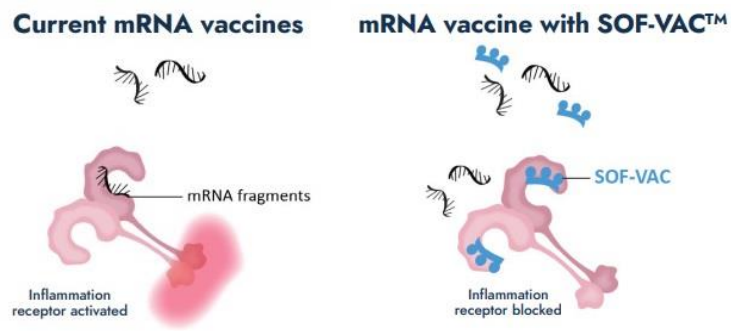
mRNA Vaccine Enhancer Shows Significant Inflammation Reduction

- **New data shows SOF-VAC™ significantly reduces mRNA-driven inflammation in animal model**
- **Effectiveness of RNA remains high**
- **Comprehensive data package achieved, actively seeking commercial partner for next stage**

Sydney, 18 October 2023: Innovative biotech company **Noxopharm Limited (ASX:NOX)** announces new data that shows its SOF-VAC™ mRNA vaccine enhancer significantly reduces inflammation driven by mRNA in an animal model.

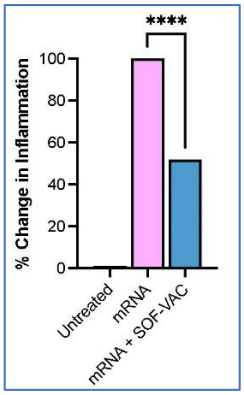
SOF-VAC is a proprietary asset designed to be combined with mRNA vaccines to reduce inflammatory responses. It works by blocking specific inflammation receptors, and is fully compatible with existing mRNA vaccine delivery systems.



In the left image, fragments of mRNA bind to inflammation receptors in the body causing overstimulation, which results in inflammation and other vaccine side effects. In the right image, when SOF-VAC is combined with the mRNA vaccine, it blocks the inflammation receptors and reduces vaccine side effects.

Results show a highly significant reduction in the mRNA-driven inflammation response in studies recently conducted by Noxopharm and its strategic partner, the Hudson Institute of Medical Research in Melbourne.

In an animal study, inflammation was reduced by around 50% (see appendix for detailed data) when comparing the inflammation induced by mRNA alone to mRNA plus SOF-VAC. This is an important finding, as many side effects of mRNA vaccines are due to inflammation.



Compounded average percentage shows a highly significant decrease in levels of nine inflammatory biomarkers (p<0.001) *detected in the blood of mice six hours post-injection with mRNA alone or mRNA co-packaged with SOF-VAC.*

The ability of SOF-VAC to reduce the inflammatory side effects of mRNA has several potential benefits, such as:

- Enabling mRNA vaccines to be given with higher doses – creating longer-lasting protection and a decrease in the frequency of booster shots required.

- Supporting the combination of mRNA vaccines (or other types of RNA vaccines) for different diseases into one syringe.

- Supporting future mRNA (or other RNA) drugs that require high and repeated doses to help treat a variety of diseases.

During the studies, SOF-VAC was combined with mRNA in a way that did not affect the function of the mRNA, which is important to ensure the effectiveness of vaccines.

Noxopharm has now largely concluded its planned development work on SOF-VAC, and is actively seeking a commercial partner to take the asset forward to the next stages of its development.

The company has also recently filed a substantial Patent Cooperation Treaty (PCT) application, which is an essential part of the process of securing robust IP protection in several countries simultaneously.

At a wider level, there is growing awareness of the importance of reducing inflammation in the context of mRNA vaccines, as evidenced by the recent awarding of the Nobel Prize in Medicine to pioneering work in this field that led to the development of the COVID vaccines. This recognition illustrates how critical and relevant the suppression of inflammation is, and all further development of mRNA vaccines and drugs needs to address this issue.

According to Precedence Research, the mRNA market in 2022 was US$40 billion, and is expected to grow to US$137 billion by 2032 at a compound annual growth rate of 13%.

Noxopharm CEO Dr Gisela Mautner said: “Our results are a significant milestone in the development of SOF-VAC. They show that it works in reducing inflammation, which should translate into fewer side effects from mRNA vaccines. This is of major importance as vaccines are given to populations that are essentially healthy, and who do not want to be negatively affected by a preventative vaccine administration.

