23	2009-525498		
Mexico	2009.2.23	MX/A/2009/002064	2012.4.9	297926
USA	2009.2.20	12/438,354	2012.4.10	8153122
Vietnam	2009.3.23	1-2009-00568		
Korea	2007.7.1	2007-0084868	2009.12.07	931976

- Humanized antibody against human L1CAM and method for preparing the antibody (application number 10-2012-00092965, application date 2012.8.24)

- Antibodies specifically binding to L1CAM in humans and mice, and use thereof (application number: 10-2011-0130590, application date: 2012.11.16).

Competitive Advantages

- Currently holding patents for targets (L1CAM) of bile duct cancer treatment: first-in-class antibody therapeutics for bile duct cancer.
- Antibody binding to both human and rodent L1CAM can be applied to other malignant cancers.
- Preclinical studies can be efficiently conducted in rodent models.
- Bile duct cancer is refractory to conventional therapy and has poor prognosis. Bile duct cancer therapeutics is categorized as an orphan drug.

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LG Life Sciences, Ltd.

Development of an Anti-myocardial Infarction Agent against Ischemia-Reperfusion Injury with A Novel Necrosis Inhibitor, LC28-0126

Code Number : KDDF-201210-07

Development and Market Objectives

- Development of a cardio-protective agent through successful completion of clinical Phases 1 & 2 using a novel class of necrosis inhibitor, LC28-0126 (CYCL001 Ver. 1.0 approved by MFDS) by demonstrating safety & tolerability in Phase 1 as well as its suppressive effect on infarct size against lethal ischemia-reperfusion (IR) injury during percutaneous coronary intervention (PCI) for the ST-segment elevation with myocardial infarction (STEMI) patients with acute myocardial infarction (AMI) in Phase 2.

Unmet Medical Need & Target Patients

Target Patients

- The STEMI patients with AMI were selected as the primary target to clearly demonstrate the efficacy of LC28-0126 in Phase 2.
- The non-STEMI patients will be tested after completion of Phase 2 in STEMI patients.

Unmet Medical Needs

- More than 1,000,000 cases of myocardial infarction (MI) occur in the US every year and the high prevalence rate of 600 cases/100,000 population was reported. However, no drugs are currently available to effectively treat this condition.
- The patients with AMI without PCI settings typically exhibit 70% of infarcted area, causing death from heart attack.
- The PCI administration for the patients with AMI ultimately could extend their life, but paradoxically, > 30% of the infarcted area still remains due to lethal reperfusion injury caused by excess blood and oxygen provided at the time of the procedure.
  Consequently, 5 ~ 10% of the patients with PCI setting die within a year, or the patients should endure significant medical expenses due to serious clinical complications in their lives.
- All drugs that were successfully developed in preclinical stage failed in the clinical trials performed for the patients with MI as they did not demonstrate fundamental reductions in size of the myocardial infarct. The underlying reason is due to the fact that the size of infarct is decisively influenced by the degree of necrosis of myocardial cells.
- Therefore, there exist significant unmet medical needs in the development of a treatment drug which can reduce the infarct area of 30% post PCI, down to < 5%. LC28-0126 a strong novel necrosis inhibitor that specifically targets the mitochondria was developed by LG Life Sciences. This is the first time in the world LC28-0126 a novel necrosis inhibitor to be tested in the clinical trial for AMI patients, suggesting its clinical implications in the area of ACS (Acute Coronary Syndrome) for which there are no adequate treatments.

Status

- A clinical Phase 1 trial with healthy volunteers was completed in 4Q, 2014, Korea. The clinical Phase 2a for AMI with 60 STEMI patients has been completed in 4Q, 2015. **Additional clinical Phase 2a for 100 STEMI patients approved by MFDS (2015) has been initiated in April, 2016**.
- A backup study of chemical synthesis is also underway.
- Out-licensing or collaborative research opportunities including the "LGLS-Necrosis Program" are available.
- Partnership for the clinical studies for MI is possible.

Intellectual Property

- 3 material patents and several use patents covered worldwide.

Competitive Advantages

- Thus far, anti-platelet agents have been used as secondary drugs to vasodilatation in PCI procedure. Three clinical candidates of MI inhibitors have been tried to demonstrate efficacy for reduction in the infarct size for STEMI patients in clinical trials: cyclosporine A, Phase 3; Bendavia & TRO-40303, Phase 2. However, all of these candidates have recently failed in the clinical trials for STEMI patients with AMI, which might be mainly due to the action mechanism of these apoptosis inhibitors that could not fundamentally block myocardial necrosis.
- Drugs that can effectively reduce the size of myocardial infarct against lethal IR injury during PCI administration do not yet exist. Therefore, there exist significant medical unmet needs in the development of drugs, that is, strong necrosis inhibitors that can fundamentally block myocardial cell necrosis, the main cell-death mechanism of myocardial infarction.
- Therefore, LGLS LC28-0126 showing inhibitory effects on cellular necrosis and (2) strong efficacy of reduction in infarct size in the rat MI model is expected to potentially demonstrate **the fundamental reduction in infarct size** against lethal reperfusion injury in the clinical settings.

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LG Life Sciences, Ltd.

Korea Drug Development Fund

SK Biopharmaceuticals

YKP3089, an Innovative Drug for the Treatment of Epilepsy: Late-Phase Global Clinical Development

Code Number : KDDF-201110-14

Development and Market Objectives

- SKBP successfully completed multinational Phase 2a and Phase 2b trials to evaluate efficacy and safety of YKP3089 to treat epilepsy. In EOP2 meeting, FDA agreed that YKP3089 had shown sufficient and repetitive efficacy upon those two studies, therefore the agency accepted two studies as pivotal ones.
  By FDA guidance, SKBP is now conducting OLE to confirm its safety and in parallel NDA registration is being prepared. SKBP plans to commercialize by itself in the US market targeting '18 market launch. Based on YKP3089 clinical profile, SKBP plans to conduct additional clinical trials, in addition to partial onset seizure, to expand YKP3089's indication in other seizure type including generalized seizures as well as LGS.

Unmet Medical Need & Target Patients

Target patients

- Epilepsy is categorized into two major types: partial onset seizures and generalized seizures. Partial onset seizures are the more common type of seizures, representing 53 percent among all epilepsy patients. Approximately 30 to 40 percent of patients still have refractory seizures on their current drug regimens. We have confirmed the efficacy of YKP3089 in the treatment of refractory partial-onset seizures in patients whose medical needs are urgent and unmet. Especially, YKP3089 has shown significant seizure free rate (100% seizure reduction) compared to placebo in both studies.

Unmet medical need

- Epilepsy is the most common neurological disorder and its various types of seizures are difficult to control with a single drug. Despite the availability of many antiepileptic drugs acting by a variety of molecular mechanisms, there are huge medical unmet needs for approximately 30 – 40 percent of refractory seizure patients. In addition, the use of many of the currently-available drugs is compromised by their inconvenient dosage regimens or deleterious side effects, such as sedation, cognitive deficits, weight gain, and behavioral changes.

Status

- A multinational Phase 2a study in US, Korea, Poland and India and a multinational Phase 2b study in 16 countries were completed. Several drug-drug interaction studies and MOA studies are on progress.

Intellectual Property

- Composition of Matter Patent:
  - US : issued as US 7,598,279 (Filed in 2006)
  - Filed : WW including EU and Asia countries
- Process patents : PCT application filed
  - Pending : Worldwide

Competitive Advantages

- Potential of Superior Efficacy compared to standard of care drugs
  - Signals of 100% reduction in seizures (seizure free rate)
- Better Compliance for patients
  - Once daily (QD) dosing
  - Favorable safety and tolerability profile (same dropout rate due to AE compared to placebo)
  - Narrow Peak-to-trough plasma fluctuation implicating better tolerability and sustained clinical efficacy
- Strong Patent strategy provides long exclusivity with CoM as well as process patents

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HALLYM UNIVERSITY

Development of analgesic compounds for the treatment of chemotherapy-induced peripheral neuropathy

Code Number : KDDF-201406-15

Development and Market Objectives

- The development of 2 candidate substances for the treatment of chemotherapy-induced neuropathic pain, using FY-304, a derivative of 5-membered heterocyclic compounds and FY-504, the lead candidate from the Korean government's new therapeutic development project [KDDF201304-06] in order to synthesize a new compounds with excellent efficacy, high stability and fewer side effects, and which is also appropriate for broad indications.

Unmet Medical Need & Target Patients

Chemotherapy-induced Peripheral Neuropathy, CIPN Neuropathic Pain : Issues with existing medication

Drug/Combination Tested	Study Result
Lyrica®	Failed
Lidoderm®	Failed
Procrit®	Failed
Amitriptyline/ketamine/baclofen	Limited efficacy

▲ **Clinical research data for existing and combination CIPN therapies**

- Analysis of currently-available medications highlights issues related to their efficacy and side effects. Improved pain alleviation and decreased side effects related to the central nervous system are the most important factors for the development of a new medication for the neuropathic pain.
- Gabapentin, pregabalin and similar drugs are allopathic medications used to ease neuropathic pain, but their level of efficacy is currently low effective for less than 30% of patients → an improvement of more than 50% is needed).
- Side effects such as dizziness and drowsiness are associated with CNS-targeted medications and none are currently capable of addressing the underlying cause of the disease.
- High-capacity administration is currently not possible with low stability candidates.

Status

- In vitro and in vivo data show that FY-304 inhibits the TTX-resistant Na channel, highlighting the possibility for development as a CIPN alleviator.
- Using the properties of FY-304 and FY-504 from previous research efforts as the foundation, and via the synthesis of novel compounds, we are developing new substances for chemotherapy-induced neuropathic pain with excellent efficacy, high stability and fewer side effects, and which is also appropriate for broad indications.

Intellectual Property

- Patent Title: 5-membered heterocyclic derivatives, their method of manufacture and the pharmaceutical compositions arising from it (Patent No: 10-2013-0046117).
- Extent of Rights: 5-membered heterocyclic derivatives and their hydrates or pharmacologically active substances including pharmaceutical compositions that decrease pain including acute pain, chronic pain, neuropathic pain, post-operative pain, migraine, and arthralgia.

Competitive Advantages

- Patent: Extensive literature analysis suggests that the potential for exclusive patent rights is very high with no intellectual property issues identified worldwide. As a highly novel candidate, broad patent rights are expected.
- Efficacy: Neuropathic pain relief or inhibition.
- Mechanism of Action: Selective inhibition of Nav1.8 (IC50>10pM)
- Toxicity: Single dose tox(oral), Bacterial Reverse Mutation Test (Ames Test), In vitro Chromosome Aberration Assay, In vivo Micronucleus Assay and hERG assay were finished. The results were suited for goal.

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ABION Inc.

Preclinical study of Carbiferon, a next generation IFN-beta, for multiple sclerosis

Code Number : KDDF-201502-07

Development and Market Objectives

- A biobetter version of recombinant human interferon-β1a (rhIFN-β 1a) has been developed to improve its biophysical properties, such as aggregation, production and stability and pharmacokinetic properties, without jeopardizing its activity. Glycoengineering had no effect on rhIFN-β ligand-receptor binding, as no loss of specific activity was observed. R27T showed improved stability and had a reduced propensity for aggregation and an increased half-life.

Target indication : First line Tx for Relapsing Remitting Multiple Sclerosis (RRMS) & Clinically isolated syndrome (CIS)

Unmet Medical Need & Target Patients

Unmet Medical Need	Development Goal
Approval for Various MS	Target for RRMS, SPMS, and CIS
Improved Delivery Method	SC/Once per Week
Improved Tolerability	Improved Efficacy
Decreased Side Effects	Decrement of Injection Site Reaction
Lower Drug Cost	More than 10 Times Productivity form Host Cell

Status

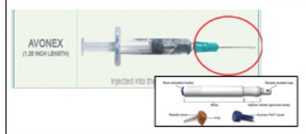
Process Development

- Cell Line development
  - High producer
  - Reduced NGNA vs. NANA content
- Culture process development
  - High productivity (Basal and feed media optimization)
  - Full glycosylation of both sites
- Purification process development
  - High Purification yield
  - Efficient separation of single vs. double glycosylation forms
- Overall anticipated productivity improvement : 15 – 50 fold increase

Intellectual Property

Patent Title	Country	Patent Date	Application No./ Patent No.	Status
Human Interferon-Beta Mutein	Korea	2007.11.27	0781666	Granted
	PCT	2006.05.11	2006-049423	Granted
	US	2012.01.24	8101716	Granted
	JP	2010.12.03	4637913	Granted
	Brazil	2008.10.21	PI0517932	Granted
	China	2012.11.07	CN1011115198	Granted
	India	2007.05.18	3732/DELNP/2007	Pending
	EP	2011.05.18	1809661	Granted
		Sweden, Switzerland, France, United Kingdom, Hungary, Ireland, Finland, Portugal, Italy, Spain, Germany		
	EP_Turkey	2011.08.30	TU 110830ZT4	Granted
	EP_Greece	2011.08.17	3075773	Granted
	EP_Austria	2011.05.18	1809661	Granted
	EP_Denmark	2011.05.18	1809661	Granted
Modified Interferon-beta Conjugated with Polyethylene Glycol	Korea	2014.07.24	10-2014-0093983	Pending
	PCT	2014.07.24	PCT/KR2014/006743	Pending

Competitive Advantages

	Avonex	Rebif	Betaseron
			
Dosage	Once per week	3 times per week	3~4 times per week
Type of Inject	i.m (ex. Buttocks Injection), Slightly Difficult	s.c.(ex. Insulin), Easy	s.c.(ex. Insulin), Easy
Problems	• High COGs(Cost of Goods) & High Price	• Repeated Dose and High Risk of Side Effect • High COGs(Cost of Goods) & High Price	• Low Solubility • High Immunogenicity
Carbferon			
Advantage	• Patient`s economic burden decrement (High yield protein production) • Improved patient`s compliance (Prolonged half life once per week (s.c.)) • Lower immunogenicity (Solubility increment)		

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Vivozon, Inc.

