KOREA-SINGAPORE R&D JOINT CALL
PRE-PROPOSAL APPLICATION FORM

Title	Therapeutics development for Idiopathic Pulmonary Fibrosis using BMT101, a pre-validated oligonucleotide drug inhibiting fibrosis
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Brief Description of Proposed Collaboration (Not to exceed 2 pages)

1. Research Aims

- List briefly the key aims/objectives of the research.

Project Goal: We will test the BMT101, an anti-scar oligonucleotide drug candidate inhibiting fibrosis, to Idiopathic Pulmonary Fibrosis (IPF) animal model. By validating therapeutic efficacy and safety, we will expand the application of BMT101 to IPF therapeutics, and partner or license-out with global pharmaceutical companies.

1st year goal: Test BMT101 in IPF animal model to validate the efficacy to inhibit pulmonary fibrosis as well as to observe general toxicity
2nd year goal: To develop BMT101 into IPF therapeutics, establish lung delivery method as well as secure comprehensive efficacy data, PK/PD and toxicity data. Based on these data, file IND by the end of 2nd year and partner/license-out with global pharmaceutical companies.

2. Research Need & Problem

- What are the need of this research and the problem of the precedent study?

Idiopathic Pulmonary Fibrosis (IPF) is a disease in which lung tissue undergoes severe fibrosis (like scar) over time by unknown cause. Many people live only about 3 to 5 years after diagnosis, mostly due to respiratory failure.

Approximately 70,000 patients in US and EU suffer from IPF. No effective cure exist except lung transplantation. Therefore, there is a great need to develop therapeutics which can slow the progress of IPF and prevent the loss of lung function.

IPF therapy market across the US and European Union (EU) will be worth more than $1.1 billion by 2017. It represents a commercially attractive patient population size with a financially appealing orphan drug status.

Currently, the only approved drug for treating IPF is Esbriet (pirfenidone) by InterMune, a small molecule drug with anti-fibrotic and anti-inflammatory activity. Pirfenidone is currently in market of EU, Japan and other countries but hold a problem of high cost with low efficacy. In addition, it is still not approved by US FDA due to toxicity and side effect.

Therefore, there is a great need to develop novel IPF therapeutics which can effectively inhibit or reduce lung fibrosis of patients as well as minimize side effects.

3. Solution Overview

- What is the proposed solution and why do you think it will work?

In this proposal, we will develop novel IPF therapeutics using BMT101, a pre-validated oligonucleotide which can inhibit fibrosis.

BMT101 effectively suppresses expression of connective tissue growth factor (CTGF) via RNAi mechanism. It shows efficient target gene silencing activity and does not trigger any toxicity based on

animal toxicology study. Currently, BMT01 is under development as an anti-scar therapeutics for wounded skin.

Several studies demonstrated that CTGF level is upregulated upon fibrosis process of IPF lung tissue, which results in excessive fibrosis. Thus, anti-fibrotic activity of BMT101 by inhibiting CTGF expression can lead to effective IPF treatment by delaying or inhibiting lung fibrosis of IPF patients.

The unique strategy of our proposal is to use a therapeutic molecule already validated for its efficacy and toxicity, which can result in acceleration of processes to clinical trial. We expect that, within two years, we will be able to complete IPF animal model efficacy and toxicology study to file IND. At the stage of entering clinical trial, we will partner or license-out this novel IPF therapeutics.

4. Solution Impact

- If successful, what is the potential impact of the solution?

By successful completion of this project, we will be able to develop safe and effective therapeutic modality for IPF, which currently has very limited options for treatment.

We expect to be able to secure significant portion of IPF therapeutic market, which is estimated to be $1.1 billion in 2017.

By collaborating with Singapore research team, our fundamental technology can be improved to the level of global standard, which can help partnering/licensing-out with global pharmas.

By expanding the application of BMT101, an anti-fibrotic drug, we can develop other therapeutics including anti-liver fibrotic drugs etc.

5. Collaborative Planning

- What is the proposed collaborative planning with Singapore A*STAR research team?
- What is your expectation for A*STAR team's research?
- How will the research leverage the expertise in Korea and Singapore?

For the successful execution of this project, we plan to organize activities between Korea and Singapore research groups.

Korea(BMT Inc.): Validate the anti-lung fibrotic efficacy of BMT101; toxicology and PK/PD study
Singapore(A*STAR): lung fibrosis animal model; optimization of oligonucleotide delivery to lung; formulation for clinical study

By integrating our technology for therapeutic molecules and the drug/gene delivery technology of A*STAR Nanobiotechnology research group, we expect to successfully develop IPF therapeutics.

Throughout the research progress, we will closely collaborate with Singapore research group to complete the mission within the time schedule. For this, we will organize mutual visit and research, as well as research progress meeting in every quarter.

At the point of successful development of IPF therapeutics, we will actively market the drug to Big Pharmas located in Singapore, to complete partnering/license-out within the schedule of this project.