Second part of HERACLES clinical trial begins

Highlights

- **HERACLES clinical trial enters next level**
- **Multiple SOF-SKN doses to be given**
- **Successful safety results allow two lowest doses to be skipped**
- **Global cutaneous lupus market worth over US$3.3 billion**

Sydney, 5 November 2025: Clinical-stage biotech company **Noxopharm Limited (ASX:NOX)** is pleased to announce the start of the second part of the HERACLES clinical trial, following successful single-dose testing.

HERACLES is a first-in-human trial for SOF-SKN™, a novel drug candidate for autoimmune diseases. The study aims to evaluate the safety and tolerability profile of SOF-SKN by testing it at different concentrations, and is taking place in Australia to capitalise on Australian expertise in lupus research and early phase clinical trials. Noxopharm will also secure federal R&D tax benefits by conducting the study locally.

Intensive testing

The trial will now see multiple doses of ascending concentrations of SOF-SKN given to participants in order to continue safety testing at a more intensive level over a longer period of time.

This approach will enable Noxopharm to ascertain how SOF-SKN behaves in a testing regimen that more closely resembles how the drug might be used by future patients in real-world conditions. Cutaneous lupus (CLE) is an incurable chronic disease, meaning that patients would potentially need to use SOF-SKN on an ongoing basis to help relieve their symptoms.

The primary goal of the Noxopharm team, again working with Doherty Clinical Trials in Melbourne, will be to make sure that SOF-SKN is safe over repeated applications of the cream. They will also investigate how well trial participants tolerate the drug, as well as measure numerous other pharmacokinetic and pharmacodynamic parameters.

Lowest doses skipped

Because SOF-SKN was safe and well tolerated at all dose levels in the successful first part of the trial, the Safety Steering Committee decided it was unnecessary to test the two lowest doses in the second part, but rather begin at the second-highest dose.

There will therefore now only be two cohorts, each with four participants receiving a dose of SOF-SKN every day for two weeks and a dose increase from one cohort to the next.

Skipping the two lowest dose cohorts means the trial will conclude more quickly and be more cost effective.

The repeated administration of the drug plus subsequent readouts are scheduled to take approximately one month for each cohort, due to a battery of tests including electrocardiograms, physical exams, participant questionnaires, numerous blood tests, skin observation scoring tests and so on. All of these are administered at multiple time points, with subsequent data collection and analysis.

With the same level of scrutiny as in the first part of the trial, this data will be evaluated and discussed by the Safety Steering Committee before it can give the green light to proceed to the next cohort and a higher dose.

Participant recruitment is currently ongoing, and the first cohort will receive their first dose in the near future.

Noxopharm CEO Dr Gisela Mautner said: "Now that we have successfully applied SOF-SKN in single doses to healthy volunteers, we are ramping up the testing to ensure it is safe across repeated doses. This is a vital aspect of the drug development process as regulatory authorities have strict safety approval processes for when and how new drugs are allowed to be given to people."

SOF-SKN is initially being developed for autoimmune diseases like cutaneous lupus erythematosus (CLE) before potential development for autoimmune-related skin diseases like psoriasis and dermatomyositis. The global CLE market is worth more than US$3.3 billion and is expected to grow significantly over the coming years.

The core Sofra™ technology could also be further utilised for rheumatoid arthritis and diabetes, plus other diseases linked to the dysregulation of the immune system.

-ENDS-

About the Sofra technology platform

Developed from a breakthrough discovery in the immune system, Sofra comprises a novel class of drugs targeting inflammatory and autoimmune diseases, as well as RNA therapeutics and vaccines.

Sofra technology has potential applications in a wide range of diseases related to the immune system such as rheumatoid arthritis, lupus and diabetes, as well as other diseases like cancer.

The global autoimmune disease therapeutics market was worth US$163.2 billion in 2024 and is expected to reach US$219.6 billion by 2035, while the worldwide immuno-oncology market was US$43 billion in 2023 and is projected to hit US$284 billion by 2033.

The proprietary platform is based on short nucleic acid sequences, the building blocks of DNA or RNA, known as oligonucleotides. These act on specific immune sensors to regulate inflammation at its source, reducing or stimulating it to control the disease. In essence, the Sofra technology for

autoimmune diseases replicates what is naturally occurring in the bodies of healthy people, but is either absent or too little in patients with autoimmune conditions.

Further information and animations: SOF-SKN / SOF-VAC

About Noxopharm

Noxopharm Limited (ASX:NOX) is a clinical-stage Australian biotech company discovering and developing novel treatments for cancer and inflammation, including a pioneering technology to improve the safety profile of a wide range of mRNA medicines.

The company utilises specialist in-house capabilities and strategic partnerships with leading researchers to build a growing pipeline of new proprietary drugs based on two technology platforms – Sofra™ (inflammation, autoimmunity, mRNA drug enhancement, and oncology) and Chroma™ (oncology).

To learn more, please visit: noxopharm.com

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Dr Gisela Mautner, CEO and Managing Director of Noxopharm, has approved the release of this document to the market on behalf of the Board of Directors.

Forward Looking Statements

This announcement may contain forward-looking statements. You can identify these statements by the fact they use words such as “aim”, “anticipate”, “assume”, “believe”, “continue”, “could”, “estimate”, “expect”, “intend”, “may”, “plan”, “predict”, “project”, “plan”, “should”, “target”, “will” or “would” or the negative of such terms or other similar expressions. Forward-looking statements are based on estimates, projections and assumptions made by Noxopharm about circumstances and events that have not yet taken place. Although Noxopharm believes the forward-looking statements to be reasonable, they are not certain. Forward-looking statements involve known and unknown risks, uncertainties and other factors that are in some cases beyond the company’s control that could cause the actual results, performance or achievements to differ materially from those expressed or implied by the forward-looking statement.