Development of oral VVZ-149, a non-opioid analgesic candidate for nociceptive and neuropathic pain

Code Number : KDDF-201506-05

Development and Market Objectives

- VVZ-149 is a small molecule that inhibits both GlyT2 and 5HT2a. GlyT2 plays an important role for pain transmission in spinal dorsal horn area. Inhibition of GlyT2 increases the amount of glycine released from glycinergic inhibitory interneuron so that pain transmission from periphery to central dorsal horn can be reduced. 5HT2a is expressed in both peptidergic and non-peptidergic nociceptive nerve terminal in periphery so that blocking of 5HT2a can decrease the activation of nociceptive nerve terminal. 5HT2a also plays an important role in spinal dorsal horn area via descending facilitatory tract increasing the sensitivity for pain. Thus, inhibiting both GlyT2 and 5HT2a can provide more efficient way to control pain. VVZ-149 has shown morphine comparable efficacies in various animal studies. Currently, Clinical phase 2 trials of VVZ-149 injections for treatment of postoperative pain are ongoing in US and Korea. If the phase 2 studies are successful, the application of VVZ-149 injections can be expanded to pain for terminal cancer patient or chemotherapy induced neuropathic pain.
- This project is to accelerate the development of oral VVZ-149 by conducting preformulation studies and GLP toxicology studies although the GLP toxicology studies had already conducted as an injection form. After oral administration of VVZ-149, most of the VVZ-149 is metabolized to an active metabolite, VVZ-368, in liver. Thus, the GLP study will elucidate any potential toxicity of the active metabolite, VVZ-368. Oral form of VVZ-149 will provide various development opportunities for various chronic pain including neuropathic pain.
- Licensing-out to global pharmaceutical companies will be expedited once the phase 2 studies of VVZ-149 injections are successful and phase 1 study for the oral form of VVZ-149 is ready.

Unmet Medical Need & Target Patients

- Analgesic market (>$60B) is a second biggest market, behind the market for anticancer drugs. Nevertheless, there are huge unmet medical needs in perspectives of safety and efficacy.
- So far, opioid analgesics and NSAIDs accounting for almost half of the market have been commonly used, but their various adverse effects have limited their use. The opioid analgesics induce nausea, respiratory depression, vomiting, itching, addiction, and tolerance etc. seriously limiting its flexible usage. The NSAIDs is widely used, however, they are not that effective for moderate-to-sever pain and cause a mechanism based ulcer in stomach or duodenum limiting their long-term use.
- Oral form of VVZ-149 will be developed for most chronic pain including migraine or neuropathic pain. The analgesic effect in arthritis (rheumatoid- or osteo-) has not been confirmed yet.

Status

- Preformulation studies have been started focusing various physicochemical properties of VVZ-149. The GLP toxicology study will be initiated at early 2016.

Intellectual Property

A. Patent Status

- Substance Patent:
  - Applied in 2011 (PCT/KR2012/010257 : NOVEL BENZAMIDE DERIVATIVE AND USE THEREOF)
  - Registered in Korea in 2015 (10-1542939)
- Mode of Action Patent:
  - Applied in 2011 (PCT/KR2012/005145 : COMBINATION OF EFFECTIVE SUBSTANCES CAUSING SYNERGISTIC EFFECTS OF MULTIPLE TARGETING AND USE THEREOF

B. Scope

- Worldwide

Competitive Advantages

- First-in-Class, non-opioid and non-NSAID analgesic
- Clear MoA : Dual-target Synergism, acting on both CNS and PNS
- Efficacy in animal studies : Comparable efficacy to morphine, clear dose-dependency, and proven PK/PD relationship in animal studies. All studies were conducted under complete randomization and blind test.
- Well studied plasma exposure levels for efficacy : Repetitive and consistent plasma exposure level for efficacy was confirmed in various animal models for neuropathic pain, formalin-induced pain, and postoperative pain. Human proof-of-concept is expected soon from the ongoing Phase 2 studies of VVZ-149 injections for post-operative pain and neuropathic pain providing early opportunity of out-licensing for the oral VVZ-149.

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Korea Institute of Science and Technology

Korea Institute of Science and Technology

A study on long-term in vivo efficacy and toxicity of KDS2010, a novel inhibitor of aberrant GABA synthesis

Code Number : KDDF-201509-06

Development and Market Objectives

- We found that reactive astrocytes aberrantly and abundantly produce the inhibitory transmitter GABA by over-expressed monoamine oxidase-B (MAO-B) in Alzheimer's disease (AD). Based on this novel target, we developed a lead compound, KDS2010, which showed potent and selective inhibitor of aberrant GABA synthesis and excellent drug-like properties in ADME/Tox. Thus we plan to evaluate KDS2010 for a pre-clinical candidate, which will serve as an effective treatment for memory impairment in Alzheimer's disease by targeting aberrant GABA synthesis in reactive astrocytes.

Unmet Medical Need & Target Patients

- Drug candidate: Inhibitor of aberrant GABA synthesis in reactive astrocytes for treatment of memory impairment in AD
- Target Patients: Alzheimer's disease (MCI to mild)
- Unmet Medical Need: There are major two categories for AD therapy. However, the existing AD therapies are only effective temporarily. Novel treatments with a long-term effectiveness are needed for the improvement of memory impairment in AD.
  - ChEIs [acetylcholine esterase inhibitors: (Aricept®, donepezil), (Exelon®, rivastigmine), (Razadyne®, galantmine)]
  - NMDA antagonist: (Namenda®, memantine)

Status

- KDS2010 shows excellent selectivity and efficacy for inhibition of aberrant GABA synthesis in reactive astrocytes in AD.
- KDS2010 fully restores the cognitive impairment of APP/PS1 mice in passive avoidance & Morris water maze test.
- It exhibits excellent drug-like properties in ADME/Tox and is confirmed off-target selectivity test (Eurofin, 87 safety panel for CNS)
- The safety evaluation of the candidate is ongoing (2 weeks repeated toxicity test with rat).
- The long-term effectiveness is being evaluated with low dose of the candidate in APP/PS1 mouse model (0.3, 1, 3 mg/kg).

Intellectual Property

- Patent application: Korea & PCT
- Preparation of patent application: end of 2016, (USA, EU, China etc)

Competitive Advantages

- A novel therapeutic strategy to address the disease-modifying therapy in AD through inhibition of aberrant GABA synthesis in reactive astrocytes.
- The candidate can be expanded for other disease indications by targeting aberrant GABA synthesis in reactive astrocytes.

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Jeil Pharmaceutical Co., Ltd.

JEIL PHARMACEUTICAL CO.,LTD.

Phase 2A Clinical Study of JPI-289 for the Treatment of Stroke

Code Number : KDDF-201512-08

Development and Market Objectives

- The aim of this project is to accomplish phase 2A clinical trial in acute ischemic stroke patients including evaluation of efficacy, PK/PD profiles, and safety/tolerability of JPI-289 at low and high doses, and to proceed phase 2B clinical development of the PARP-1 inhibitor, as a first-in-class drug for the treatment of stroke.
- Ultimately, after rapid completion of the Proof of Concept (POC, Phase 2A) clinical studies, Jeil Pharmaceutical is planning to license out, co-develop, and co-commercialize JPI-289 with global big companies.

Unmet Medical Need & Target Patients

- Stroke is a debilitating condition, with the highest death rate as a single organ disease. Incidence is expected to keep increasing over the next 20 years despite the progress in modern medical science and technology. This is largely due to a global increase in the aging population.
- No clinically effective therapies currently exist although the stroke incident rate in Korea remains high. Developments of new therapeutic strategies and standards of medical care are imperative.
- Currently, treatment for ischemic stroke with cerebral blood vessel occlusion predominantly employs a thrombolytic agent combined with surgery, and further agents including anticoagulants and platelet aggregation inhibitors for secondary prevention. Any new therapy for stroke is expected to be highly marketable, as the only thrombolytic agent, tPA (tissue Plasminogen Activator) has been approved by the FDA with limitations so far.
- Jeil Pharmaceutical will develop JPI-289, a PARP-1 inhibitor, on a commercial scale after acquiring Proof-of-Concept data via a combination therapy with tPA and/or thrombectomy in Phase 2A clinical trials. This will be followed by licensing-out and co-development with multinational partners.
- A homogeneous patient group will be selected for a combination therapy with tPA and/or thrombectomy for NDA approval, with the range of subjects and indications further expanded through PMS clinical trials.

Status

- A clinical protocol for a phase 2A clinical trial of JPI-289 was approved by Ministry of Food and Drug Safety (MFDS) and review by Institutional Review Boards (IRBs) of 8 Clinical Research Centers including Seoul National University Hospital is currently in progress.
- Administration and interim analyses for cohort 1, 2 will be performed in 2016, and based on the results, a dose for cohort 3 will be determined. Administration and analysis for cohort 3 will be started in 2017.
- A protocol for a phase 2B clinical trial in stroke patients will be developed by early 2018. After acquiring IND/IRB approvals for the phase 2B clinical trial of JPI-289, Jeil Pharmaceutical will enter phase 2B clinical trial during the second half of 2018.

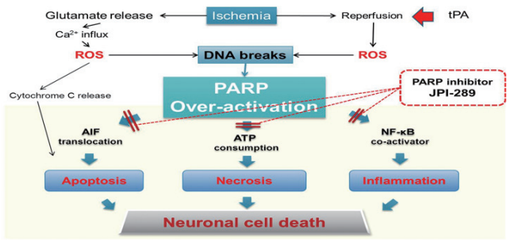
Intellectual Property

- Patent applications covering materials and preparation methods were submitted in 2008, and the registration was approved in 2010 in Korea (10-0968175), as well as in the US, Europe, China, Japan, Australia, Canada, Russia, Mexico, and Hong Kong during 2011 and 2015.
  - PCT: WO 2010/056038
- Application for the JPI-289 crystalline structure patent was submitted in 2012.
- In summary, one application in Korea and nine international applications have been registered, and review processes for registration of another application in Korea and six international applications are currently underway.

Competitive Advantages

- The majority of previous stroke candidates have been designed to inhibit apoptosis mechanisms; however, the clinical results have been inconclusive as most of the brain damages were caused by necrosis during the first 10 hours after the stroke occurs.
- JPI-289 inhibits the damages caused by necrosis, apoptosis and inflammation, at the same time, and is expected to exert significant benefits in the treatment of stroke.

Jeil Pharmaceutical Co., Ltd.



① Inhibition of PARP-1 is a significantly distinct mechanism of action when compared to other candidates and is expected to show high efficacy in clinical trials with ischemic stroke patients through the neuroprotective effects.

② Effective PARP-1 inhibition and the mechanism of action by MP-124 have been proven in a monkey model, which is the closest stroke primate animal model to human so far. In a monkey tMCAO stroke model, JPI-289 showed 49% decrease in infarction volume, which is the best result in the world when compared with that of 21% decrease in infarction volume by MP-124. Therefore, JPI-289 among PARP inhibitors is considered as one of the most promising agents for the treatment of stroke.

③ Safety of JPI-289 has been confirmed in healthy volunteers because there were no serious adverse events (SAEs) during phase 1 study. AUCs of JPI-289 in the blood were increased dose-proportionally.

④ JPI-289 is highly soluble with excellent PK parameters. Single doses of JPI-289 significantly decreased infarct volume in an SD rat stroke model. Therefore, it is expected to be suitable for acute ischemic stroke patients who are required a prompt administration and onset of efficacy.

⑤ When JPI-289 was co-administered with tPA in the rat embolic tMCAO models, the infarction volume and hemorrhage area were significantly decreased compared to those of tPA single treatment group.

⑥ Because JPI-289 can be taken as an oral administration due to relatively high bio-availability (rat: 66%, dog: 100%) as well as an injection, treatment of stroke with JPI-289 after discharge is predicted to be maximized.

⑦ JPI-289 has shown excellent safety profiles in non-clinical studies, leading to IND approval for Phase 1 clinical trials in healthy male subjects. This is in favorable contrast to MP-124, another leading candidate that has been in Phase 1 since 2009. Acquisition of clinical POC via rapid completion of Phase 2A is expected to endow an advantageous position in licensing-out to global big pharmaceutical companies.

⑧ After secure of clinical POC, the drug value will be maximized by expanding its application for other diseases (e.g. myocardial infarction, Delayed Graft Function, Acute Kidney Injury) and patient groups.

⑨ S100B, NSE will be scrutinized further to develop as a bio-marker of stroke in upcoming studies.

⑩ The synthetic process of JPI-289 has been established with API/DP production in cGMP facilities for Phase 1/2 trials. As a result, mass production for commercial purposes is tangible.

⑪ A huge market value has been established with monopolistic right until 2028.

