Licencing Deal from Hudson Institute of Medical Research Provides Noxopharm With Potential To Limit Side-Effects of RNA Therapeutics.

Highlights

- **Noxopharm subsidiary, Pharmorage, in-licences cutting edge RNA technology developed by Hudson Institute of Medical Research (Hudson)**
- **The licence is exclusive and global and comes with major opportunities, subject to clinical trials and marketing approvals, in both RNA drug discovery and mRNA vaccine manufacture**
- **RNA drugs already under development by Hudson will add to existing Pharmorage assets and help position the Company at the forefront of chronic inflammatory/autoimmune diseases drug development**
- **The mRNA vaccine opportunity lies in the potential to limit unwanted inflammatory side-effects, an exciting commercial opportunity with the mRNA vaccine market predicted to reach US$23 billion by 2035[1]**

Sydney 17 November 2021: Australian clinical-stage drug development company Noxopharm Limited (ASX:NOX) is pleased to announce that Noxopharm, through its wholly-owned subsidiary, Pharmorage Pty Ltd ('Pharmorage'), has entered into a licence agreement with Hudson Institute of Medical Research ('Hudson').

The key **financial terms of the licence agreement** between Noxopharm and Hudson are (i) no upfront fees, (ii) material milestone payments relating to late-stage clinical development on initiation of Phase 3 trials and receipt of marketing approvals, (iii) a two digit percentage of any upfront sub-licence fees, and (iii) a single digit royalty on net sales. The licence is effective immediately and the licence term lasts as long as royalty payments continue. The licence is subject to standard termination clauses.

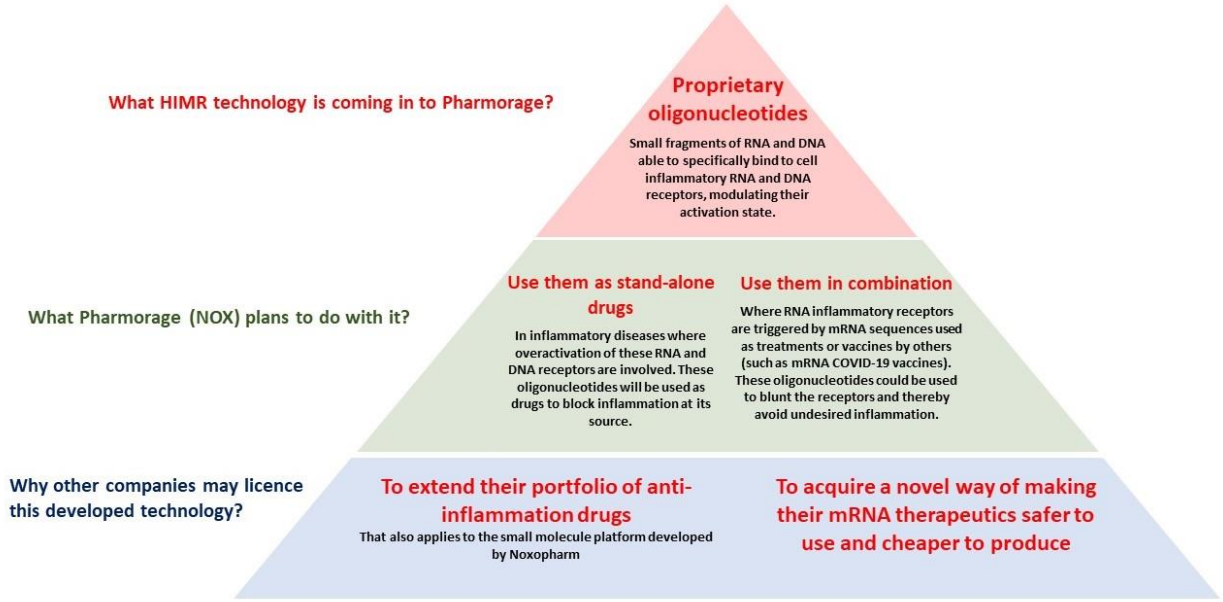
Pharmorage is wholly responsible for the development of the technology and retention of the licence depends on meeting certain development milestones that the Company believes are practical and achievable in terms of capital expenditure and time.

