T89

Clinical Studies

Dantonic® is a modernized and industrialized botanical drug formula of Danshen (Radix Salviae Miltiorrhizae, RSM) and Sanqi (Radix Notoginseng, RN) as active ingredients and Borneol as absorption enhancer. Dantonic® was approved as a prescription drug for the treatment of chronic stable angina pectoris in patients with coronary heart disease by the State Food and Drug Administration of China (CFDA) in 1993.

Dantonic® is currently approved in 24 countries (not in the USA yet) for the treatment and prevention of chronic stable angina pectoris and other cardiovascular disease related conditions. More than 2 billion doses have been prescribed worldwide. It is coded as T89 in the US development. T89 has been studied in well controlled US and global clinical trial.

T89 Phase I study (Dose escalating studies)

Phase I studies were carried out in China, Australia and Japan. The studies showed that T89 has a very good safety profile.

T89 Safety and Tolerance Studies

Study No.	Title	Main Findings
T89-01-CN	Dose escalating study in Chinese healthy subjects	Well tolerated with no safety concerns up to 650 mg, single dose
T89-05-AU	Dose escalating study in Australian healthy subjects	Well tolerated with no safety concerns up to 800 mg, single dose
T89-10-JP	Dose-escalate study to investigate the safety and tolerability of T89 in Japanese healthy subjects	Single administration of T89 150mg, 300mg; repeating dose 225mg bid for 14 days. Well tolerated.

T89 Phase II Trial (Clinical Trial No: NCT00797953)

A Randomized, Multi-Center, Double-blind, Placebo-controlled Phase II clinical trial was conducted in the Unites States from November 2007-December 2010. The study was to evaluate the efficacy and safety of T89 in a patient with Chronic Stable Angina Pectoris. A total of 124

patients who met inclusion and exclusion criteria was randomized into three (3) groups: T89 low dose (125mg, twice daily), T 89 high dose (187.5 mg, twice daily) and placebo control.

The primary endpoint was total exercise duration (TED) change at 4 and 8 weeks after drug administration from baseline. The result was very promising, compared with baseline data, total exercise duration (TED) significantly increased in both T89 treatment groups without severe drug-related AEs reported.

T89 Phase III study (Clinical trial No: NCT01659580)

Based on the positive results in T89 Phase II study, a double-blind, randomized, multi-nation, multi-center, placebo controlled Phase III clinical study was designed. This pivotal Phase III clinical trial was to confirm the efficacy and safety of the drug at 150mg and 225mg (twice daily) doses in the prevention and treatment of angina pectoris in patients with Chronic Stable Angina.

This large-scale clinical study was conducted in 137 clinical sites across the world including Canada, Georgia, Mexico, the Unites States, Russian Federation and Ukraine. Nine hundred and sixty (960) subjects who met inclusion and exclusion criteria were randomized into four (4) groups: T89 high dose (225 mg twice per day), T89 low dose (150 mg twice per day), Sanqi plus Bingpian (225 mg twice daily) and placebo control groups. The primary efficacy endpoint is the change of symptom-limited Total Exercise Duration at the end of the 4th week of treatment from baseline and compared with those data from placebo control. The study was conducted during July 2012-March 2016. Data had been analyzed and study results had been presented to the US FDA.

Now, this clinical study has been completed and data and statistical analysis are underway. The outcome of the Phase III trial could lead to the first multi-herbal prescription drug to be in the North American pharmaceutical marketplace which will provide a healthier treatment option for patients with stable angina.