“We have now taken SOF-VAC to the point where we consider the data is strong enough for it to be of interest to other companies, and so are stepping up our efforts to find the right partner to continue its clinical development. This includes presentations at targeted international conferences, as well as other activities.”

Hudson Institute Associate Professor Michael Gantier said: “The development of RNA-based therapeutics is one of the most exciting areas of medicine, and these results are the outcome of many years of research. Our demonstration that molecules as short as SOF-VAC can have such targeted anti-inflammatory effects is genuinely novel, and gives SOF-VAC an advantage for use not only in vaccines, but also in the many RNA-based drugs we see coming down the pipeline.”

-ENDS-

About Noxopharm

Noxopharm Limited (ASX:NOX) is an innovative Australian biotech company discovering and developing novel treatments for cancer and inflammation, including a pioneering technology to enhance mRNA vaccines.

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 – Chroma™ (oncology) and Sofra™ (inflammation, autoimmunity, and mRNA vaccine enhancement).

Noxopharm also has a major shareholding in US biotech company Nyrada Inc (ASX:NYR), which focuses on drug development for cardiovascular and neurological diseases.

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 (including but not limited to the COVID-19 pandemic) that could cause the actual results, performance or achievements to differ materially from those expressed or implied by the forward-looking statement.

APPENDIX

Background

Human beings' immune system consists of two parts: the innate and the adaptive immune system.

To protect against infection, humans have evolved specialised receptors that recognise foreign RNA and DNA derived from bacteria and viruses. These receptors are part of what is called the innate immune system, the body's first line of defence.

When this foreign DNA or RNA is detected by these receptors, the innate immune system is triggered to respond to the viral or bacterial infection by producing inflammatory messengers called cytokines. One example of these specialised receptors is Toll-like receptor 7 (TLR7).

When an mRNA vaccine is injected, the mRNA triggers receptors such as TLR7, leading to inflammation (termed reactogenicity in this context) that causes vaccine side effects such as fever, headache, fatigue and muscle soreness.

The mRNA also triggers the adaptive immune system, which helps to produce proteins and eventually kills the viruses or bacteria.

The need to minimise side effects restricts the amount of mRNA that can be administered in each vaccine dose. This in turn limits the vaccine's activity on the adaptive immune system, and therefore the degree and duration of immunity gained from vaccination.

The effect of mRNA vaccines on TLR7 is therefore a major limiting factor influencing vaccine tolerability and efficacy. As such, technologies that facilitate the provision of higher mRNA doses without producing unpleasant side effects will improve vaccination program outcomes and contribute to overall public health.

Detailed Results

The Sofra™ technology platform is based upon short nucleic acid sequences, which are the building blocks of DNA or RNA, known as oligonucleotides (oligos). These oligos act on nucleic acid sensors of the innate immune system such as TLR7 to modulate inflammation at its source. Some oligos have been designed to increase inflammation, others to inhibit it.

Associate Professor Michael Gantier's group at the Hudson Institute of Medical Research has carried out extensive research on how oligos modulate inflammation. They have published several works in the prestigious peer-reviewed international journal *Nucleic Acids Research*, which involved examining over 700 oligos, identifying those with the strongest activity, and selecting them for inclusion in Noxopharm's Sofra platform.

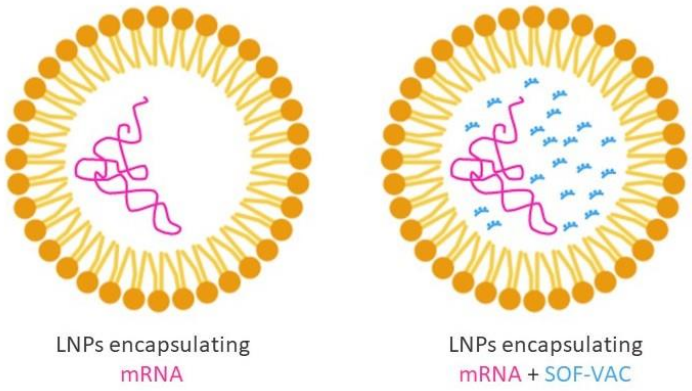
Oligos are generally defined as having 35 or fewer bases (individual letters of the DNA or RNA code). SOF-VAC comprises novel oligos of only three bases, known as 3-mers, that have demonstrated potent inhibitory activity on TLR7. SOF-VAC binds to TLR7 inflammation receptors and blocks them, thereby reducing mRNA vaccine-induced inflammation at its source.