The IP underpinning the licenced technology is the **subject of two patent applications**.

The licence is for what both parties regard as potentially ground-breaking RNA technology developed over 15 years and highly relevant to the development of RNA drugs and mRNA vaccines. The licence is exclusive and world-wide, serving in the Company's view to make Noxopharm, through Pharmorage, a foundation player in the field of RNA technology and putting it at the forefront in Australia of this emerging field.

Noxopharm CEO and Managing Director, Graham Kelly, said, "*This licence is a major coup for the Company and is validation of our ability to translate research from the laboratory to the clinic. Pharmorage already had a strong business relationship with Hudson with a major initiative in anti-inflammatory drug development. The RNA technology and its anti-inflammatory functions is an obvious fit and an opportunity with which we are delighted to be entrusted.*

The commercial terms are largely back-ended and designed to leave our other programs like the Veyonda clinical program unaffected by this new and exciting additional opportunity. The mRNA vaccine opportunity in particular does show strong potential for future out-licensing opportunities. With the whole world, including children down to 5 years of age, looking at being vaccinated against SARS-CoV-2, the dual benefits of reducing unwanted side-effects and increasing manufacturing efficiency have to be attractive. And with mRNA vaccine technology looking increasingly likely to extend eventually to most if not all viral diseases, this is an extraordinarily timely development."



With RNA technology now seen as a key contributor to future drug and vaccine development,[1,2] foundation RNA technologies offer major value propositions for companies with valuable intellectual property (IP). Noxopharm and Hudson see this as a valuable ground-floor opportunity to be an integral part of that growing market.

The Hudson technology platform is focused on the use of RNA fragments (oligonucleotides) to reduce inappropriate inflammation. The platform achieves this in a number of novel ways, two of which Pharmorage intends to pursue. The first is the development of drugs as treatments of inflammatory and autoimmune diseases. The second is to apply it to improve the safety and manufacturing efficiency of mRNA vaccines.

RNA drug programs

The success of mRNA COVID-19 vaccines has put a spotlight on RNA technology, but the technology was already well in play with RNA drugs being used in the treatment of muscular dystrophy and hypercholesterolaemia. Cholesterol-lowering drug, inclisiran, was the subject of a 2020 USD9.7 billion acquisition by Novartis. RNA drugs are seen as having a role in the treatment of chronic diseases where life-long treatment is otherwise required on a daily basis because of their ability to provide a durable treatment response (3-6 months) with a single administration.[3]

The licence comes with several lead RNA drugs being developed as treatments for chronic inflammatory and autoimmune diseases. These drugs target key immune sensors at the root of the inflammatory response. They have been successfully tested in cell models, with Pharmorage now to advance them into animal models. The cost of these studies is within the R&D budget allocated to Pharmorage.

These assets join the existing Pharmorage tank-binding kinase 1 (TBK1) inhibitor asset as potential novel treatments for chronic inflammation diseases such as rheumatoid arthritis, cardiovascular disease, various respiratory diseases, NASH etc. and autoimmune diseases such as multiple sclerosis, motor neuron disease, psoriasis, lupus, inflammatory bowel disease etc.

mRNA Vaccine Program

One key issue of mRNA vaccine technology is unwanted inflammatory side-effects including fatigue, severe headache, chills, and injection-site pain.[4] This issue can be tempered by injecting less mRNA, but this strategy limits the strength of the immune response and therefore can be less protective against infections.[5]

Another approach, used by both Pfizer-BioNTech and Moderna mRNA vaccines, involves a chemical modification of the mRNA designed to limit this side-effect by reducing activation of a cell immune sensor known as TLR7.[5,6] This allows these two vaccines to use ~2.5-8 times more mRNA than if it were non-modified.[5] The patent underpinning the use of this modification is currently held by U.S. private biotechnology company, CellScript LLC, and in force until 2027, and is licensed to both Pfizer-BioNTech and Moderna. However, an unintended downside of the modification is a reduction in the efficiency of vaccine production by 20-40% and it can also have an untoward effect on protein translation.[6]

The Hudson technology provides a way of switching off TLR7 without reducing manufacturing efficiencies. With this IP going to the heart of vaccine manufacturing efficiencies, Noxopharm sees it being of major interest to current manufacturers and developers of mRNA vaccines for coronavirus and other viral infections.

