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

Title	Preclinical Evaluation of the Renal Denervation System for Resistant Hypertension
Korea Principal Investigator	Park Jaehyung, PhD

Brief Description of Proposed Collaboration (Not to exceed 2 pages)

1. Research Aims

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

- Handok is developing the first generation renal denervation system (renal artery ablation catheter and dedicated radio-frequency generator) for resistant hypertension. World-wide market size for resistant hypertension could reach about 20B in USD (Transparency Market Research/Wall Street Journal Report).
- By utilizing the Korea-Singapore R&D Joint Call, Handok plans to evaluate the first generation through the preclinical GLP test in order to launch clinical studies and market release in time. The other goal is to test the feasibility of several features that can be implemented in the upcoming 2nd and 3rd generation system through a separate preclinical study.

2. Research Need & Problem

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

- The current catheter in market is mainly using a single electrode that access to renal arteries through femoral approach.
- This catheter delivers RF energy to create 6 to 8 lesions along each renal artery. The procedure takes 30 to 40 minutes, and highly depends upon operating physicians.
- The procedure requires highly trained physicians. Because it is difficult to validate whether the lesions are created at the optimal. Naturally, the procedural safety can be hard to be validated.

In addition, no features are available for checking the procedural effectiveness at pre, intra and post procedure.

- Handok is developing the renal denervation systems that can provide solutions, but has difficulties in evaluating the systems through the preclinical GLP test because there is no GLP lab in Korea, which is specialized for evaluating the cardiovascular products using large subjects.

3. Solution Overview

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

- Handok has already created a few patents for catheter design, and developed the first generation system that can enable the femoral and radial delivery. This system can also create simultaneously the multiple, optimally spaced lesions along the renal arteries, which could significantly reduce the procedure time, and improve the safety and effectiveness of the procedure. To launch the clinical studies and product release successfully, Handok plans to accomplish the preclinical GLP test through the R&D Joint Call.
- In addition, like the other products in the current market, Handok's first generation system would not be equipped with the features that can measure the procedural safety and effectiveness. Handok plans to test the feasibility of several features that can be implemented in the upcoming 2nd and 3rd generation system through a separate preclinical study.

4. Solution Impact

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

- Handok plans to complete developing the first generation system in 2014, to launch the first clinical study by Q2, 2015, and to enter the market by Q1, 2017.
- The objective preclinical GLP evaluation and report by the accredited center should speed up Handok's clinical and commercial plans greatly. In addition, some intravascular sensors, the feasibility of which will be tested in a separate preclinical study. The upcoming 2nd and 3rd

generation system implemented with these sensors could be the important arsenal to penetrate the market and secure market share.
- Successful market entry to resistant hypertension can be a pathway to other diseases such as heart failure, chronic kidney disease and diabetes where the sympathetic activities are abnormally elevated.
- Handok plans to achieve about 630M USD sale by 2022 through early market release in Korea, direct sales in global markets, technology out-licensing and/or partnering with global players.

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?

- Handok plans complete a preclinical GLP test for the first generation system in an accredited center (with relevant researchers) in Singapore by A*STAR.
- In addition, Handok plans to test, with relevant researchers in A*STAR, the feasibility of commercially-available intravascular sensors that could measure the procedural safety and effectiveness.