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Bio-Pharm Solutions

Global Bio-Pharm/Life Science
B-PS
(주)바이오팜솔루션즈

Preclinical study of new chemical entity for orphan disease: infantile spasms

Code Number : KDDF-201512-10

Development and Market Objectives

- To obtain US FDA Phase 1/2 study approval for infantile spasms (also known as West syndrome), a rare seizure disorder that occurs in young children, usually under one year of age.
- To increase the value of the compound by applying for the US FDA's expedited review programs, which would result in faster review times and earlier marketing approval of our orphan drug for infantile spasms.

Unmet Medical Need & Target Patients

Target population

- 2 to 24-month-old infants presenting with spasms (myoclonic jerks) of the body, and hypsarrhythmia or modified hypsarrhythmia on video EEG recording.

Unmet Medical Needs

- A significant portion of children with infantile spasms are refractory to the currently approved treatments, adenocorticotropic hormone and vigabatrin, and thus a more effective treatment option is needed at this time.
- As the currently approved treatments for infantile spasms have significant side effects, an effective treatment with a superior side-effect profile is needed.
- Approximately 60% of children with infantile spasms develop other types of epilepsy, such as Lennox-Gastaut syndrome, as they age.
- Mental retardation occurs in 70-90% of children with infantile spasms.
- Drugs with antiepileptogenic properties may be needed to prevent children with infantile spasms from progressing to Lennox-Gastaut syndrome, other types of epilepsy and also side effects including mental retardation.

Status

- Phase 1 study to assess safety, tolerability and pharmacokinetics in healthy volunteers has been completed under a US FDA IND and Health Canada CTA.
- Juvenile toxicity studies to support clinical Phase 1/2 study approval are ongoing.
- Preparations for a pre-IND meeting with the US FDA and for the submission of an orphan drug designation application are ongoing.

Intellectual Property

- Composition of Matter Patent:
  - Filed in 2010 (PCT/KR2011/004862: PHENYLCARBAMATE COMPOUND AND MUSCLE RELAXANT CONTAINING THE SAME)
  - Received patent allowance in the US, Canada, Korea, Japan, and China.
- Process Patent:
  - Filed in 2011 (PCT/KR2011/010105: PROCESS FOR PREPARATION OF PHENYL CARBAMATE DERIVATIVES)
  - Received patent allowance in the US, Japan, Korea, and China.
- Method of Use Patent:
  - Epilepsy: Filed in 2011 (PCT/KR2012/011474: PHENYL CARBAMATE COMPOUNDS FOR USE IN PREVENTING OR TREATING EPILESY)
  - Pain: Filed in 2011 (PCT/KR2012/011470: PHENYL CARBAMATE COMPOUNDS FOR USE IN ALLEVIATING OR TREATING PAIN AND NEUROPATHIC PAIN): Received patent allowance in the US.
  - Stroke: Filed in 2011 (PCT/KR2012/011471: PHENYL CARBAMATE COMPOUNDS FOR USE IN PREVENTING OR TREATING STROKE): Received patent allowance in the US.
  - 11 other method of use patents are currently in patent prosecution.

Competitive Advantages

- Efficacy
  - Considerably superior efficacy compared to vigabatrin, an FDA approved drug, in a published symptomatic infantile spasms rat model.
  - Potent anticonvulsant properties in a broad spectrum of epilepsy models.
  - Potent efficacy in refractory epilepsy models, notably in models of benzodiazepine-resistant status epilepticus.
  - NIH/NINDS Anticonvulsant Screening Program has documented a comprehensive profile of the compound in a Red Book due to the excellent efficacy of the compound.

Bio-Pharm Solutions

• MoA
- Has a unique mechanism of action not presently associated with currently-used antiepileptic drugs.

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Yungjin Pharm. Co., Ltd.

YUNGJIN PHARM

US FDA Phase 2a Completion and KFDA Phase 2b Approval of YPL-001 (Chronic Obstructive Pulmonary Disease Drug)

Code Number : KDDF-201410-05

Development and Market Objectives

• YPL-001 is a natural product developed by Yungjin pharm for COPD treatment. It is the 1st Koran natural products with phase I IND approved by FDA and has been government funded project since 2011. Phase IIa is undergoing in 3 USA hospitals now and we are looking for licensing out partners or co-development partner after phase IIa.

Unmet Medical Need & Target Patients

Unmet Medical Needs

• Efficacy
- The primary unmet medical need of COPD is to find a treatment preventing the disease progression from stage 2 or 3 to stage 3 or 4

• Steroid sensitivity
- COPD patients have a tendency of reduced responsiveness to steroids as their disease progresses. So symptoms get worse even using steroids especially for stage 3 or 4 patients. Thus, to reduce corticosteroid resistance in patients is important in acute or frequent COPD exacerbations.

• Safety
- COPD requires long-term treatment. Most of existing treatments for COPD have safety issues. Development of product with less side effects is needed.

• Formulation
- Most COPD drugs are inhalant type which need patient education for usage. Oral dosage form is easy and convenient for dosing, usually cheaper than device type drug which is helpful especially in underdeveloped country.

Target patients

• COPD patients are classified based on their degree of severity - Mild (Stage 1), Moderate (Stage 2), Severe (Stage 3), Very severe (Stage 4). The ultimate and primary goal of treatments is to prevent exacerbation of COPD. For such purpose, long term safety and prevention the development of resistance should be secured. None of the existing drugs have been proven to stop the disease progression from Stage 1 or 2 to Stage 3 or 4. YPL-001 is for stage 2 or 3 patients to prevent COPD exacerbation.

Status

• Yungjin has completed Phase 1a (Single Ascending Dose Study) and 1b study (Multiple Ascending Dose Study). The IND and IRB have been done for Phase IIa and currently patients recruiting are ongoing.

Intellectual Property

• Patent registered: total 17 patents completed
- Korea(4), USA(2), Europe(6), Japan(1), China(1), India(1), Canada(1), Australia(1)

• Patent pending: Korea(1), US(1), PCT(2)
- Covering worldwide

Competitive Advantages

• Unique MoA
- Reduce inflammatory response and increase steroid sensitivity as HDAC2 activator (First In Class)

• Well- controlled CMC
- Phytoequivalence established
- Identified components (> 90 % (w/w))
- Standardized API by GAP*

• Formulation
- Oral dosage form: easy compliance compared to inhalants

• Exclusivity
- Well protected intellectual property through several patent application

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DONGWHA PHARM. CO., LTD.

DONGWHA PHARM SINCE1897

Pre-clinical study & clinical IND approval for the development of anti-allergic asthma drug

Code Number : KDDF-201512-03

Development and Market Objectives

- DW2008 is a natural product that inhibits both allergic inflammation and bronchoconstriction, and is currently under nonclinical GLP study for developing anti-allergic asthma drug. We plan to test on the toxicity and additional efficacy of DW2008 for global licensing-out, as well as for local launching.

Unmet Medical Need & Target Patients

Target population

- Asthmatic patients who are ranked at step2(Mild) ~ step5(Severe) of GINA guideline.
- Asthmatic patients, especially old age patients and pediatric patients, who show poor medication compliance in inhalation therapy.
- Asthmatic patients who are not improved with leukotriene receptor antagonists.
- Asthmatic patients who show steroid resistance.

Unmet Needs

- Inhalation Corticosteroids(ICS) are current 1'st line therapeutic drugs of asthma, which exert good anti-inflammatory activities. But, ICS also show lots of regional adverse effects, steroid phobia, poor medication compliance.
- Bronchodilators temporarily relieve asthmatic symptoms as relievers. But, they rather have risk for an asthma exacerbation in case of long term treatment, because they have not anti-inflammatory activities. They are also inhalers that cause poor medication compliance.
- Leukotrine receptor antagonists(LTRA) are oral asthmatic drugs with over 90% market share, and have good medication compliance. But, they are usually used as add-on therapy to ICS, due to their insufficient efficacy.
- Whereas there are inhaler combination drugs "ICS+LARB", there are no oral drugs with anti-allergic inflammatory effects and bronchodilation effects.

Status

- The candidate DW2008 is currently under GLP preclinical study according to OECD, ICH guideline in Korea
- The candidate DW2008 is currently under drug positioning study in 5 asthma subtype animal models and searching specific biomarkers for setting up optimal patient selection criteria.

Intellectual Property

- Patent pending: Korea (2) PCT(1)
- Covering worldwide

Competitive Advantages

- Efficacy & MoA
  - Dual effects (anti-allergic inflammatory effect and bronchodilation effect)
  - Superior effects of DW2008 versus Montelukast(allergy inflammation) or Ambroxol(Mucosal Secretion)
  - Th2/Th17 selectivity
  - Identification of multiple targets relating to anti-allergic inflammation and bronchodilation
- CMC
  - Well-controlled CMC
  - Using GAP(Good agriculture practice) certificated botanical material
  - Identification of over 80% components (in HPLC peak area)
- Compliance and Others
  - Better medical compliance than inhalation
  - Beyond indications to other allergic diseases or respiratory diseases, such as rhinitis, atopic dermatitis, and COPD.

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Bioneer Corporation

BIONEER Innovation • Value • Discovery

Selection of optimized lead compounds for preclinical studies for idopathic pulmonary fibrosis using a novel RNAi-based nanoparticle technology SAMiRNA™, with a goal of IND application

Code Number : KDDF-201312-11

Development and Market Objectives

- Our objective is to develop the effective therapeutic drugs for the treatment of Idiopathic Pulmonary Fibrosis (IPF), a respiratory fibrotic diseases. It will be the first siRNA-based therapeutic drug against IPF, fatal respiratory diseases with no available efficient drugs yet. We are developing multiple preclinical candidate substances for idiopathic lung fibrosis with overall evaluations of efficacy and PK/PD analysis, applying the SAMiRNA™ RNAi nanoparticle technology covered by patent protection.

Unmet Medical Need & Target Patients

Unmet medical need

- The mortality rate for lung fibrosis is extremely high, with a 5-year survival rate lower than 30%.
  - Esbriet® (Pirfenidone) and Ofev® (Nintedanib), which are approved by FDA in 2014, is expensive and exhibits limited efficacy. Urgent need for the development of new effective drug which can actively reverse the process of fibrosis
  - By developing potent antifibrotic agents, applications can be extended to diseases that are frequently accompanied by fibrosis (such as NASH, systemic scleroderma, etc).

Target patients

- Patients aged 50 and older, with lung fibrosis confirmed by high resolution computed Tomography (HRCT) or by surgical biopsy, with mild to moderate symptoms between 50% to 80% on a post-bronchodilator forced vital capacity pulmonary function test.

Status

- ***In-vitro* screening** : Several hundreds of siRNA molecules were in-vitro screened to find highly specific and potent siRNAs against these target genes. Hundreds of SAMiRNA™ have been synthesized and screened for the highly potent therapeutic candidates.
- ***PK/PD*** : PK/PD analysis of SAMiRNA was performed by in vivo imaging of biodistribution and real-time qPCR-based quantification of gene knock-down in various organs. SAMiRNA-IPF is delivered to lung only in the IPF induced model animals both of Bleomycin-induced and TGF-b transgenic model, consequently knock down.
- ***in vivo* efficacy test**: The efficacy of the SAMiRNA-IPF drug has been evaluated with TGF-ß transgenic & Bleomycin induced mouse models of pulmonary fibrosis. Based on these comprehensive evaluations, the candidates show the more significant therapeutic potential for IPF treatment than Pirfenidone of InterMune, Inc and FG-3019 (CTGF mAb) of Fibrogen, Inc.

Country	Application Date	Application Number	Registration Date	Registration Number	Name of Invention
KR	2009-05-14	10-2009-042297	2013-01-16	1224828	siRNA conjugate and preparing method thereof
KR	2009-05-14	10-2012-0069988	2013-03-05	1241852	
KR	2009-05-14	10-2012-0114011	2014-04-30	1392973	
US	2010-05-13	13/319885	2014-07-15	8779114	
US	2010-05-13	13/613071	2014-07-08	8772472	
US	2014-05-30	14/291,540	2015-12-15	9211343	
EP	2010-05-13	10775118	2015-08-26	2463371	
JP	2010-05-13	2012-510752	2015-06-12	5758381	
JP	2013-05-08	2013-098798	2015-08-28	5797688	
CN	2010-05-13	2010800213243	2015-07-01	ZL201080021324.3	
CN	2010-05-13	201210301551.2	2015-06-17	ZL201203015512	
CN	2013-04-25	201310147988.X	2015-09-16	ZL01310147988X	
CA	2010-05-13	2761794			
CA	2014-11-20	2,761,749			
AU	2010-05-13	2010248239	2015-05-07	2010248239	
AU	2015-01-13	2015200143			
BR	2010-05-13	1012141-2			
IN	2010-05-13	2336/MUMNP/2011			
RU	2010-05-13	2011150787	2015-07-01	2558258	
KR	2015-04-06	10-2015-7008814			Composition for the prevention or treatment of respiratory diseases including gene-specific double strand oligo-RNA
US	2015-04-05	14/433627			
EP	2015-04-05	13843342			
CN	2015-05-06	201380058057			
JP	2015-04-03	2015-535571			
AU	2015-04-05	2013325384			
CA	2015-04-05	2887069			
BR	2015-04-05	11-2015-007637-8			
IN	2015-04-05	1964/CHENP/2015			

Bioneer Corporation

Country	Application Date	Application Number	Registration Date	Registration Number	Name of Invention
KR	2016-01-26	10-2016-7002234			Respiratory disease related genes-specific siRNA, double-stranded oligo RNA molecules comprising the siRNA, and composition for the prevention or treatment of respiratory diseases comprising the same
US	2016-01-02	14/902,566			
JP					
CN					
EP	2016-02-03	14820458.9			
CA	2016-01-04	2917320			
AU	2016-01-22	2014284836			
RU					
BR	2016-01-05	BR 11 2016 000163 0			
IN					
MX	2016-01-07	MX/a/2016/000019			
KR	2015-04-06	10-2015-0048443			Novel double strand oligo RNA and pharmaceutical compositions for preventing or treating fibrosis or respiratory diseases containing the same
PCT	2015-04-06	PCT/ KR2015/003400			

Intellectual Property

- Patents for the SAMiRNA™ RNAi drug platform (siRNA conjugate and preparing method thereof) have been filed for domestic and major international markets, including patents for specific fibrosis-related genes. The period of monopoly by 2035 will be obtained in the major markets by follow-up patent applications with further studies.

