



## ASX Company Announcement

### Sun Biomedical Limited to Acquire Dimerix Bioscience

#### Highlights

- Dimerix is a platform drug discovery and clinical stage biotechnology company;
- Dimerix is currently recruiting in to Phase 2 clinical study;
- Dimerix's lead therapeutic product, DMX200, is targeted at patients with Chronic Kidney Disease (CKD);
- CKD is a large problem with over 26 million people affected in US alone. CKD market in US exceeds \$11B in sales per annum and continues to grow;
- Dimerix initial strategy is to pursue an orphan indication, Nephrotic Syndrome, and subsequently partner the development of programs in larger disease indications;
- Dimerix is engaged in research collaborations with top pharmaceutical companies using its proprietary GPCR (G protein coupled receptors) drug discovery platform;
- Management team and advisory board are in place and ready to take the lead project forward. Near term value inflection point – data from Phase 2 study Part A in patients with proteinuria; and
- Capital raising of \$1.6M via the placement to sophisticated clients of Forrest Capital to accompany the acquisition resulting in available working capital of approximately \$3.5M.

**13 May 2015** - The Board of Sun Biomedical Ltd, an Australian biotechnology company, is pleased to announce that the Company has signed an implementation agreement to acquire 100% of Dimerix Bioscience Ltd (**Dimerix**), a public unlisted clinical stage drug discovery and development company, based in Melbourne. Dimerix's lead clinical program is a Phase 2 study in patients with Chronic Kidney Disease, using its novel combination therapy, DMX200. The acquisition will transform Sun Biomedical into an advanced clinical stage company with an asset that has the potential to make a considerable impact in the treatment of Chronic Kidney Disease. Upon successful results from the Phase 2 study, Dimerix intends to pursue the pathway of registration of a product for an orphan indication, such as Nephrotic Syndrome.

Dimerix's team has applied its patented GPCR drug discovery technology for its own internal research identifying and developing therapeutic treatments. Dimerix leverages its knowledge of drug target interaction and develops new combination therapies using already marketed compounds for new medical indications. This positions Dimerix's therapies with a fast route to market due to extensive safety data for the selected compounds removing the requirement for Phase I studies and allowing to proceed directly to Phase II efficacy studies.

#### Overview of the Transaction

Subject to executing acquisition agreements with all Dimerix shareholders and Sun Biomedical shareholders approving the transaction, Sun Biomedical will:

- acquire 100% of the issued shares of Dimerix Bioscience Limited (Dimerix) (Acquisition); and
- in connection with the Acquisition, undertake a placement of up to 160,000,000 fully paid ordinary shares in the Company (Shares) to sophisticated and professional investor clients of Forrest Capital each at an issue price of \$0.01 to raise up to \$1.6 million (before costs) (Capital Raising). 60 million shares of the placement will be issued following execution of acquisition agreements by all Dimerix shareholders using the Company's share issue capacity under ASX Listing Rule 7.1, with the

balance of 100 million shares subject to shareholder approval at a meeting of shareholders in June 2015;

- issue 60 million Advisor Options to Forrest Capital (or its nominees) exercisable at A\$0.010 per option on or before 30 June 2017
- the Company will enter into an acquisition agreement with each of the Dimerix shareholders (**Vendors**) (to acquire 100% ownership of Dimerix for total consideration of:
  - 750,000,041 Shares;
  - 30,851,592 management options exercisable at A\$0.020 on or before 30 June 2017;
  - 75,000,040 Class A Performance Shares convertible into 75,000,040 Shares upon receipt by the Company or Dimerix of a notice of allowance from the United States Patent and Trademark Office in relation to the US patent application number 13/979,127 (or any divisional or continuation thereof) within 24 months of completion of the transaction;
  - 75,000,040 Class B Performance Shares convertible into 75,000,040 Shares upon the Company's board of directors making an investment decision to proceed to file an application to the US Food and Drug Administration for a pre-Investigational New Drug ("pre-IND") meeting to progress development of DMX200 following the receipt of data generated under the current clinical trial for chronic kidney disease supporting further progression of the technology within 48 months of completion of the transaction; and
  - 75,000,040 Class C Performance Shares convertible into 75,000,040 Shares upon receipt of ethics approval allowing commencement of a second clinical trial derived from the Dimerix platform and in relation to an indication that is not covered under the existing Austin Human Research Ethics Committee approval within 48 months of completion of the transaction),
- completion of the transaction will be subject to certain conditions which must be satisfied or waived within 2 months of the date of the implementation agreement, including:
  - Sun Biomedical obtaining all necessary shareholder approvals;
  - all of the Dimerix shareholders entering into acquisition agreements with Sun Biomedical in respect of their shares in Dimerix;
  - Sun Biomedical receiving firm commitments and cleared funds for the full amount of the Capital Raising; and
  - no material breach of the warranties given in the implementation agreement having occurred.
- Voluntary escrow provisions will apply in the case of Vendor Shares to be issued to directors and promoters of Dimerix and their related parties as well as some seed shareholders of Dimerix. These details and other particulars of the transaction will be outlined in a notice of meeting which will be mailed to all Company shareholders as soon as available.