Noxopharm's recent studies involved three distinct outcomes:

1. Successful co-packaging of SOF-VAC into an mRNA delivery system
2. Reduction of mRNA-induced inflammation by SOF-VAC
3. Continued full RNA effectiveness when combined with SOF-VAC

Co-packaging of SOF-VAC into an mRNA delivery system

The first step of the studies was to co-package SOF-VAC and an mRNA inside ALC-0315 ionizable lipid-based nanoparticles (LNPs), an FDA-approved mRNA delivery system that has been successfully deployed for Pfizer/BioNTech's BNT162b2 mRNA COVID-19 vaccine. The studies showed that SOF-VAC can be successfully co-packaged with mRNA inside this delivery system without impacting the integrity of the LNPs.



Images created using BioRender

Figure 1: LNP delivery system

Reduction of mRNA-induced inflammation by SOF-VAC

To determine if SOF-VAC was effective at reducing mRNA-induced inflammation (reactogenicity) in an animal model, inflammatory cytokine levels were measured in the blood six hours post-injection. Averaged across nine cytokines (i.e. inflammatory markers), an approximate 50% reduction (48.2%) in cytokine levels was detected (**Fig. 2**), including highly significant decreases ($p<0.001$) in several critical cytokines driving post-vaccine inflammation and side effects.

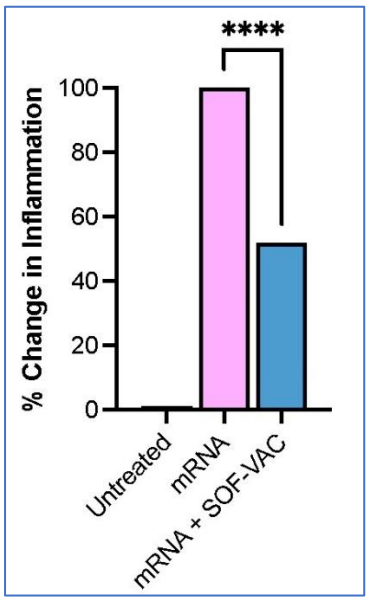


Figure 2. Compounded average percentage showing highly significant decrease in levels of nine inflammatory cytokines ($p<0.001$) detected in the blood of mice six hours post-injection with mRNA alone or mRNA co-packaged with SOF-VAC.

n=6 mice/treatment group from one experiment.

Continued full RNA effectiveness when combined with SOF-VAC

The mRNA used in the study was translated by cells in the body to make a protein (luciferase), allowing for in-life bioluminescent detection and quantification of mRNA expression using a specialised imaging machine.

Since mRNA expression is directly correlated with vaccine activity, i.e. the immunity induced by vaccination, it was critical to show that SOF-VAC did not reduce mRNA translation. Importantly, measurement of luciferase activity in the mice at six hours post-injection showed no significant difference in protein expression between the mice that received the luciferase mRNA alone and those that received luciferase mRNA co-packaged with SOF-VAC (**Fig. 3**), which means that the function of the mRNA was fully preserved.

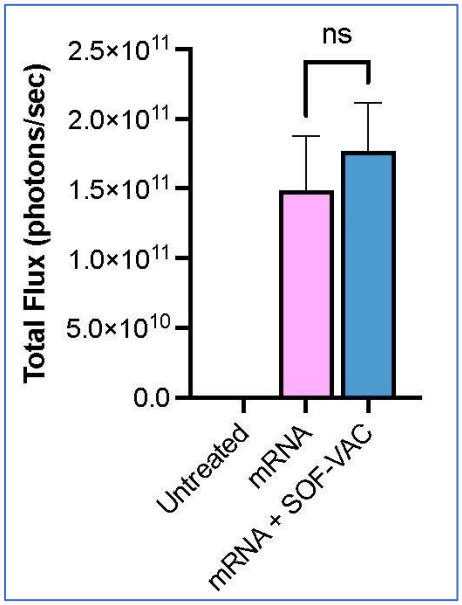


Figure 3. Measurement of mRNA expression (bioluminescence) in mice six hours post-injection with luciferase mRNA alone or mRNA co-packaged with SOF-VAC.

Data is shown as Mean ± S.E.M. n=6 mice/treatment group from one experiment.