Several lead TLR7 inhibitors have already been characterised in cell models and are ready for pre-clinical evaluation in animal models. The identified business opportunity is of the potential out-licensing to vaccine developers and manufacturers in the future.

Associate Professor Michael Gantier of Hudson and the lead scientist responsible for this technology, said, "*Following on our efforts to characterise how TLR7 sensing is impacted by RNA chemical modifications,[7] we have discovered a new class of TLR7 inhibitors that can outcompete immune sensing of therapeutic RNAs such as those used in mRNA vaccines; we propose that these inhibitors could be used in conjunction with therapeutic RNAs to limit their side-effects in patients and maximise their therapeutic potential***".**

Further details of the licenced RNA technology platform are available on www.pharmorage.com

Glossary

RNA. Ribonucleic acid, a nucleic acid present in all living cells. There are many types of RNAs in a cell which directly contribute to cellular function
mRNA. messenger RNA. mRNA is the means by which the genes (DNA) instruct the cell to synthesise proteins
mRNA vaccines. These vaccines comprise mRNA that causes the cell to synthesise a specific viral (or bacterial) protein that is the basis of triggering an immune response. Compared to conventional vaccines, mRNA vaccines do not require the presence of the whole infective agent, are more versatile and can direct immune responses to a pathogen's Achilles' heel (eg, the spike protein for SARS-CoV-2)
RNA drugs. RNA technology offers the ability to create drugs that block the production of specific proteins, rather than to block the action of proteins that is the basis of most conventional drugs. The potential advantage of this is that single administrations of RNA drugs can provide effective treatment for extended periods (3-6 months), considered an attractive method of treatment for life-long diseases. Currently, RNA drugs are used in the treatment of muscular dystrophy and hypercholesterolaemia
TLR7. Toll-like receptors (TLR) are a class of proteins that play key roles in alerting the innate immune system to the presence of infective agents. TLR7 specifically responds to single-strand RNA by triggering the production of inflammatory cytokines.

References

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

About Hudson Institute of Medical Research
A global bioscience medical research leader, Hudson Institute's sole focus is on powering breakthrough scientific discoveries into improved health care that will transform lives. It strives to improve human health through groundbreaking, collaborative, medical research discoveries and the translation of these to real world impact.

The Institute's 455 scientists research five areas of medical need:

- Inflammation
- Reproductive health and pregnancy
- Infant and child health
- Cancer
- Hormones and health

About Pharmorage

Pharmorage Pty Ltd is a wholly-owned subsidiary of Noxopharm created in 2020 and specializing in the discovery and development of drugs to treat chronic illnesses associated with abnormal inflammatory and immune responses relating to chronic inflammatory and autoimmune diseases and septic shock.

To learn more, please visit www.pharmorage.com

About Noxopharm

Noxopharm Limited (ASX:NOX) is an Australian clinical-stage drug development company focused on the treatment of cancer and cytokine release syndrome (septic shock).

Veyonda® is the Company's first pipe-line drug candidate currently in Phase 2 clinical trialling. Veyonda® has two main drug actions – a moderating effect on the ceramide/sphingosine-1-phosphate balance and inhibition of STING signalling. Activity against the former target contributes to its dual-acting oncotoxic and immunomodulatory functions designed to enhance the effectiveness and safety of standard oncology treatments, i.e., chemotherapies, radiation therapies and immune checkpoint inhibitors. Activity against the latter target provides an anti-inflammatory effect, as well as contributing to an anti-cancer action, but also potentially blocking septic shock.

Noxopharm is running comprehensive drug discovery programs in both oncology and inflammation, and is the major shareholder of US biotechnology company, Nyrada Inc (ASX:NYR), active in the areas of drug development for cardiovascular and neurological diseases.

To learn more, please visit: noxopharm.com

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Forward Looking Statements

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