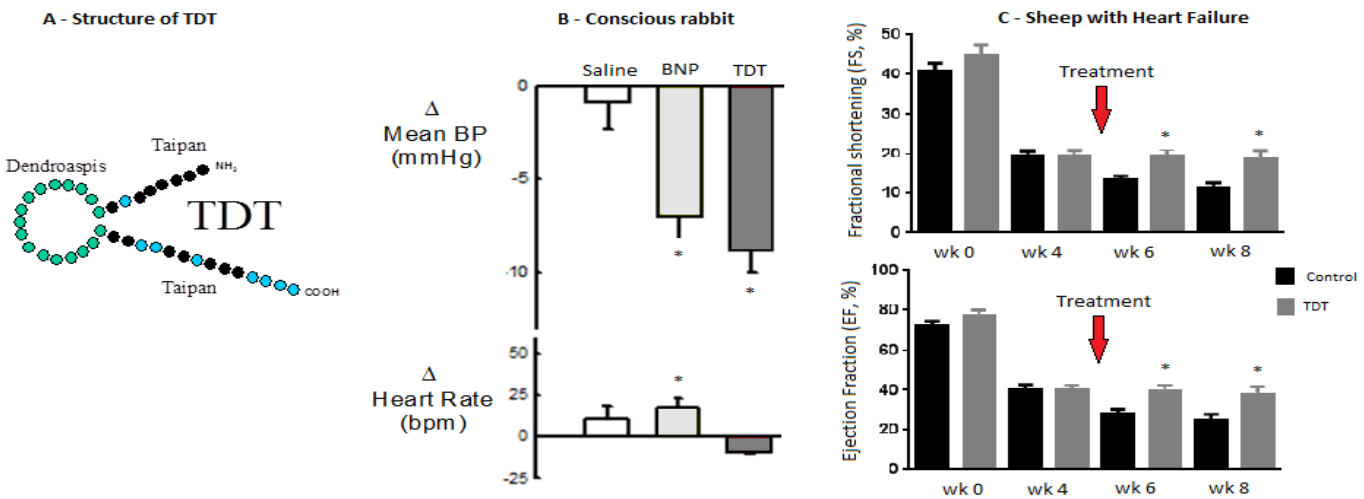
Baker IDI
HEART & DIABETES INSTITUTE

A natriuretic peptide derived from snake venom as a new treatment for Heart Failure

- Lead indication: Acutely Decompensated Heart Failure
- Follow-up indication: Heart Failure patients after discharge
- Aims at improving discharge success, decreasing hospital readmission rate and improving quality of life.

SUMMARY OF INVESTMENT OPPORTUNITY:
Baker IDI researchers have designed a potent natriuretic peptide that has the potential not only to provide a treatment for HF patients in hospital, but also for stable HF patients after discharge. Natriuretic peptides are normally released by a failing heart to reduce the symptoms of heart failure through multiple actions: increasing blood volume, reducing cardiac contractility and lowering cardiac output. Current treatments for HF still elicit many side effects, often treat only single symptoms, and rarely address the progression of the disease. After identifying the novel NP, the investigators have developed strong proof-of-concept data and confirmed the desired pharmacology and a minimal side-effect profile that is superior to existing NP products. Importantly, they have demonstrated efficacy in two different animal models of HF (rat and sheep). These data provide the basis for development of a new product to treat HF with the aim of improving discharge success, decreasing hospital readmission rate and improving quality of life.

TECHNOLOGY:
We have designed a chimera of “natriuretic-like” peptides found in the venoms of the Taipan and the Dendroaspis snakes (TDT). We optimized its biological stability, and showed efficacy using rat and sheep models of HF; we also demonstrated reduced tachycardia compared with existing NPs.



A) Structure of TDT with the Dendroaspis ring (green) and Taipan TNPc tails (blue black)
B) Single injection of TDT decreased blood pressure in conscious rabbits without inducing tachycardia.
C) Ovine model of high rate pacing induced dilated cardiomyopathy. Daily injections of TDT resulted in significantly higher fractional shortening and LVEF compared to untreated animals regardless of the ongoing high rate pacing, demonstrating efficacy for prevention of worsening cardiac function in this animal model.

PROBLEM / TARGET MARKET:

Heart failure represents a new epidemic of cardiovascular disease, with a prevalence of over 5.8 million in the USA, and over 26 million worldwide, and rising.

In addition to the cost in human suffering, HF represents a considerable burden to the health-care system, responsible for costs of more than $30B annually in the USA alone. Projections show that by 2030, the total cost of HF will increase to $69.7B. Heart failure is also the leading cause of hospitalization in people over 65. In 2010, more than 1 million hospital discharges in the US, 1.6 million in EU, had HF listed as the primary diagnosis. This is a major unmet medical need since 1 in 4 patients discharged with "stable" HF return to hospital within 30 days; 2 in 4 return within 60 days.

Sales of HF therapeutics in 2015 totalled approximately $3.2B in the seven major markets (US, 5EU, and Japan), and are expected to grow to $11.5B by 2025 (CAGR 13.5%).

Although the HF market has numerous well established therapies and the pipeline is promising, there is a considerable level of unmet need. HF-PEF, acute HF, and treatments for patients with multiple comorbidities represent three major unmet needs in the HF space.

For acute HF, loop diuretics are the first and only line of treatment for patients in most of the 7MM; these patients are at an extraordinarily high risk of death during hospitalization and after discharge.

TDT will be formulated as subcutaneous injection for patients hospitalised for acute HF due to worsening chronic HF, advanced HF or *de novo* acute HF, wherein the durable pharmacological action and potency would provide a single low volume dose. The product would be positioned as an add-on therapy to IV loop diuretics. The size of this patient segment was estimated at 2.76 million in 2015, and growing to 3.03 million hospitalisations in 2025.

STAGE OF DEVELOPMENT:

- Drug optimised for potency and stability
- Efficacy using rat and sheep models of HF
- Next steps: formal preclinical toxicology study and Phase I safety trial

COMPETITIVE ADVANTAGE:

- Highly potent molecule
- Durability of pharmacological action
- No observed tachycardia or other negative side effects compared with existing NPs
- TDT is not broken down by neprilysin (more likely to have stronger renal effects)

INTELLECTUAL PROPERTY:

patent WO2006/005140 (granted in US and EU) entitled "Proteinaceous compounds and uses therefore". This patent has been filed in the name of The University of Queensland and Baker IDI Heart and Diabetes Research Institute; it protects the composition of matter IP related to the Taipan peptide, including over one hundred novel analogues of TNP and chimeras with other existing NPs.

New claims for the TDT product may arise during formulation of the product for outpatient use, which is considered as the follow-on indication.

TEAM:

Professor Geoffrey Head, head of the Neuropharmacology Laboratory at Baker IDI

Professor David Kaye, Heart failure and transplant physician at the Alfred Hospital Melbourne, head of the Heart Failure Research Group and the Translation Domain at Baker IDI

Dr Melissa Byrne, pre-clinical research manager for the Heart Failure Research Group at Baker IDI, specialist in the use of animal models of disease for the translation of basic science into pre-clinical research and longer term clinical outcomes

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