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## Appendix

### 1. Review of Clinical Assets

#### 1.1. Dimerix – DMX200 Clinical Trial & Pipeline Opportunities

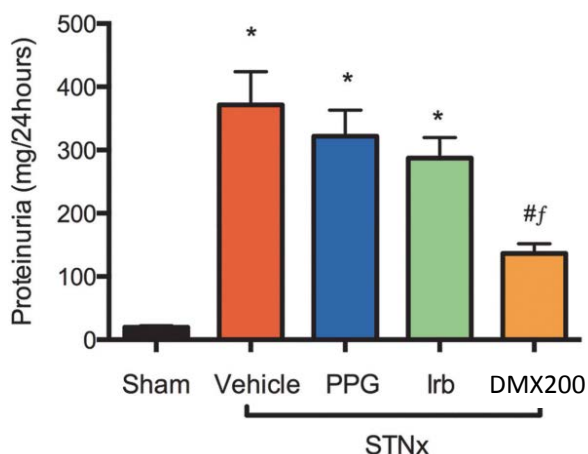
Dimerix lead therapy known as DMX200 recently commenced a Phase 2 clinical trial in Australia under the Clinical Trial Notification (CTN) pathway for the treatment of patients with chronic kidney disease (CKD). Ethics was granted in September 2014 and patient screening commenced shortly after. Patients are required to be stabilized on the standard of care therapy prior to dosing with DMX200.

Safety and reduction of the amount of protein leaking into the urine, proteinuria, are endpoints for this study. Data from the clinical trial is expected to be available during CY 1H 2016.

Dimerix has additional opportunities that the company intends to progress through animal studies in the next 0 – 12 months; these include:

- i. application of its lead therapy in other diseases including diabetic retinopathy and non-alcoholic steatohepatitis (NASH);
- ii. application of alternative drug combinations in multiple sclerosis and cancer fatigue.

#### 1.2. DMX200 — A new approach for CKD



**Figure 1.** DMX200 significantly reduces proteinuria in animal model.

Using its proprietary technology Dimerix has identified a combination of two drugs that, when administered together in the appropriate ratio, improves the outcome of chronic kidney disease in the animal models of the disease.

This combination known as DMX200, involves drugs targeting the angiotensin II Type 1 (AT1R) and the chemokine 2 receptors (CCR2).

The studies in the 5/6 sub-total nephrectomy (STNx) rat model of chronic kidney disease, compared the efficacy of the DMX200 combination of Irbesartan (IRB) and propagermanium (PPG), acting on the angiotensin II and chemokine receptors respectively, to treatment with either drug alone.

DMX200, when compared to either drug alone:

- i. Significantly reduced the amount of proteinuria (see Figure 1);
- ii. Significantly reduced the amount of macrophage infiltration into the kidney, and;
- iii. Significantly reduced the loss of podocytes in the kidney.

These data, in combination with the laboratory pharmacology produced using Dimerix's core technology, provide a compelling case to progress the DMX200 formulation into Phase II clinical trials for chronic kidney disease. The data was recently published in one of the top peer-reviewed journals (Ayoub *et.al.*, PLoS One 2015, Mar 25, 10(3))

### **1.3. Clinical Rationale**

#### **1.3.1. Rationale for Development of Propagermanium - Irbesartan Combination Therapy**

Dimerix Bioscience has data suggesting a combination approach involving the simultaneous antagonism of both the angiotensin receptor (AT1R) and the chemokine receptor (CCR2) may provide improved anti-proteinuria efficacy. The combination proposed by Dimerix consists of the AT1R blocker Irbesartan together with the CCR2 pathway inhibitor – propagermanium. Dimerix have completed three pre-clinical studies examining this hypothesis in the STNx rat model of chronic kidney disease and proteinuria. In these three studies AT1R and CCR2 blockade have been shown to act synergistically to reduce proteinuria and podocyte loss to a greater level than when treated with blockade of either AT1 or CCR2 alone.