Competitive Advantages

- Robust SAMiRNA™ technology fundamental patents for lung fibrosis-related siRNA sequences
- Synergy for the lung fibrosis treatment effect will be verified by administration of an siRNA cocktail simultaneously targeting two critical genes.
- Favorable comparisons for therapeutic effect in various animal models (TGF-β transgenic mouse model, smoking model, bleomycin-induced lung fibrosis mouse model)
- Market assessment will be faster due to a shorter clinical trial period, as idiopathic lung fibrosis medicines are classified as orphan drug.
- Potential extended applications for the diseases in other organs which are frequently accompanied with fibrosis symptoms (hepatocirrhosis, kidney fibrosis, etc).

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ImmuneMed Inc.

Development of newly defined antiviral drug that selectively acts on the virus infected cells

Code Number : KDDF-201406-08

Development and Market Objectives

- Virus Suppressing Factor (VSF) is an antiviral immunoglobulin that inhibits various pathological activities essential to viral replication. It specifically targets on receptor of virus infected cells and have been classified as an investigational new drug following lead candidate nomination and preclinical trials through the optimization of humanized VSF (HzVSF), providing a new concept for the treatment of viral diseases.

Unmet Medical Need & Target Patients

Target patients

- This candidate is under development for the treatment of hepatitis B and C. Infected patients with clinical symptoms caused by immunophathologic phenomena, such as inflammation arising from viral infection will be prioritized.
- Initial target indication
  Hepatitis C: There are an estimated 170 million international patients (with more than 350 thousand people dying from the disease each year), and more than 600 thousand domestic patients.
- Secondary target indication
  Hepatitis B: There are an estimated 400 million international patients (with more than 1 million people dying from the disease each year), and more than 2 million domestic patients.
- Tertiary target indication
  Other serious viral diseases that cause clinical symptoms arising from inflammation by virus infection.

Unmet medical needs

- The existing antiviral therapies are only effective for specified viral strains
- There is a strong unmet need for new therapies that can reduce the excessive immune reaction, such as inflammation caused by viral infection
- Novel treatments with a wide range of anti-viral and anti-inflammatory activity are needed for the treatment of patients who do not receive therapeutic benefit from existing drugs.
- A new drug that can synergize with existing treatment options for combination therapy is needed.

Status

- Epibase in vitro immunogenicity screening was performed for deduction of the candidate which was less active as immunogen in clinical usage. Efficacy test for HCV and HBV was carried out in vitro. The anti-viral efficacy against HCV genotype 1a, 1b and 2a of the candidate was tested and was similar with sofosbuvir (SOVALDI) which is currently used for the treatment of HCV. In addition, the candidate inhibited HBV cccDNA replication. And currently, the candidate is validating for efficacy against HCV and HBV using SCID/Alb-uPA mouse model which is engrafted with human liver. The candidate is also evaluating with the Woodchuck model using Woodchuck hepatitis virus (WHV) which shows the similar clinical symptoms with HBV-infected patients.
- To validate the efficacy of the candidate for Ebola, the experiment is performing in vitro and in vivo (guinea pig and HNP) at Biosafety Level 4 (BSL4) facility in University of Texas Medical Branch at Galveston, US.

Intellectual Property

- Patent Name: Novel anti-viral VSF protein and hybridoma producing same
  - 2 registration patents, 1 public PCT
  - Registration Countries: Korea, USA
  - Patent Registration Number / Registration Date
    United States of America, 7,514,082 / 2009.04.07.
    Republic of Korea, 0425030 / 2004.03.17.
    PCT, WO 2003064461 A1 / 2003.01.30.
- Patent Name: An antibody specifically binding to separated peptide derived from XXXX, or a fragment thereof binding to the peptide
  - 2 patent application
  - Applied Countries: Republic of Korea, PCT
  - Patent Registration Number / Registration Date
    Republic of Korea, 10-2015-0082132/ 2015.06.10
    PCT, PCT/KR2015/005917/2015.06.12

ImmuneMed Inc.

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Competitive Advantages

- In contrast to existing treatment options, we are developing a first–in-class humanized antibody that exhibits dual properties of antiviral and anti-inflammatory effects, which can selectively act on virus infected cells.
- There is a high likelihood for success, because the drug is phenotype-based, rather than target-based therapeutic.
- There are many opportunities of indication expansion in various acute and chronic viral diseases.
- It is expected to have synergy with both anti-viral and anti-inflammatory effects when used in combination with currently available antiviral therapies.

CrystalGenomics, Inc.

Development of IV/PO interchangeable antibiotics inhibiting fatty acid biosynthesis for MRSA

Code Number : KDDF-201412-14

Development and Market Objectives

- The objective is to develop an oral/IV switchable fatty acid biosynthesis inhibitor as a MRSA antibiotic by developing both the intravenous and oral formulations of CG400549, an antibiotic candidate which inhibits Fab I, an enzyme that plays a critical role in bacterial protein synthesis, through completion of phase 1 studies and obtaining phase 2 study approval for both formulations.

Unmet Medical Need & Target Patients

- Despite the fact that development of antibiotics for bacterial infections had made a significant progress, it had been confirmed that the bacteria will eventually develop resistance against specific antibiotics over time. This meant that the development of new antibiotics and the emergence of bacterial strains that are resistant to corresponding antibiotics, was an inevitable cycle that kept repeating itself and therefore, continuous development of novel antibiotics became an absolute requirement for treating bacterial infections.
- The prevalence rate of MRSA infection is rising globally and the reason why this bacterial strain is getting spotlight attention is the fact that it not only has resistance to existing antibiotics but also, it is the most common bacteria that causes hospital-acquired infections and, it could be fatal for the immunocompromised and week/elderly patients.
- Although antibiotics such as vancomycin, linezolid, daptomycin and others are currently available for treating MRSA, these are associated with not only significant adverse events but also, it has been recently been brought to attention that there are also resistance issues with these antibiotics. Therefore, development of new antibiotics with novel structure & target, superb efficacy and excellent safety profile, is needed.

Status

- Using the prototype oral formulation, high safety margin has been secured through single dose and multiple dose (28 days) toxicity studies. Additionally, up to 4~8 fold higher efficacy against currently available competitor products, has been confirmed.
- Safety in humans have been confirmed through phase 1 clinical studies and efficacy in humans have been confirmed in the phase 2a skin infection study conducted in the US where all recruited subjects infected with MRSA were completely cured after receiving CG400549.
- Devising future development plans to reflect the changed clinical study guidelines in accordance with the GAIN Act, a US legislation that went effective in 2013 and, simultaneously preparing a "bridging study" to enable use of the newly developed and improved oral formulation in the next stage.
- In parallel to development of the new oral formulation, development of an injectable formulation for human use has been completed. A focused development is underway as clues to dramatically improve the current injectable formulation, have been found.

Intellectual Property

- Fab I INHIBITOR AND PROCESS FOR PREPARING SAME
  - A compound which is effective for inhibiting Fab I, and a method for treating a bacterial infection.
  - Patent registered in PCT/KR, US, EP, CN, JP, CA and IN.

Competitive Advantages

- The mechanism of action of CG400549 is different from currently available antibiotics and has a novel chemical structure which has never been used as an antibacterial agent previously. New class antibiotic has been a rare occurrence in the field of antibiotic development as Pfizer's Zyvox was the first new class antibiotic in 30 years. CG400549 has demonstrated having the best efficacy when it was evaluated against other MRSA agents recommended by the Infectious Diseases Society of America (IDSA) for testing efficacy in MRSA strains derived from the actual patients. Also, its efficacy in humans was confirmed when 100% of subjects who were enrolled in the phase 2a study, were completely cured from the MRSA infection.
- CG400549 was designed from CrystalGenomics' proprietary structure-based novel drug discovery platform to attack a disease protein which does not exist in humans but critical for the survival of

CrystalGenomics, Inc.

super bacteria. Therefore, since CG400549 is able to eradicate super bacteria while having virtually no affect in humans, its superb safety profile stands out as one of the strongest differentiation attributes compared to other antibiotics. Based on the available clinical data thus far, the usual side effects associated with IDSA recommended MRSA agents which are diverse and serious, have not been observed with CG400549.

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Qurient

Qurient Therapeutics

Phase 1 Clinical development of Q203 : A novel drug candidate against MDR/XDR tuberculosis

Code Number : KDDF-201509-02

Development and Market Objectives

- Secure safety and tolerability of Q203 through single and multiple dose phase 1 studies in healthy volunteers, which enable proceeding to phase 2 studies in tuberculosis (TB) patients.
- Seek co-development opportunities for further clinical development of Q203

Unmet Medical Need & Target Patients

Target Patient Group

- Multi-drug resistant tuberculosis (MDR-TB) patients, who do not respond to current standard regimen.
- Drug susceptible and resistant TB patients who can benefit from Q203 treatment.

Unmet Medical Needs

- TB is a significant worldwide health problem. According to the World Health Organization (WHO), TB ranks as the second leading cause of death from an infectious disease worldwide, after the human immunodeficiency virus (HIV). Estimated 9.0 million people developed TB and 1.5 million died from the disease in 2013. In addition, globally, 3.5% of new and 20.5% of previously treated TB cases were estimated to have had multi-drug resistant TB (MDR-TB) or extensively drug resistant TB (XDR-TB) and global treatment success rate was only 48% and 22%, respectively. According to the Centers for Disease Control and Prevention (CDC) in the United States, the cost of hospitalization for one XDR-TB patient is estimated to average $483,000 USD.
- There had been no new drug approved for TB in past forty years until 2012. Shortcomings of recently approved drugs against drug resistant TB [bedaquiline (SirturoTM, Janssen) and delaminid (DeltybaTM, Otsuka, approved by EMA in 2013)] include unavailability of clear combination dosing regimen and/or safety concerns (QTc interval prolongation, abnormal hepatic function and/or increased risk of death). There is a need for additional medical therapies that act through novel mechanism of action in order to offer efficacy against both drug sensitive and drug resistant TB and to provide necessary options for combinational regimen, with an acceptable tolerability profile.

Status

- Q203 has shown potent efficacy in TB animal model.
- Q203 has shown potent bactericidal efficacy against MDR/XDR tuberculosis bacillus in clinical isolates.
- A novel mechanism of action - targeting the QcrB subunit of the cytochrome bc1 complex in the tuberculosis bacillus electron transfer system has been identified.
- Q203 has been shown safety through GLP toxicology and safety pharmacology studies in rodent and non-rodent species.
- Q203 has been approved for Phase 1 clinical trial from U.S. FDA
- Q203 has been designated as an Orphan Drug from U.S. FDA

Phase 1 clinical studies are now in progress in U.S.

Intellectual Property

- Q203 patent is registered in U.S, China, Singapore, New Zealand and under review in the other 20 countries.

Competitive Advantages

- **First-in-Class drug candidate:** Q203 has a novel mechanism of action such that Q203 deplete energy metabolism of TB by inhibiting M.Tb. cytochrome bc1 complex specifically.
- **Strong efficacy:** Q203 exhibits potent efficacy in chronic tuberculosis animal models at low dose strength.
- **Efficacy against drug resistant patient isolates:** Q203 demonstrated strong efficacy against MDR/XDR TB patient isolates.
- **High selectivity:** Q203 is highly selective for M. tb. Cytochrome bc1 complex against it bacterial or mammalian counterparts.
- **Potential improvement of patient quality of life:** Q203 demonstrated reduction of post-infection inflammation in lung during the animal studies, which may lead to reduced degree of lung damage after treatment

Qurient

- **Relatively low COG:** Relatively simple process route may lead to low COG in commercial production.
- **Safety:** Q203 demonstrated good safety and tolerability profile in the GLP pre-clinical studies.

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CJ HealthCare

Global Development of CJ-12420, the next generation acid suppressant

Code Number : KDDF-201404-10

Development and Market Objectives

- CJ-12420 belongs to a new class of acid secretion inhibitors called potassium-competitive acid blockers (P-CAB). Based on the outstanding pharmacology results of pre-clinical and phase 1 clinical studies, we would like to maximize the licensing value of CJ-12420 by executing preclinical and clinical studies for differentiated efficacy and long-term safety. CJ-12420, the next generation acid suppressant, is expected to be a global blockbuster drug with clinical development in the world's key "pharmerging" markets including China.

Unmet Medical Need & Target Patients

Target Patient Population:

- Target patients of CJ-12420 are people with acid related diseases such as peptic ulcer, gastroesophageal reflux disease, and H.pylori infection.

