Dimerix

Immediate Release

UPDATE ON PROJECT PARASOL AND KEY APPOINTMENT TO MEDICAL ADVISORY BOARD

- The PARASOL working group has conducted an analysis of FSGS data and confirmed the strong correlation between an improvement in eGFR and a reduced risk of end-stage kidney disease, confirming the use of eGFR as an approved surrogate endpoint for FDA approval
- The PARASOL working group also provided strong data to support the relationship between a reduction in proteinuria and the reduced risk of kidney disease progression
- Subject to FDA confirmation, a reduction in proteinuria may also become a validated endpoint for full FDA approval
- Potential benefit for Dimerix ACTION3 clinical trial with possible range of proteinuria endpoints that could be accepted as a primary endpoint for marketing approval, subject to FDA confirmation, and no changes are anticipated for the study design given both eGFR and proteinuria data are already being collected for a total period of 2 years
- Expert nephrologist and Co-Chair of the PARASOL working group, Dr Laura Mariani, has been appointed to Dimerix Medical Advisory Board
- A blinded interim analysis is planned after the first 144 patients reach 35-week treatment, expected around mid-2025
- To date, 129 patients have been randomised/dosed in the ACTION3 Phase 3 clinical trial, with 16 patients in stabilisation, titration or screening ahead of potential randomisation (subject to meeting inclusion/exclusion criteria)

MELBOURNE, Australia, 28 October 2024: Dimerix Limited (ASX: DXB), a biopharmaceutical company with a Phase 3 clinical asset in kidney disease, is pleased to provide an update on the PARASOL Scientific Workshop held in Washington DC on 7-8 October 2024, and published on 25 October 2024, as well as advise that Dimerix has appointed Dr Laura Mariani to its ACTION3 Medical Advisory Board.

The PARASOL (**P**roteinuria **a**nd GF**R** as Clinical Trial Endpoints in Foc**a**l **S**egmental Gl**o**merulosc**l**erosis) working group is a collaborative academic and regulator-led international effort that has been established with the aim to define the quantitative relationships between changes in biomarkers such as proteinuria and eGFR and long-term outcomes for FSGS patients and further support the use of alternative proteinuria-based endpoints as a basis to provide both accelerated and traditional marketing approval in FSGS kidney disease.[1] Dimerix is supporting this working group, including participating in workshops held in June 2024 and October 2024.

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The October 2024 PARASOL Scientific Workshop, which included clinicians, patients, key opinion leaders, statisticians, FDA and industry sponsors of FSGS clinical trials, presented a preliminary analysis of the pooled globally available observational data of FSGS patients. It is important to note that the PARASOL data set uses observational data, is broad ranging, includes patients across a wide range of demographics, age and regions, and is not specifically limited to randomised trial data with the same population as the Dimerix ACTION3 Phase 3 clinical trial.

The PARASOL project team presented the preliminary data analysis at the American Society of Nephrology (ASN) meeting in San Diego on 25th October 2024, with the analysis confirming, amongst other things, the strong correlation between the surrogate endpoint of improvement in eGFR and the clinical endpoint of reduced risk of end-stage kidney disease, noting eGFR is currently the primary endpoint in its ACTION3 Phae 3 clinical trial.

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It was also broadly recognised that patients with FSGS, unlike other types of kidney disease, often have residual scarring of the kidney that may prevent some patients reaching the low level of proteinuria seen in other kidney diseases (where complete remission is defined as <0.3 g/g protein in the urine). The PARASOL dataset has now shown that higher proteinuria thresholds including 0.7 g/g, 1.0 g/g, and up to 1.5 g/g have shown significant benefit with regard to reducing risk of progression to renal failure. Importantly, this provides a range of potential proteinuria targets for drug candidates targeting FSGS, subject to confirmation with the FDA.

There was general agreement from the FDA at the workshop that PARASOL working group has likely provided sufficient data to support the relationship between a reduction in proteinuria and decreased risk of kidney disease progression. The FDA may now have sufficient data to grant FDA approval on proteinuria endpoints (as an alternative to eGFR alone or proteinuria and eGFR). However, it is likely each industry sponsor (company) will have to present justification to the FDA for which proposed proteinuria threshold should be applicable to their drug candidate, along with their drug candidate safety profile and the biological plausibility for how their drug candidate directly works to reduce proteinuria and/or preserve kidney function.

For Dimerix and its ACTION3 Phase 3 clinical trial and subject to FDA approval, it is likely that the Company may now have a range of proteinuria endpoints that could be acceptable as a primary endpoint for FDA approval. Importantly, no changes are anticipated to the study, given both eGFR and proteinuria data are being collected for a total of 2 years. With regards to next steps, Dimerix intends on requesting a meeting with the FDA to reach agreement on the appropriate proteinuria endpoints for DMX-200 in the ACTION3 Phase 3 clinical trial.

Dimerix is very pleased that Dr Laura Mariani has agreed to join the ACTION3 Medical Advisory Board. Dr Mariani serves as the Co-Chair of the Project PARASOL working group and is currently Assistant Professor in the Division of Nephrology at the University of Michigan with research interests in observational studies in glomerular disease, including NEPTUNE and CureGN. Her primary research interest is in developing and applying statistical methods for clinical outcome definition and prediction of kidney disease progression as well as linking clinical phenotype to novel biomarkers and high dimensional omics data to better understand disease mechanisms that can be targeted for therapy in glomerular disease.