In the current Phase 2 clinical study it is planned to use the same agents as studied in the pre-clinical studies. IRB is approved for human use and is well established in the treatment of patients with renal disease. There are currently no approved selective CCR2 receptor blockers, although a number of pharmaceutical companies are testing various investigational CCR2 inhibitors as monotherapies for a range of indications. Propagermanium has been selected for clinical development because it has activity as a CCR2 inhibitor (Reference: Kitagawa K, Wada T, Furuichi K, Hashimoto H, Ishiwata Y, Asano M, Takeya M, Kuziel WA, Matsushima K, Mukaida N, Yokoyama H. Blockade of CCR2 ameliorates progressive fibrosis in kidney. *Am J Pathol.* 2004 Jul; 165(1):237-46), has a long history of human use and is the only commercially available CCR2 product. Irbesartan is an off-patent angiotensin receptor blocker and is a standard of care.

## **2. Review of Marketing and Development Strategy Rationale**

### **2.1. Lead Indication - Chronic Kidney Disease**

Chronic kidney disease (CKD) can result from diabetes, high blood pressure and diseases that cause inflammation in the kidneys. As CKD progresses it can lead to end-stage renal disease (ESRD), where the kidneys fail completely. A person with ESRD must receive a kidney transplant or regular blood-cleansing treatments called dialysis.

CKD is a large problem with over 26 million people affected in the United States alone, with 8.5 million having Stage 3 (of 5 stages) or worse disease progression. US Sales of an estimated US\$2.3 billion are mainly derived from Stage 5 CKD with Stages 3 and 4 representing largely untapped markets.

### **2.2. CKD -Medical Need**

Chronic kidney disease (CKD) is a major public health problem in Australia and throughout the world.

It is estimated that 10% of all adults presenting to a general practice in Australia have CKD. One in ten Australian adults show at least one indicator of kidney damage.

Progression of CKD ultimately results in kidney failure requiring dialysis. The cost of treating end stage kidney failure is estimated to be around \$12 billion to the Australian Government from 2009 to 2020.

Kidney disease contributes to approximately 15% of all hospitalizations in Australia. Individuals with CKD have a 2 to 3-fold greater risk of cardiac death than individuals without CKD.

Recent studies have confirmed that even early CKD constitutes a significant risk factor for cardiovascular events and death. For people with CKD, the risk of dying from cardiovascular events is up to 20 times greater than requiring dialysis or transplantation.

As such there is a large unmet need for therapies that may stop or reduce the progression of CKD. It is for this reason that Dimerix are developing DMX200 and based on encouraging animal data are now recruiting patients in its Phase 2 clinical study.

However CKD is comprised of a number of sub indications such as Nephrotic Syndrome, which has a small patient population enabling the orphan drug pathway to be initiated, and Diabetic Nephropathy which is increasingly common due to the increasing prevalence of Type II diabetes.

### **2.3. Rational for Clinical Development Approach**

Kidney disease can arise from diabetic and non-diabetic disorders. Several large interventional studies have uniformly found that proteinuria is a major risk factor for the progression of renal disease. Furthermore, a reduction of proteinuria regardless of whether kidney disease is from diabetic or non-diabetic disorders has been associated with a decreased risk of adverse renal end-points. Proteinuria can be measured from urine samples provided in a clinical study with reduction monitored over a twelve week time period for proposed dosing levels. As a result, for some indications, in the United States, the Food and Drug Administration (FDA) will consider a reduction in proteinuria as a primary endpoint to approve treatments.

The DMX200 Phase 2 clinical program in chronic kidney disease will measure the reduction in proteinuria from patients with both diabetic and non-diabetic disorders. Phase 1 is not required due to the extensive clinical history of the components of DMX200.

Dimerix intends to initially target development of the treatment for Nephrotic Syndrome, as an orphan indication, to leverage the reduced statistical burden imposed by regulatory bodies for such diseases. Nephrotic syndrome affects approximately 20,000 – 25,000 patients in the United States and there is currently a lack of approved treatments for this condition.

In the United States, an orphan-drug designation is granted for novel drugs that treat a rare disease or condition affecting fewer than 200,000 patients in the U.S. Orphan drugs have faster development time lines and lower R&D expenses, due to the reduced size of the trials required by the FDA. Once on the market, they tend to have less competition, lower marketing costs, and a longer life-cycle with less risk of generic erosion.

The DMX200 trial is planned to include up to 60 patients (in two parts) and will be conducted initially at three sites in Melbourne.

Proof of concept of reduction in proteinuria, is expected to enable outlicensing of DMX200 to a large partner to develop it for prevalent indications such as Diabetic Nephropathy.

### **2.4. DMX200 – Additional Indications**

DMX200 could also be used for non-renal complications such as such as diabetic retinopathy NASH.

There is a large market for treatment of diabetic retinopathy (over 8 million in the US alone as per National Eye Institute); however approvals for new treatments in large medical indications like this will require more complex trials measuring multiple end points over longer periods.

Dimerix strategy is thus to initially target orphan indications and use this data to support partnering with a major pharmaceutical companies to address the significantly larger, and more complex, market segments including diabetic nephropathy, diabetic retinopathy, and NASH.