Unmet Medical Needs:

- Acid-related diseases means various digestive disorders associated with gastric acid including gastric ulcer, duodenal ulcer, erosive esophagitis, and non-erosive reflux disease, etc. Acid related diseases can be cured, or at least the symptoms can be alleviated significantly by inhibiting gastric acid secretion.
- It has been reported that these diseases are increasing due to aging, obesity, alcohol, and caffeine. We expect more than 250 million patients to exist in the global pharmaceutical market by 2020. Thereare more than $ 30 billion prescription drugs for gastrointestinal disorders by 2020, which is the largest market in the entire drug treatment industry.
- Especially, gastroesophageal reflux disease(GERD) is a disease type in developed countries and its incidence in the developed world is very high at about 20%. Due to the increasingly growing factors such as aging, obesity, mental stress, GERD incidence is continuously rising. GERD is the conditions of discomfort or complications due to the stomach contents reflux or back up into the esophagus. It is classified into erosive esophagitis (EE) and non-erosive reflux disease (NERD), and may cause severe complications. Heartburn and acid reflux symptoms are typical symptoms. GERD is a chronic condition in most cases, and its recurrence rate is very high.
- Acid suppressants have been the biggest-selling drugs worldwide since the release of H2 receptor antagonists in 1970s and introduction of proton pump inhibitors in late 1980s. Proton pump inhibitor(PPI) currently holds the major part of acid suppressant market, but has identifiable limitations related to its mode of action; it requires several days to achieve maximum suppression, is less efficacious when administered post-prandially, and has large individual differences. The purpose of this study is to develop CJ-12420, the next generation acid suppressant as a global blockbuster drug that overcomes the limitations addressed by currently available PPI.

Status

- CJ-12420 showed potent inhibitory effect on H+/K+-ATPase from human, pig, and dog. We also confirm the high selectivity between Na+/K+-ATPase and H+/K+-ATPase.
- CJ-12420 totally suppressed acid secretion in Heidenhain pouch (HP) dog compared to 80% inhibition of Revaprazan at 3mg/kg. Phase 1 results showed dose dependent acid suppression, potent efficacy and fast onset time. CJ-12420 is currently undergoing Phase III clinical trials after successfully concluding phase 2 clinical trials in Korea last year. Compared to existing antiulcer drugs, CJ-12420 has been shown to relieve symptoms more quickly with prolonged effects in clinical trials.

Intellectual Property

- Patents on substance and other subject matters are granted in the major countries including Korea, China, Honkong, and the United States.

Competitive Advantages

- PPIs, current mainstay of acid related disease, are acid-activated pro-drugs that require consumption of food for stimulation of proton pumps because they only bind to active proton pumps.

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CJ-12420, on the other hand, binds to both resting and stimulated pumps, which exerts potent efficacy under any gastric conditions.

- **Pharmacology**
  - Inhibition of both resting and activated gastric H+/K+-ATPase
  - Highly selective inhibition of gastric H+/K+-ATPase
- **Pharmacokinetics and Drug Metabolism**
  - Rapid absorption
  - Low risk for drug-drug interaction
- **Safety**
  - Safe and well tolerated in various clinical studies including 300 patients
  - No clinically significant liver toxicity reported
- **Pharmacokinetics/Pharmacodynamics**
  - Rapid absorption within 0.5 to 1.5 hour
  - Rapidly increased median pH>4
  - Complete control of NAB upon administration before bed
  - Remarkably similar acid suppression profile in both fed and fasting state

- We are planning to conduct preclinical and clinical studies for demonstrating distinctive efficacay/safety data in parallel with our own domestic phase 3 trial. Via those study results, we are expecting to enhance licensing value and to establish stable business foundation for global market entry. The important thing for licensee would be not only differentiated pharmacology and development risk but also domestic market entry of drug. Quicker market entry can make them achieve profit more. Therefore, the fast launch to their market make the drug very attractive and increase licensing value. We are also striving to maximize the licensing value through preemptive execution of long-term toxicity studies, and initiation of clinical development in China.

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Sookmyung Women's University

SOOKMYUNG WOMEN'S UNIVERSITY

Development of lead componds for rheumatoid arthritis therapy by using cytokine-derived peptide SIS-1

Code Number : KDDF-201404-04

Development and Market Objectives

- The development objective is to generate lead compounds as a novel therapy to treat rheumatoid arthritis based on a Erdr1-derived peptide SIS-1 that has been observed to exhibit anti-inflammatory effects and improvement of rheumatoid arthritis in CIA mouse model.

Unmet Medical Need & Target Patients

- Currently prescribed drugs to treat rheumatoid arthritis include TNF inhibitors, which are primarily focused on easing of symptoms rather than a cure of the disease. The percentage of patients reporting a 70% improvement in terms of symptoms is only around 15%, while that of the patient group with very low reactivity (patients who do not reach ACR20) is approximately 30%. In addition, considering drug resistance issues and severe side effects, the developments of new medicines that address these problems are critically needed.
- Recently, interest in the use of biologicals with a different mechanism-of-action to TNF inhibitors has been increasing. Therefore, needs of new developmental therapeutics with novel mechanisms has been recognized by the medical community.
- Our research team attempts to develop therapeutic lead compounds for rheumatoid arthritis therapy by using Erdr1-derived peptide SIS-1 with novel mechanism-of-action. It targets a novel inflammatory cytokine control mechanism by focusing on the fact that the amount of inflammatory cytokines such as IL-17 remains high after treatment in TNF-refractory patient groups. Evidence suggests that the amount of inflammatory cytokines such as IL-18/IL-32 increases in rheumatoid arthritis patients.

Status

- Establishment of the optimal efficacy of SIS-1 for RA therapy in CIA mouse model
- Generation of three lead compounds for RA therapy in CIA mouse model
- Verifying the inhibitory function of Erdr1/SIS-1/three lead compounds toward inflammatory cytokines
- Verifying the inhibitory function of Erdr1/SIS-1/ three lead compounds toward polarized Th17 cells
- Verifying the inhibitory function of Erdr1/SIS-1/ three lead compounds toward osteoclast differentiation
- Identification of two targets for Erdr1/SIS-1 binding

Intellectual Property

- PCT application PCTKR20131005912
- Domestic registration 10-1510941
- Domestic application 10-2012-0072513
- Domestic application 10-2016-0028227
- Domestic application 10-2016-0028229
- Securing of substance patent
- Progressing with patent protection in 10 major countries

Competitive Advantages

- Development of a novel therapeutic target that is highly effective on TNF inhibitor refractory patients by targeting a different mechanism to that of TNF inhibition.
- 'First-in-class' investigation of the therapeutic potential of Erdr1 which has been implicated with anti-cancer and anti-inflammatory effects
- Domestic licensing-out is in progress via joint research with domestic and overseas pharmaceutical companies through continuous contact. The possibility of a successful international licensing deal is high.

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HANDOK INC.

Clinical Development of Therapeutic Agent for Auto-Inflammatory Diseases

Code Number : KDDF-201404-05

Development and Market Objectives

- The final research goal is approval in Korea for 3 rare disease indications by 2017 and global or local licensing-out.

Unmet Medical Need & Target Patients

Target Patient Population

- CAPS(cryopyrin-associated periodic syndrome): NOMID(neonatal onset multisystem inflammatory disease), MWS(Muckle-Wells syndrome) and FCAS(familial cold autoinflammatory syndrome)
- SOJIA(systemic onset juvenile idiopathic arthritis)
- AOSD(adult onset still's disease)

Unmet Medical Needs

- No drug has been approved for the treatment of patients with CAPS, SOJIA, or AOSD in Korea. The patients with CAPS can be treated with Anakinra which is imported through Rare Disease Centre and covered by insurance, but Anakinra is inconvenient as it should be injected daily. The anti-IL-1 therapeutics such as neutralizing antibody and receptor typed biologics are not imported to Korea and these drugs are too expensive to use. SOJIA and AOSD cause more severe symptoms than general rheumatoid arthritis and there's no standard therapy to treat patients with SOJIA and AOSD. SOJIA patients can be treated with steroid but it could evoke severe adverse events with long term use especially for children and adolescents. And for the patients with AOSD, there's no approved drug globally with the indication of the disease and it is mainly treated with NSAID, corticosteroid and MTX (combined with corticosteroid). But the response rates for theses drugs are not favorable so clinical needs for the new drugs to treat with disease CAPS, SOJIA and AOSD are absolute.

Status

- A phase II clinical trial in patients with CAPS (cryopyrin-associated periodic syndrome) that was approved by Korean regulatory agency in Oct. 2015 is up and running.

Intellectual Property

Number	Registration number	Register	Patent Title	Country	Domestic/ Overseas	Registration Date
1	10-1333958	HANDOK INC	Human interleukin-1 acceptor antagonist-hybrid F c fusion protein	Korea	Domestic	Nov. 21, 2013
2	PCT/ KR2011/ 007809	HANDOK INC	Human interleukin-1 acceptor antagonist-hybrid F c fusion protein	Overseas	Overseas	Oct. 19, 2011
3	8883134	HANDOK INC	Human interleukin-1 acceptor antagonist-hybrid F c fusion protein	US	Overseas	Nov. 11, 2014

Competitive Advantages

- Inhibits both Interleukin 1-alpha and Interleukin 1-beta.
- With new hybrid Fc technology, in vivo half- life of the fusion protein is increased, and safety and convenience for patients has been improved significantly by eliminating ADCC and CDC function while retaining fusion protein activity levels.

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HanAll BioPharma Co., Ltd.

Development of New Antibody Therapeutics of Novel Mechanism for the Treatment of Severe Autoimmune Diseases

Code Number : KDDF-201410-02

Development and Market Objectives

- The final objective of this project is to develop a novel antibody drug, HL161, for the treatment of various autoimmune diseases mainly caused by autoantibodies.

Unmet Medical Need & Target Patients

- The first target indications are pathogenic IgG-mediated autoimmune diseases like pemphigus vulgaris, neuromyelitis optica and myasthenia gravis. In addition, immune complex-mediated glomerular diseases like lupus nephritis and membraneous nephropathy could be applied.
- There is no specific medicine for these indications. In the case of pathogenic IgG-mediated autoimmune diseases, high dose of steroid, high dose of IVIG therapy and plasmapheresis are current treatment option for the patients. However, current treatment options have significant limitations in terms of efficacy, safety and treatment cost. So, the development of a new treatment option is urgently required.

Status

- Two fully human anti-FcRn candidate antibodies were selected from human immunoglobulin transgenic rats.
- Candidate antibodies have high affinity to hFcRn and blocking effect against IgG:FcRn interaction.
- Fc-engineered HL161 antibodies were constructed to eliminate additional effector functions such as ADCC and CDC.
- Two final candidate antibodies, HL161AN, and HL161BKN remarkably reduce IgG levels up to about 80% in cynomolgus monkeys.
- Nonclinical Toxicity study is ongoing.
- Investigational New Drug (IND) for first-in-human study will be filed at Mar. 2017.

Intellectual Property

Country	Application No. Publication No.	Application Date Publication Date	Title	Status
PCT	PCT/KR2015/04424 WO2015-167293	2015.04.30 2015.11.05	ANTIBODY BINDING TO FCRN FOR TREATING AUTOIMMUNE DISEASES	Published
AR	20150103466	2015.10.26		Filed
TW	104135358	2015.10.28		Filed

Competitive Advantages

- There are concerns over an imbalance between supply and demand of plasma-derived product, IVIG, due to an increased demand for plasma. However, this supply and demand issues for HL161 anti-FcRn monoclonal antibody will be stable because it will be produced by recombinant technology.
- In the case of IVIG, the price for a single treatment reaches $10,000~20,000 with standard dosage of 1~2g/kg, but the treatment cost of HL161 will be significantly lower than IVIG since it will be effective at 10~20mg/kg in the patients.
- HL161 can effectively suppresses autoimmunity against autoantigens through increasing catabolism of pathogenic autoantibodies, thus exert therapeutic effect on various severe autoimmune diseases.
- HL161 shows excellent efficacy in comparison with IVIG and anti-FcRn antibodies that other companies are developing.

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CKD Pharmaceuticals, Inc

Development of CKD-506, an HDAC6 selective inhibitor, for rheumatoid arthritis treatment

Code Number : KDDF-201412-07

Development and Market Objectives

- CKD-506 is a current preclinical candidate to treat rheumatoid arthritis by repressing inflammatory cytokine and by inducing CTLA4 expression.

Unmet Medical Need & Target Patients

Target Patient Population

Methotrexate or biologics-resistant RA patients

- Rheumatoid arthritis (RA) is a chronic inflammatory disease which affects about 1% of world population. It usually results in severe joint pain and bone deformation.
- The goal of RA treatment is to improve symptoms and slow the progress of the disease. The first line therapy is methotrexate. However, in short term use, about 30 to 40% of RA patients develop resistance against methotrexate. In long term use, 80% of RA patients develop the resistance.
- If the methotrexate treatment for 3 months does not improve the symptom, the RA patients are prescribed with the expensive biologics drugs such as Orencia (CTLA4-Fc) or other TNFα neutralizing agents. For the last 10 years, the biologics use increased gradually.
- Some patients develop resistance against biologics drugs but the exact mechanism of resistance is unclear. One hypothesis of such resistance is anti drug antibody. It has been known that the anti drug antibody for about 30% of RA patients exposed to biologics reduces the efficacy of biologics due to the augmented clearance of the biologics.
- CKD-506 represses inflammation synergistically with methotrexate by reducing TNFα secretion and inducing CTLA4 expression even in the presence of anti drug antibody against biologics. Thus, it is strongly believed that CKD-506 can be used for both methotrexate resistant and biologics resistant patients.

