For Immediate Release

ASX/Media Release

Research published in *Scientific Reports* uses state-of-the-art CRISPR technology to validate relevance of the Dimerix Receptor-HIT technology in real time

MELBOURNE, Australia, 13 June 2017: Dimerix Limited (ASX: DXB), a clinical-stage biotechnology company discovering and developing new therapeutic treatments identified using its proprietary assay technology today announced the publication of important research by Chief Scientific Advisor, Associate Professor Kevin Pfleger and colleagues in the leading peer reviewed journal *Scientific Reports* (1).

Using state-of-the-art CRISPR technology, the team at the Harry Perkins Institute of Medical Research led by Associate Professor Pfleger has developed world first tools for studying functional receptor interactions in real time. This has enabled them to validate the relevance of the Dimerix Receptor-Heteromer Investigation Technology (Receptor-HIT) platform technology to monitor receptor complexes by labelling and monitoring endogenous receptors with tags for bioluminescence resonance energy transfer (BRET). This publication shows that even when cells express receptors under the low levels of expression that occur naturally, the Receptor-HIT technology is sufficiently sensitive to detect and observe the kinetics of receptor heteromer complexes *in vitro*.

Associate Professor Pfleger highlighted that “This work has considerable potential for improving drug discovery and profiling, leveraging both Dimerix’s Receptor-HIT platform and the latest advances in genome editing”.

The Receptor-HIT technology was used to identify DMX-200 (2), Dimerix’s lead clinical stage drug development program, in Phase II trials for the treatment of chronic kidney disease. It is often difficult to be sure that discoveries made in the laboratory will translate into a therapeutic effect in humans. This new research adds further confidence to the mode of action in patients being treated with DMX-200.

Dimerix’s CEO Kathy Harrison said, “Validation of the power of platform technologies which rely on analysis *in vitro* can be challenging. This pivotal piece of work has shown that the relevance of the heterodimers (the core premise of Receptor-HIT technology) can be demonstrated in cells in real time under endogenous promoter conditions, as occurs in the physiological setting.”

Associate Professor Pfleger is one of the world’s foremost authorities on the use of BRET technologies to study G protein-coupled receptors (GPCRs). He published the seminal review and protocol for BRET in *Nature Methods* (3) and *Nature Protocols* (4) respectively, more recently published the first demonstration of BRET GPCR ligand binding assays again in *Nature Methods* (5), and is co-inventor of the Receptor-HIT technology assigned to Dimerix from The University of Western Australia (UWA). This research was supported by the Australian Research Council Linkage Grant announced in May 2016 for which Dimerix is a partner organisation.

Based at the Harry Perkins Institute of Medical Research and UWA Centre for Medical Research, Associate Professor Kevin Pfleger was Chief Scientific Officer of the Company from 2008 until Dimerix became a public company in June 2014.

(1) White CW, Vanyai HK, See HB, Johnstone EKM and Pfleger KDG (2017): Using nanoBRET and CRISPR/Cas9 to monitor proximity to a genome-edited protein in real-time. *Sci Rep*. **7**:3187 (Published online on 9th June and available at http://rdcu.be/tllA)
(2) Ayoub MA, Zhang Y, Kelly RS, See HB, Johnstone EKM, McCall EA, Williams JH, Kelly DJ and Pfleger KDG (2015) Functional Interaction between Angiotensin II Receptor Type 1 and Chemokine (C-C motif) Receptor 2 with Implications for Chronic Kidney Disease. *PLoS ONE* **10**: e0119803
(3) Pfleger KDG and Eidne KA (2006) Illuminating insights into protein-protein interactions using bioluminescence resonance energy transfer (BRET). *Nat Methods* **3**:165-174
(4) Pfleger KDG, Seeber RM and Eidne KA (2006) Bioluminescence resonance energy transfer (BRET) for the real-time detection of protein-protein interactions. *Nat Protoc* **1**: 337-345
(5) Stoddart LA, Johnstone EKM, Wheal AJ, Goulding J, Robers MB, Machleidt T, Wood KV, Hill SJ and Pfleger KDG (2015) Application of BRET to monitor ligand binding to GPCRs. *Nat Methods* **12**: 661-663

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Dimerix Bioscience Pty Ltd
Dimerix Limited's wholly owned subsidiary Dimerix Bioscience Pty Ltd is a clinical-stage pharmaceutical company committed to discovering and developing new therapeutic models identified using its proprietary assay, termed Receptor-Heteromer Investigation Technology (Receptor-HIT). This assay enables the identification of pairs of receptors that function in a joint manner (interact) when ligands, small molecule drugs, peptides or antibodies, bind to them. The Receptor-HIT technology was used to identify DMX-200 in an internal drug development program, initially for the treatment of a subset of patients with chronic kidney disease. In addition to its own therapeutic programs, the company also earns revenue by providing this technology to global pharmaceutical companies. For more information see www.dimerix.com

DMX 200
DMX-200 is being developed as an adjunct therapy, adding propagermanuim to a stable dose of irbesartan. Irbesartan is an off-patent angiotensin II type I receptor blocker indicated for the treatment of hypertension and nephropathy in Type II diabetic patients. Propagermanium (PPG) is a chemokine receptor (CCR2) blocker, which has been used for the treatment of Hepatitis B in Japan and is available in the USA for its anti-inflammatory properties. DMX-200 has been shown to improve the outcome of chronic kidney disease by reducing proteinuria by more than 50 per cent in animal models (2).

The DMX-200 Phase II Trial
The trial is a single arm, open label study in adult patients with chronic kidney disease (with proteinuria). The primary end points are the incidence and severity of adverse events and the clinically significant changes in the safety profile of participants. The secondary end points are obtained from statistical analysis of biomarker data at each time point including change from baseline, and the proportion of responders defined as those participants achieving normalisation of proteinuria (proteinuria within normal limits) or those participants achieving a 50 per cent reduction in proteinuria.

The trial has two parts. Part A is a dose escalation trial recruiting up to 30 patients and completed enrolment at the end of November 2016. All patients recruited to the trial will be on stable irbesartan therapy, and will be treated with propagermanium dosed orally three times per day. Each patient will

commence on 30mg PPG/day and the dose increased each 28 days to a maximum of 240mg/day, or until proteinuria is absent or reduced to a level the clinician considers acceptable. The Company expects to complete Part A in mid 2017. Part B is an expansion study, in which up to 30 patients will be given the optimal dose identified from Part A.

Chronic Kidney Disease

Chronic kidney disease can result from diabetes, high blood pressure and diseases that cause inflammation specifically in the kidneys. Proteinuria is the most common manifestation of the disease. As the disease progresses it can lead to end-stage renal disease (ESRD) where the kidneys fail. The only treatment for ESRD is a kidney transplant or regular blood-cleansing treatments called dialysis. More than 26 million people suffer from the disease in the United States.