"I am delighted to join the Dimerix Medical Advisory Board at such an exciting time in their FSGS program. The objective of PARASOL is to advance the understanding and use of proteinuria and eGFR-based surrogate endpoints for accelerated and traditional approval of new treatments for FSGS patients, thus facilitating the development of new therapies. There remains a high unmet need for new treatments for this progressive disease, and I look forward to working with Dimerix to progress DMX-200 as a promising potential new treatment for FSGS patients".

Dr Laura Mariani, Co-Chair Project PARASOL, Associate Professor, Director, Clinical & Patient Cohorts, University of Michigan Division of Nephrology

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Authorised for lodgement by the Board of the Company

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About ACTION3 FSGS Phase 3 Study

The Phase 3 study, which is titled **"A**ngiotensin II Type 1 Receptor (AT1R) & **C**hemokine Receptor 2 (CCR2) **T**argets for **I**nflammat**o**ry **N**ephrosis", or ACTION3 for short, is a pivotal (Phase 3), multi-centre, randomised, double-blind, placebo-controlled study of the efficacy and safety of DMX200 in patients with FSGS who are receiving a stable dose of an angiotensin II receptor blocker (ARB). Once the ARB dose is stable, patients will be randomized to receive either DMX200 (120 mg capsule twice daily) or placebo.

The single Phase 3 trial in FSGS patients has interim analysis points built in that are designed to capture evidence of proteinuria and kidney function (eGFR slope) during the trial, aimed at generating sufficient evidence to support marketing approval.

Further information about the study can be found on ClinicalTrials.gov (Study Identifier: NCT05183646) or Australian New Zealand Clinical Trials Registry (ANZCTR) (Study Identifier ACTRN12622000066785).

About Dimerix

Dimerix (ASX: DXB) is a clinical-stage biopharmaceutical company working to improve the lives of patients with inflammatory diseases, including kidney diseases. Dimerix is currently focussed on developing its proprietary Phase 3 product candidate DMX-200 (QYTOVRA® in some territories), for Focal Segmental Glomerulosclerosis (FSGS) kidney disease, and is also developing DMX-700 for respiratory disease. DMX-200 and DMX-700 were both identified using Dimerix' proprietary assay, Receptor Heteromer Investigation Technology (Receptor-HIT), which is a scalable and globally applicable technology platform enabling the understanding of receptor interactions to rapidly screen and identify new drug opportunities.

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About DMX 200

DMX 200 is the adjunct therapy of a chemokine receptor (CCR2) antagonist administered to patients already receiving an angiotensin II type I receptor (AT1R) blocker - the standard of care treatment for hypertension and kidney disease. DMX 200 is protected by granted patents in various territories until 2032, with patent applications submitted globally that may extend patent protection to 2042, in addition to any exclusivity period that may apply in key territories. In 2020, Dimerix completed two Phase 2 studies: one in FSGS and one in diabetic kidney disease, following a successful Phase 2a trial in patients with a range of chronic kidney diseases in 2017. No significant adverse safety events were reported in any trial, and all studies resulted in encouraging data that could provide meaningful clinical outcomes for patients with kidney disease.

About FSGS

FSGS is a rare disease that attacks the kidney's filtering units, where blood is cleaned (called the 'glomeruli'), causing irreversible scarring. This leads to permanent kidney damage and eventual end-stage failure of the organ, requiring dialysis or transplantation. For those diagnosed with FSGS the prognosis is not good. The average time from a diagnosis of FSGS to the onset of complete kidney failure is only five years and it affects both adults and children as young as two years old.[2] For those who are fortunate enough to receive a kidney transplant, approximately 60% will get re-occurring FSGS in the transplanted kidney.[3] At this time, there are no drugs specifically approved for FSGS anywhere in the world, so the treatment options and prognosis are limited. FSGS is a billion-dollar plus market: the number of people with FSGS in the US alone is just over 80,000,[2] and worldwide about 220,000.[4] The illness has a global compound annual growth rate of 8%, with over 5,400 new cases diagnosed in the US alone each year.[5] Because there is no effective treatment, Dimerix has received Orphan Drug Designation for DMX 200 in both the US and Europe for FSGS. Orphan Drug Designation is granted to support the development of products for rare diseases and qualifies Dimerix for various development incentives including: seven years (FDA) and ten years (EMA) of market exclusivity if regulatory marketing approval is received, exemption from certain application fees, and a fast-tracked regulatory pathway to marketing approval. Dimerix reported positive Phase 2a data in FSGS patients in July 2020.

References

1 See Project PARASOL website: https://www.is-gd.org/parasol

2 Guruswamy Sangameswaran KD, Baradhi KM. (2021) Focal Segmental Glomerulosclerosis), online: https://www.ncbi.nlm.nih.gov/books/NBK532272/

3 Front. Immunol., (July 2019) | https://doi.org/10.3389/fimmu.2019.01669

4 Delve Insight Market Research Report (2022): Focal segmental glomerulosclerosis (FSGS) – Market Insight, Epidemiology and market forecast – 2032; https://www.delveinsight.com/report-store/focal-segmental-glomerulosclerosis-fsgs-market;

5 Nephcure Kidney International (2020); Focal Segmental Glomerulosclerosis, online https://nephcure.org/livingwithkidneydisease/understanding-glomerular-disease/understanding-fsgs/

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