Unmet Medical Needs

- Methotrexate may induce liver toxicity and methotrexate resistance as explained above.
- The demand of new oral small molecule drug is increasing to improve patient compliance (oral drug instead of IV injection) and to reduce high cost of biologics use (20,000USD/patients-year).
- Although tofacitinib, a new oral Jak3 inhibitor, was launched for the treatment of rheumatoid arthritis, it induces LDL cholesterol in a dose dependent manner (15% induction with 5 mg bid and 30% induction with 10 mg bid) and has an increased risk of carcinogenesis.
- Other drug candidates such as p38 MAPK inhibitor or Syk inhibitor have been discontinued due to toxicity or lack of efficacy.
- The demand on new oral small molecule drug is huge to enhance patient compliance and cost.

Status

- CKD-506 is at pre-IND stage
  - CKD-506 showed significant therapeutic efficacy in RA animal models.
  - Oral treatment of CKD-506 improved various inflammatory indices such as bone deformation and joint edema.
  - The action mechanism of CKD-506 can be applied to other inflammatory diseases such as inflammatory bowel disease (IBD).
  - The GLP toxicity and ADME study has been completed in global CRO.

Intellectual Property

- PCT was filed in 2014.
  - **Patent**: Novel compounds for selective histone deacetylase inhibitors, and pharmaceutical composition comprising the same
  - **Status**

	Application number	Filing date
KR	2014-0051151	2014-04-29
KR	PCT/KR2014/003776	2014-04-29

Competitive Advantages

- Orally available small molecule drug that potentially replaces the current biologics.
- Partnering Opportunity : Seeking for a global partner for development and commercialization

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Oscotec Inc.

Development of SYK inhibitor for Rheumatoid Arthritis

Code Number : **KDDF-201509-05**

Development and Market Objectives

- SKI-O-703 (mesylate salt of SKI-O-592) is currently under Phase I clinical studies for the treatment of rheumatoid arthritis in USA. SKI-O-703 inhibits spleen tyrosine kinase (SYK) which is well known as a characterized drug target for autoimmune diseases.
- The preclinical study was completed at the CRO in USA (2015). SKI-O-703 showed a good Tox profile and excellent safety margins in rat and dog via oral administration (>30-fold margin of safety).
- Our market objective is to out-license SKI-O-703 to a global pharmaceutical company. Oscotec Inc. aims to complete a phase I clinical trial in compliance with the US FDA.

Unmet Medical Need & Target Patients

Unmet medical needs:

- Low molecular weight drugs from the DMARDs family are the current gold-standard for treatment of rheumatoid arthritis. However, they suffer from low efficacy, frequent cases of non-responsiveness and a variety of adverse events.
- Biologics often exhibit reasonable efficacy, but many patients are non-responsive to them. Moreover, high costs, limited administration routes (injection is the only validated administration route) and potential tumor formation are points of concern in using biologics for anti-rheumatic applications. Therefore, the key unmet needs for rheumatoid arthritis medicines are summarized as follows:
  - Achievement of adequate therapeutic efficacy for patients who are non-responsive to existing medicines,
  - Management of adverse events to a lower level coupled with high selectivity,
  - Maintenance of economic feasibility through low molecular weight synthetic drugs,
  - Improvement in convenience via oral administration.

Target patient population:

- Patients with rheumatoid arthritis, those who are non-responsive to MTX and biologics.

Status

- The candidate SKI-O-703 is currently in phase I clinical study in compliance with the US FDA.

Intellectual Property

- The legal groundwork has been laid for the development of SKI-O-592 (free base of SKI-O-703), which will protect its novelty and competitiveness. Patents for key scaffolds were filed in US and 18 countries following PCT application and some of those including US were registered. A patent that includes SKI-O-592 has been filed for US and PCT patents.

Competitive Advantages

- Fostamatinib (R788) developed by Rigel Pharmaceuticals, Inc. jointly with AstraZeneca was discontinued after Phase III clinical trials due to low efficacy and severe adverse events which were caused from low selectivity. P505-15, from Portola Pharmaceuticals Inc. exhibited high selectivity, but revealed a high level of toxicity and low bioavailability.
- Our clinical candidate SKI-O-703 demonstrated a superior selectivity to SYK, an improved bioavailability and a low level of toxicity. It has been established from in vivo models that SKI-O-703 has better efficacy and safety characteristics when compared to existing SYK inhibitors. We are currently in contacts with global pharmaceutical companies for future out-licensing.

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Dinona Inc.

Development and preclinical study of MD3 antibody therapeutics for induction therapy of allo-islet transplantation

Code Number : **KDDF-201212-01**

Development and Market Objectives

- To develop an induction treatment for the suppression of adverse reactions resulting from allo-islet transplantation.
- Pre-clinical efficacy tests for candidate antibodies, MD3 have been completed and IND approval is scheduled for completion in the near future.

Unmet Medical Need & Target Patients

The target Patient

- The target patient group consists of Type 1 diabetes patients who require islet transplantation, and includes patients with adverse reactions to islet or pancreatic transplantation, as well as patients who require islet transplantation after a kidney transplant. Severe Type 2 diabetes patients who require insulin injections may also be suitable.

Unmet Medical Needs

- The drop ratio for allo-islet transplants within one year or less has significantly improved to between 3 and 5 percent, as a result of the development of efficient immune modulation technology. However, long-term transplantation success over a period of one year remains disappointingly low. The ratio of insulin independent patients five years after islet transplantation drops to approximately 15 percent. A key cause of this phenomenon is toxicity arising from the prolonged injection of immunosuppressive preservers. There is a critical need for research and development to address this problem.

Status

- MCB was established, the whole processes related CMC was completely developed. GMP manufacturing for IND is going to conducted in Q3~Q4, 2015. Also, Non-human primate toxicity study will be ended up by Q4, 2016.

Intellectual Property

- Patents : 2 registered
- PCT Applications : 3
- Scope/extent analysis currently being conducted in different countries
  - Material: A candidate antibody highly specific for human ICAM-1 and an additional antibody that recognizes both primate and human ICAM-1.
  - Indication: Adverse reaction of cell or organ transplantation, graft-versus-host reaction, autoimmune diseases.

Competitive Advantages

- Succeeded in transplanting the world's longest pig islet into a diabetic monkey.
- Induced antigen-specific T-cell immune tolerance in non-human primates.
- Confirmed that the immune reaction toward infection in animals injected with MD-3 antibody was within the normal range and that CMV was not re-activated.
- Throughout repeated primate tests, excellent efficacy and safety confirmed.
- Treatment can be used for islet transplantation, and also as an indicant for solid-organ transplants, repression of the formation of anti-drug antibodies (ADA) and autoimmune diseases.

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Hanyang University

(Hanyang University Department of Biology)

HANYANG UNIVERSITY

Generation of lead compound of transcutaneous delivery peptide (TDP) for atopic dermatitis

Code Number : KDDF-201312-15

Development and Market Objectives

- Our primary objective is to develop a safe and unique biomaterial for the treatment of intractable allergic disease (atopic dermatitis). A cell-penetrating peptide has been investigated with extensive research and developed into a transcutaneous delivery peptide, a drug delivery system that can penetrate the skin barrier.

Unmet Medical Need & Target Patients

Target Patients

- Atopic dermatitis is a chronically recurring typical allergy-type skin disease frequently accompanied by severe itchiness. The condition is widespread from toddlers to adults and the number of reported cases continues to rise. The primary target patients for our therapeutic are those with evident dermatitis symptoms including itching, dryness and eczema.

Unmet Medical Needs

- Common treatment modalities are prescribed according to treatment stage.

Degree	Treatment Stage	Treatment Method
Dry skin	1	Basic Treatment: Moisturization, inflammatory suppression, identification of allergen
Slight ~ Moderately Serious	2	Prescription of mild local steroid agents and a local calcineurin inhibitor
Moderately Serious ~ Serious	3	Prescription of a high potency local calcineurin inhibitor
Serious (incurable)	4	Systemic Treatment: systemic steroid prescription with cyclosporine A, UV treatment

Table 1. Common treatments for atopic dermatitis

- Progress in the development of safe and effective medicines for the treatment of atopic dermatitis has been limited (Datamonitor). This has been largely due to the fact that the modes of onset and pathological mechanisms have only been recently elucidated.
- Local steroid application is the most common treatment, but is only suitable for providing temporary relief due to side effects including skin shrinkage, blood vessel extension, bleaching, the appearance of purple spots and issues with the development of tolerance. Oral and intravenous steroid treatment is used for moderately serious atopic dermatitis. However, despite high efficacy, the steroid rebound effect is considered as a risk when prescribing this treatment. The side effect can manifest as growth impairment, obesity and other complications caused by an increased appetite. Similarly, high risks are associated with CyA and calcineurin inhibitors including red spots, flu symptoms and headaches when used continuously. As such, widespread dissatisfaction and considerable unmet medical needs exist for the treatment of atopic dermatitis.
- New treatments that are safer and address the underlying pathophysiology of atopic dermatitis are urgently needed.

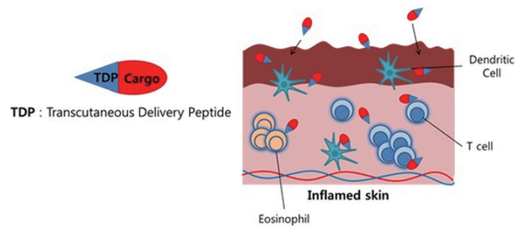
Status

- We have confirmed a highly effective human cell-penetrating peptide sequence that can deliver functional biomaterial (both protein and peptide) into cells.
- Optimization of the cell-penetrating peptide is ongoing, to improve the delivery of functional biological payloads into cells through the epidermis and dermis with high efficiency.
- Two types of candidate protein have been selected, based on the mode of action characterized for atopic dermatitis.

Intellectual Property

- Patents have been filed covering 6 types of cell-penetrating peptide, including sequence and domain information, as well as the cargo delivery functionality.
  (Application Numbers: 2012-0152966 / 10-2013-0120096 / 10-2013-0120095 / 10-2013-0120094).

Competitive Advantages



- This treatment is projected to deliver therapeutic proteins directly into cells safely and effectively using a cell-penetrating peptide based on a human protein sequence that is distinct from existing cell penetrating peptide methods (TAT, VP22: viral origin).
- Using proteins and peptides of human origin for skin treatment confers additional advantages in terms of safety and efficiency.
- The method for intracellular delivery of proteins and peptides for the inhibition of atopic dermatitis signalling is in an excellent competitive position because the market for atopic dermatitis treatment is still largely dependent on steroid agents, while the effect of newly-developed monoclonal antibodies have not been verified.
- In addition, the skin penetrating peptide currently under development has potential applications in diverse fields including not only atopic dermatitis, but also for other skin diseases and skin care needs.

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Medytox Inc.

Development of Novel T Cell Targeting Immuno-Modulators for Type 1 Diabetes Mellitus (T1DM)

Code Number : KDDF-201310-13

Development & Market Objectives

- We aim to develop a first-in-class disease-modifying medicine for Type 1 Diabetes Mellitus (T1DM) patients with minimized side effects.

Unmet Medical Need & Target Patients

- T1DM, juvenile-onset diabetes, is an autoimmune disease characterized by T cell-mediated destruction of pancreatic β cells, resulting in insulin deficiency and hyperglycemia. The incidence of T1DM has been growing rapidly, with an estimated 2 million T1DM patients worldwide and approximately 70 thousand in children under the age of 14 diagnosed annually. Although, injectable insulin therapy is an available life-saving first-line treatment, a significant unmet need exists for a highly reliable treatment option that can address the discomfort of daily subcutaneous injections and the side-effects of hypoglycemia.

Status

- We are currently developing human T cell-specific monoclonal antibodies (mAbs) and validating the candidates through in vitro/in vivo efficacy and reliability assessments. For further pre-clinical tests on selected mAbs, we have generated a transgenic T1DM mouse model, which express human TCR components. Evaluation of the selected mAbs is underway using the humanized transgenic T1DM mouse model.

Intellectually Property

- Two domestic and PCT applications filed, respectively.

Competitive Advantages

- In contrast to insulin-therapy which only alleviates symptoms, our goal is to develop a disease-modifying therapy with long-term efficacy (> 6 months). Our humanized transgenic T1DM mouse model facilitates developing superior candidates. We shall develop innovative biological immuno-modulators free from non-specific activation or side effects.

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Ewha Womans University

Development of intranasal insulin using TCTP-PTD

Code Number : KDDF-201402-01

Development and Market Objectives

- Our goal is to develop an alternative non-invasive method of insulin administration for diabetic patients who are treated with insulin injection. We are currently optimizing a nasal insulin candidate based on TCTP-PTD, originating from TCTP (translationally controlled tumor protein) which can facilitate the nasal delivery of insulin.

Unmet Medical Need & Target Patients

- Patients receiving long-term insulin therapy with invasive hypodermic injections can become averse to treatment due to pain, fear and issues related to discomfort. In addition, repeated injections can cause side effects including abnormal absorption and infections arising from skin damage. In particular, children and the elderly experience difficulty in self-administration using injectors. Therefore, the development of more user-friendly methods of insulin administration, alternative routes of insulin administration, is needed.

Status

- Using various analogues of TCTP-PTD, the lead optimization and pre-formulation study of a nasal insulin is underway.

Intellectual Property

- [A composition for improving of insulin transmucosal ability] - Patent registered in Korea (2015)
- [A peptide with ability to penetrate plasma membrane] – Patent application filed in Korea (2016)

Competitive Advantages

- Unlike PTDs derived from other virus or transcription factors, TCTP-PTD (which is derived from human protein, TCTP), is expected to be a safe and versatile approach for intranasal or noninvasive delivery of bioactive molecules such as insulin. Nasal delivery of insulin using TCTP-PTD may serve the user-friendly medications that are safe and effective for the treatment of diabetes, thereby improving the clinical usefulness of insulin therapy.

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Genexine, Inc.

Conduct and Completion of a Global Clinical Phase I Trial of a Next-Generation Human Growth Hormone Product

Code Number : **KDDF-201502-11**

Development and Market Objectives

- Global clinical development phase 2 for Adult growth hormone deficiency (AGHD) patients and approval of global clinical development phase 2 for pediatric growth hormone deficiency (PGHD) patient.
- The market objective is a global license out to major pharmaceutical company in global basis.

Unmet Medical Need & Target Patients

- For AGHD, the target population includes patients with pituitary growth hormone secretion disorder with brain tumors, radiation therapy or surgery after a brain hemorrhage, or decreased body profile.
- For PGHD, the target population includes pediatric patients with growth hormone secretion disorder or damage in the pituitary, or the growth curve of only 5cm/year or less than 2 SD score of growth in the age group, or patients with low blood sugar, depression and mental immaturity.
- When the therapeutic regimen requires more frequent treatment, the possibility of patient compliance tends to be decreased. This may result in growth defect as well as mental stress with reduced quality of life of patients. Some of the sustained release formulation to be used for a thick needle, this formulation may cause pain, injection site pain, this may be a serious problem, especially in children.

Status

- KDDF funded Phase 1 study with healthy volunteers has completed, the global clinical trials for AGHD study is completed up to the first and second groups received doses, this trial is approved in 8 countries including South Korean and France. Patient recruitment is underway for the third dose group.
- The global trial for PGHD patients is in the process of approval targeting 15 European countries including Russia and Spain.

Intellectual Property

- The hyFc, a proprietary platform technology developed by Genexine, Inc., is already protected by registered patents in many countries including the United States and Korea.

Competitive Advantages

- Development a bi-weekly or monthly administration product by using the hyFc technology
  - The hyFc was developed by hybridizing IgD and IgG4. The IgD portion of hyFc have characteristics of high hinge flexibility and IgG4 have long half-life by Fc region mediated by FcRn. It is also designed to remove ADCC and CDC functions. Long-acting mechanism of GX-H9 is mediated by FcRn recycling which allow bi-weekly or monthly administration.
  - GX-H9 has higher bioavailability when compared to Pegylation or other long-acting technologies. By using the hyFc technology, greater efficacy was shown with lower doses in animal models compared to existing products. Therefore, GX-H9 is expected to show superior efficacy in humans.
  - The hyFc technology not based on any chemical reaction but on the natural process, which should result in all natural protein metabolites. Therefore, this technology may have distinguished advantage in terms of adverse event during trials.

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Genexine, Inc.

Global Phase 2 study in pediatric patients (PGHD) of next generation human growth hormone drug (GX-H9) and global License out

Code Number : **KDDF-201509-12**

Development and Market Objectives

- Genexine has a platform technology called "hybrid Fc (hyFc)" designed for the long-acting Fc fusion proteins by hybridizing IgD and IgG4
- Genexine's hyFc growth hormone (GX-H9) has potential for differentiated best-in-class profile; safe and long-acting, without significant reduced efficacy
- Growth hormone market size is about $3.5 B in 2013 and expected to increase to $4.7 B by 2018 (Wall Street Journal 2014)

Unmet Medical Need & Target Patients

Unmet medical needs

- Much less pain due to less frequent injections using fine needle
  - High level of compliance guaranteed due to less frequent injections
  - High growth due to high level of compliance

Target patient

- Pediatric growth hormone deficiency (PGHD):
  - Growth hormone secretary impairment or deficiency due to an abnormal pituitary gland
  - Lowest 3% of common-age growth rate or growth less than 5cm per year (growth delay or dwarfism)
  - Short stature, low growth velocity for age, increased fat around waist, younger look and delayed tooth development
- Adult growth hormone deficiency (AGHD):
  - Adult onset associated with pituitary damage by surgery, brain tumor, infections, injury or radiation therapy
  - Childhood onset as a result of congenital, genetic, acquired or idiopathic causes
  - Overweight, increased body & abdominal fat, skin thinning & dryness, reduced muscle mass, low energy and low mood

Status

- On-going EU/KR Phase 2 study for growth hormone deficiency (GHD) patients in both adult and pediatric populations, and it is a co-development project with Handok, Inc.

Intellectual Property

- Issued: US, EU, Japan, China, Korea, Canada, Singapore, Israel, Australia, Russia
- Filed or under review: Brazil, Hong Kong, India

Competitive Advantages

- Efficacy related dose response robustness
- Safe and long-acting technology
- Straight forward manufacturing process
- Best weekly and first semi-monthly
- Strong IP protection of hyFc technology

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Yuhan Co., Ltd.

Preclinical in vivo study to evaluate the additional mechanism of action(MoA) and to demonstrate the enhanced therapeutic efficacy following the repeated dosing of YH14618

Code Number : KDDF-201404-09

Development and Market Objectives

- In a previous first-in-human study following single intradiscal injection of YH14618 in patients with degenerative disc disease suffering from chronic low back pain, YH14618 showed potential therapeutic efficacy. The objective of the current preclinical study is to generate robust molecular mechanistic data related to disc regeneration and pain control that may translate into enhanced clinical efficacy following repeated dosing of YH14618 in patients with degenerative disc disease.

Unmet Medical Need & Target Patients

Unmet Medical Needs

- Currently, there are no approved treatments that can modify degenerative changes in the disc.
- Pain killers have temporary efficacy, with concerns for side effects related to long-term use, while surgical intervention is not satisfying the needs of patients, despite high operation costs.
- Therefore, there is a high clinical demand for the development of safe and efficacious drugs that can modify the disease course and provide sufficient sustainable pain control.

Target Patient Population

- Patients with mild to moderate degenerative disc disease who have not experienced adequate control of chronic low back pain on NSAIDs or other conservative treatments.

Status

- A first-in-human clinical trial in patients with degenerative disc disease has been completed.
- An additional preclinical study is being carried out by a global CRO.
- A phase 2 clinical study is underway (YH14618-202; NCT02320019; KDDF-201408-07) with topline results expected in May 2016.

Intellectual Property

- International patents in over 20 countries have been granted, including patent registration in Korea.

Competitive Advantages

- Competitors such as cell therapies and recombinant proteins are being developed but their pharmacological efficacy on disc regeneration and pain control in patients with degenerative disc has not been confirmed.
- YH14618, a first-in-class disease modifying therapeutic for the treatment of degenerative disc disease, offers clinical benefit for both long term pain relief and prevention of disease progression.
- YH14618 is a peptide composed of natural amino acids with excellent safety and commercially competitive qualities.

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Yuhan Co., Ltd.

Phase 2b study of YH14618 for degenerative disc disease

Code Number : KDDF-201408-07

Development and Market Objectives

- YH14618 is a novel peptide under development as an intradiscal injection for the treatment of patients with symptomatic lumbar degenerative disc disease, to achieve the treatment goals of improvement in chronic back pain and prevention of disease progression via its modulatory effect on TGFβ1.
- The initial safety, tolerability and therapeutic efficacy of YH14618 has been investigated in a Phase 1/2a clinical trial (YH14618-201). The current study (YH14618-202; ClinicalTrial.gov Identifier: NCT02320019) is a double-blind, placebo-controlled clinical trial designed to establish proof-of-concept for the safety and efficacy of YH14618, by comparing the proportion of VAS (Visual Analogue Scale) responders, defined as those who achieve a ≥ 50% reduction from baseline score for low back pain, at Week 12 following intradiscal injection. Patients diagnosed with one or two symptomatic lumbar degenerative discs with persistent low back pain despite at least 3 months of conservative therapy are eligible.

Unmet Medical Need & Target Patients

Target Patient Population

- Patients diagnosed with one or two symptomatic lumbar (L1/L2 ~ L5/S1) degenerative discs, defined as a Pfirrmann grade of 2 to 4 (on MRI). Patients must have suffered from persistent low back pain with VAS ≥40 mm and modified Oswestry disability index (mODI) of ≥30%, despite at least 3 months of conservative therapy.

Unmet Medical Needs

- Low back pain is a common condition with approximately 80% of the population reported to experience the condition at least once during their lifetime. Although an estimated 5% of this population will develop chronic low back pain, only 20~40% of these patients respond satisfactorily to currently available treatments. Many factors can contribute to the onset of chronic low back pain, however, discogenic factors are known to be the major cause, affecting 26~42% of patients. Discogenic low back pain is a serious medical and social problem, with total health care costs in the United States estimated to exceed $100 billion per year. Degenerative disc disease can arise from the natural process of aging, but eventually becomes irreversible, and can begin when adolescents are in their twenties. Pain and the impaired mobility associated with degenerative disc disease typically affect adults between the ages of 30 and 50.
- Current treatment options for discogenic low back pain range from medicinal anti-inflammatory and pain relief strategies to invasive procedures including spine fusion and spinal arthroplasty. However, these treatments are limited to relieving symptoms, with no attempt to restore the disc structure. Additionally, there are unsatisfactory outcomes with surgical intervention due to high cost, complications, and recurrence of pain. None of the currently available treatment options satisfactorily meet the treatment goals for DDD which include long-term improvement in chronic back pain and restoration of disc structure.

Status

- First-in-human phase 1/2a clinical trial (YH14618-201) has been completed in a total of 50 patients with symptomatic lumbar disc degenerative disease.
- A 2b clinical study (YH14618-202) in a target of 320 subjects with lumbar disc degenerative disease is currently being conducted and the subject recruitment has been completed in Jan 2016.
- In vivo study using a rabbit model of degenerative disc disease is underway to evaluate the synergistic effect of repeated dosing (KDDF-201404-09).

Intellectual Property

- Patents have been granted in approximately 20 countries including the Republic of Korea.

Competitive Advantages

- Currently, for patients with degenerative disc disease and chronic low back pain, there is no approved treatment that addresses the underlying pathophysiology responsible for the disease. Pain

Yuhan Co., Ltd.

killers such as NSAIDs and other conservative analgesics have only temporary efficacy in general, with concerns for side effects related to long-term use. Surgical intervention is a significant undertaking and frequently does not comprehensively resolve the unmet needs of patients despite high costs. Therefore, a significant clinical demand exists for the development of safe and efficacious solutions that can modify the disease course and provide sufficient and sustainable pain control. YH14618, a first-in-class disease modifying peptide for the treatment of degenerative disc disease, is being developed as a differentiated therapeutic offering clinical benefit for both long-term pain relief and prevention of disease progression.

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OliX Pharmaceuticals, Inc.

Preclinical study and IND approval of anti-scarring therapeutics BMT101, self-delivering RNAi molecule

Code Number : KDDF-201408-14

Development and Market Objectives

- Our objective is to obtain preclinical safety data and complete an IND application/approval for BMT101, a new preventive medicine for intractable hypertrophic scarring, developed by using OliX's self-delivering RNAi technology.

Unmet Medical Need & Target Patients

- In general, hypertrophic scarring has an incidence which is 3 times higher in Asians and other ethnicities, compared to the Caucasian population. In the US, it has been reported that approximately 45% of patients who suffer from illnesses, surgical operations and burns end up with scarring, and in Asians and other ethnicities, approximately 44.6% will develop a hypertrophic scar.
- Surgical interventions, laser treatment, ointments and patch-type treatments continue to remain the most common treatments. However, these treatments typically have limited effects on reducing the hypertrophic scar. For more effective treatment and prevention, a treatment that eradicates the formation of the hypertrophic scar is needed. Currently, no FDA approved drug exists for this indication.

Status

- After asymmetric siRNA library sequence screening for CTGF, a key gene for the information of hypertrophic scars, our self-delivering RNAi technology was introduced to the corresponding sequence for the development of a new candidate substance, BMT101, for an anti-scarring therapeuticBMT101's anti-scar efficacy was verified in-vitro through the confirmation of its selective silencing effects for CTGF and other fibrosis factors
- Through PK/PD testing, BMT101 has been determined as only topically active, and it has been confirmed that there are virtually no side effects with systemic exposure.
- Using animal models of scarring, we have demonstrated the efficacy of BMT101 as an anti-scarring therapeutic and are currently undergoing IND-enabling preclinical studies.

Intellectual Property

- A patent is held for 'Novel siRNA Structure for Minimizing Off-target Effects and Relaxing Saturation of RNAi Machinery and the Use Thereof' (issue no. 10-0949791, issue date March 19th, 2010(Korea), PCT issued. Patent issued or pending in Europe, Japan, China, Australia, and USA)
- 'Nucleic Acid Molecules Inducing RNA interference with Cell-penetrating Ability and the Use Thereof (issue no. 10-1581655, issue date November 3rd, 2015(Korea). PCT issued. Patent pending in several key territories)

Competitive Advantages

- Our cp-lasiRNA technology enables self-delivery into cells without the need for delivery vehicles, such as cationic lipids or polymers, so there are no delivery vehicle-related side effects. Additionally, via pharmacodynamics test and preliminary toxicity test of BMT101, we have confirmed the low possibility for side effects due to systemic exposure.
  - Unlike the conventional siRNA, when treated with BMT101, the quantity of IFN-α was almost identical to the negative control group, and this suggests that BMT101 does not elicit non-specific immune effects.
  - Through the development of a new intractable anti-hypertrophic scarring therapeutic, BMT101, it may be possible to expand its indication to other diseases that are related to fibrosis from overexpression of CTGF.
    BMT101 is 10 times more potent than other competing candidates and has outstanding competitiveness in terms of side effects and cost of production.

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HANDOK INC.

Development of Anti-Glaucoma Drug with a Novel Mechanism of Action

Code Number : KDDF-201410-09

Development and Market Objectives

- To discover and develop a preclinical candidate with novel mechanism, good efficacy and excellent safety profile for novel treatment options for glaucoma patients.

Unmet Medical Need & Target Patients

- There are approximately 583,000 patients suffered from glaucoma in South Korea and about 66% of patients are over 50's in age. Various treatment options including prostaglandin derivatives are well-established, however, there are highly unmet medical needs in that significant percentage of glaucoma patient population does not respond to the standard medications in terms of IOP (IntraOcular Pressure) reduction, and some patient groups demonstrate a variety of side effects.
- Therefore, a novel therapeutics, as a single agent and/or combination with current drugs, in order to overcome the current issues is highly needed in the glaucoma market

Status

- We have identified a novel target as well as its new mechanism of action, and we have successfully validated a possibility that its antagonism would provide first-in-class therapeutics for glaucoma treatment. The current lead series compounds showed excellent efficacy in vitro and in vivo.
- Currently, the project is at the lead optimization stage, through which the compound profile is being improved and will be ready for preclinical candidate selection.

Intellectual Property

- The patent for materials was submitted to the USPTO in Jan. 2016

Competitive Advantages

- This is a first-in-class glaucoma therapeutics with the goal to have superior efficacy and lower side effect over current standard therapies.
- Due to its novel mechanism, which has never been explored in glaucoma therapeutics, it would show a good efficacy with sufficient IOP reduction especially in the patients who do not respond sufficiently to the current standards. And with the same reason, it may well have a synergistic efficacy in combination with standard therapies, which would provide another rationale to use this compound to the refractory patient groups. Overall, compounds having abovementioned features will generate a good market share in the glaucoma therapeutic sector.

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Enzychem Lifesciences Corporation

The development of a new oral drug to treat Chemotherapy Induced Neutropenia (CIN)

Code Number : KDDF-201410-10

Development and Market Objectives

- Neutropenia is a common dose-limiting toxicity during the treatment with myelosuppressive cancer drugs. Chemotherapy-induced neutropenia (CIN) often leads to a dosing delay and/or reduction of dose resulting in the compromised chemotherapy. The current standard of care is a parental product (G-CSF), and it suffers from various side effects and limited use only in febrile neutropenia. Our goal is to develop an orally efficacious drug that can be generally applicable to both febrile and afebrile neutropenia with an excellent safety profile.

Unmet Medical Need & Target Patients

- A recent review reported that 16.8% out of 2,131 patients who received various chemotherapies experienced febrile CIN (J Oncol Pharm Pract 20 (3): 190, 2014). Another review reported that 10.7% out of 2,692 cancer patients experienced febrile CIN, and 29.3% experienced Grade 3-4 CIN (febrile and afebrile combined). (J Natl Compr Canc Netw. 6:109, 2008.)
- In the clinic, G-CSF injection is the standard of care to increase the numbers of neutrophils and to prevent infection. However, G-CSF products are expensive, inconvenient to use, indicated to only febrile neutropenia, and problematic due to several side effects/toxicities such as pain, fever, rash and splenic rupture, etc. Therefore, a new therapeutic agent that can overcome the various issues of current therapy, G-CSF, in terms of convenience, target patients, cost and safety is warranted.

Status

- The core battery of safety studies testing up to the maximum doses of 2000 mg/kg in the nonclinical animals did not raise any safety concern. A variety of nonclinical studies and Phase 2a study demonstrated the efficacy of EC-18 after oral administration. The mechanism of actions of EC-18 shows attenuation of chemotherapy-induced neutrophil extravasation from blood vessels. Phase 1 clinical study was successfully finished in US and Korea. Currently, phase 2 clinical trial is under preparation. In addition, various investigations including formulation optimization, absorption mechanism, DMPK, and toxicity are ongoing.

Intellectual Property

- Method for treating, controlling or mitigating neutropenia comprising administration of a monoacetyldiacylglycerol
- Methods for treating, controlling or mitigating neutropenia and other conditions, comprising administration of a monoacetyldiacylglycerol simultaneously, sequentially or in combination with a granulocyte colony stimulating factor (G-CSF)
- Methods for treating, controlling or mitigating neutropenia and/or thrombocytopenia, in patients receiving chemotherapeutic agents, such as lenalidomide and monoacetyldiacylglycerol

Competitive Advantages

- Patient population: G-CSF is mostly indicated for febrile neutropenia whereas EC-18 can be used in both febrile and afebrile neutropenia (Grade 3-4).
- Route of administration: G-CSF is administered parentally whereas EC-18 is an oral drug.
- Superior efficacy: G-CSF cannot be administered until 24 hours after the completion of chemotherapy whereas, EC-18 can be administered prior to the initiation of chemotherapy to effectively prevent neutropenia.
- Safety: Common side effects of G-CSF include pain, fever, rash and splenic rupture, whereas those were not found in EC-18 so far.

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Enzychem Lifesciences Corporation

ENZYCHEM LIFESCIENCES

Global phase 1 clinical development of new oral drug for the treatment of Chemotherapy Induced Neutropenia

Code Number : KDDF-201506-03

Development and Market Objectives

- Neutropenia is a common dose-limiting toxicity during the treatment with myelosuppressive cancer drugs. Chemotherapy-induced neutropenia (CIN) often leads to a dosing delay and/or reduction of dose resulting in the compromised chemotherapy. The current standard of care is a parental product (G-CSF), and it suffers from various side effects and limited use only in febrile neutropenia. Our goal is to develop an orally efficacious drug that can be generally applicable to both febrile and afebrile neutropenia with an excellent safety profile.

Unmet Medical Need & Target Patients

- A recent review reported that 16.8% out of 2,131 patients who received various chemotherapies experienced febrile CIN (J Oncol Pharm Pract 20 (3): 190, 2014). Another review reported that 10.7% out of 2,692 cancer patients experienced febrile CIN, and 29.3% experienced Grade 3-4 CIN (febrile and afebrile combined). (J Natl Compr Canc Netw. 6:109, 2008.)
- In the clinic, G-CSF injection is the standard of care to increase the numbers of neutrophils and to prevent infection. However, G-CSF products are expensive, inconvenient to use, indicated to only febrile neutropenia, and problematic due to several side effects/toxicities such as pain, fever, rash and splenic rupture, etc. Therefore, a new therapeutic agent that can overcome the various issues of current therapy, G-CSF, in terms of convenience, target patients, cost and safety is warranted.

Status

- The core battery of safety studies testing up to the maximum doses of 2000 mg/kg in the nonclinical animals did not raise any safety concern. A variety of nonclinical studies and Phase 2a study demonstrated the efficacy of EC-18 after oral administration. The mechanism of actions of EC-18 shows attenuation of chemotherapy-induced neutrophil extravasation from blood vessels. Phase 1 clinical study was successfully finished in US and Korea. Currently, phase 2 clinical trial is under preparation. In addition, various investigations including formulation optimization, absorption mechanism, DMPK, and toxicity are ongoing.

Intellectual Property

- Method for treating, controlling or mitigating neutropenia comprising administration of a monoacetyldiacylglycerol
- Methods for treating, controlling or mitigating neutropenia and other conditions, comprising administration of a monoacetyldiacylglycerol simultaneously, sequentially or in combination with a granulocyte colony stimulating factor (G-CSF)
- Methods for treating, controlling or mitigating neutropenia and/or thrombocytopenia, in patients receiving a chemotherapeutic agents, lenalidomide, and monoacetyldiacylglycerol

Competitive Advantages

- Patient population: G-CSF is mostly indicated for febrile neutropenia whereas EC-18 can be used in both febrile and afebrile neutropenia (Grade 3-4).
- Route of administration: G-CSF is administered parentally whereas EC-18 is an oral drug.
- Superior efficacy: G-CSF cannot be administered until 24 hours after the completion of chemotherapy whereas, EC-18 can be administered prior to the initiation of chemotherapy to effectively prevent neutropenia.
- Safety: Common side effects of G-CSF include pain, fever, rash and splenic rupture, whereas those were not found in EC-18 so far.

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Taejoon Pharmaceutical Co., Ltd.

TAEJOON PHARM

Nonclinical studies of novel antibody TJO-054 for treatment of wet AMD

Code Number : KDDF-201509-15

Development and Market Objectives

- First-in-class anti-VEGFR2 antibody for treatment of wet AMD
  - Nonclinical study of ocular PK/toxicity and IND approval for Phase 1 clinical trial
  - Manufacturing the material TJO-054 for clinical study phase 1
  - Pre-formulation study to develop the high concentration antibody product suitable for intravitreal injection

Unmet Medical Need & Target Patients

- Wet age-related macular degeneration (wet AMD) is the leading cause of severe vision loss in people over age 60.
- Anti-VEGF-A therapy, Lucentis® and Eylea®, for neovascular AMD has become a standard treatment for neovascular AMD. However, developments of new treatments are needed due to induction of unresponsiveness to some patients with current treatment.
- Taejoon's TJO-054 aims to target wet AMD patients including the non-responders to current anti-VEGF-A drugs.

Status

- Nonclinical efficacy test shows that TJO-054 has inhibitory effects of wet AMD.
- Safety of TJO-054 has been approved in a phase 1 clinical study of systemic administration to solid cancer patients.
- We are planning to get IND approval of phase 1 clinical trial for ocular administration.
- It is shown that TJO-054 is the only antibody that possesses cross-species cross reactivity for rodents in the scope of all the VEGFR-2/KDR targeting antibodies. Thus, TJO-054 can evaluate efficacy and safety in rodent models and can easily find availability for expanding indications by translational research.

Intellectual Property

- Taejoon Pharm. possesses global commercial/business rights of TJO-054 for ocular indication (including wet AMD) by a license contract with original developer.
- It is expected to apply for additional patents once TJO-054 confirms any new mechanism or newly high concentration formulation is developed for suitable ocular administration.

Competitive Advantages

- TJO-054 is a fully human monoclonal antibody to bind VEGFR-2/KDR on abnormal vasculature related to new angiogenesis diseases including wet AMD and cancers.
- In choroidal neovascularization, the main cause of wet AMD, VEGFR2 signaling by not only VEGF-A but also VEGF-C, -D is also important. However, current anti-VEGF drugs (Lucentis® and Eylea®) cannot block VEGFR2 signaling by VEGF-C and –D. In contrast, TJO-054 is able to block VEGF signaling by VEGF-C, -D as well as VEGF-A, thus expects to improve the efficacy as well as reduce unresponsiveness compared to current treatments.

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Korea University

고려대학교 KOREA UNIVERSITY

Development of therapeutic agent for duchenne muscular dystrophy by targeting NMD

Code Number : KDDF-201304-03

Development and Market Objectives

- To develop a medicine for hereditary conditions including duchenne muscular dystrophy (DMD), a rare disease arising from nonsense mutations, by developing novel compounds through cellular-based screening and optimization.

Unmet Medical Need & Target Patients

- DMD is a rare disease, but affects more than 30,000 people in America and Europe. No lasting treatment for DMD currently exists on the market.
- The development of treatments that can improve dystrophin protein expression, a primary factor in DMD, is critically needed.
- Other hereditary diseases derived from nonsense mutations can potentially be diagnosed by genomic analysis, but current medicinal methods are very limited.
- Hereditary diseases that arise from nonsense mutations cause more serious symptoms than those of other genetic disorders. Therefore, radical treatments targeting these diseases are urgently needed.
- Prolonged treatment with a low molecular weight compound is ideal.

Status

- NMD / Researching and discovering inhibitor nonsense mutations
- Lead materialization of identified lead candidates
- Currently in progress with research to explore the possibility of clinical trials with DMD patients.

Intellectual Property

- The pathological cause of rare diseases derived from nonsense mutations and DMD is relatively simple. For the case of DMD, the function of dystrophin is downregulated, and therefore, the conduct of preclinical-clinical translation for radical treatments is expected to be easier than for other diseases. This allows project planning in the near future for the discovery of new compounds without patent infringement.

Extent of Patent

- New compounds that inhibit NMD specifically, and their derivatives.
- The new compounds in # 1, and protein translation inhibitors and their derivatives
- The new compounds in # 1 and hereditary disease medicines and their derivatives

Competitive Advantages

- Our research team is currently in the process of discovering NMD inhibitors by targeting all stages of NMD using an NMD-relevant cell line optimized for inhibitor screening. Inhibitors discovered from this process will have a big advantage in that we can apply it to DMD which arises from NMD, and many other hereditary diseases.
- This research will be undertaken through cooperation with the Green Cross Corp., a leading pharmaceutical company in Korea that has successful experience in developing new drugs, and Professor Chae Jong Hee's team from Seoul National University Hospital, whose primary research focus is in DMD clinical trials.

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