Immuron Reports Positive Results in NASH Clinical Trial

Oral IMM-124E Significantly Reduces LPS, a Major Factor in Liver Inflammation

Headlines:

- ***First-In Class Anti-LPS Mechanism of Action confirmed for IMM-124E***
- ***Results demonstrate excellent safety and tolerability***
- ***Statistically significant reduction in serum endotoxin/ Lipopolysaccharide (LPS) levels compared to placebo***
- ***Statistically significant reduction in mean serum ALT in patients with elevated pre-treatment ALT***
- ***Statistically significant reduction of additional serum NASH biomarkers associated with liver damage – AST and CK-18***
- ***IMM-124E retained within the GI tract and not absorbed into the bloodstream, contributing to favourable safety profile***
- ***Anti-LPS mechanism of IMM-124E may have wider therapeutic applications beyond NASH***

Melbourne, Australia, March 8, 2018: Immuron Limited (ASX: IMC; NASDAQ: IMRN), an Australian microbiome biopharmaceutical company focused on developing and commercializing orally delivered targeted polyclonal antibodies for the treatment of inflammatory mediated and infectious diseases, is today pleased to announce the topline results of its IMM-124E phase II **Non-Alcoholic Steatohepatitis** (NASH) clinical study.

A total of 133 biopsy-proven NASH patients were enrolled into the Immuron NASH clinical study and were treated with either IMM-124E or placebo for 6 months. The study showed that IMM-124E, a first-in-class, oral antibody therapy targeting the endotoxin Lipopolysaccharide (LPS) and other bacterial components, resulted in a statistically significant reduction of serum LPS levels in patients with NASH.

Considering the published association of serum LPS in the progression of NASH, Immuron believes the outcome of the trial is an important milestone toward commercialization of IMM-124E. Serum ALT was also significantly reduced within the 6-month treatment period meeting the study endpoint, demonstrating a significantly greater

proportion of patients with at least 30% reduction in serum ALT compared to placebo. Additional biomarkers associated with NASH and liver damaged were also reduced by IMM-124E including aspartate transaminase (AST) and cytokeratin-18 (CK-18).

"***This is truly a proof of concept for this first-in-class drug candidate.***" said Arun Sanyal, Professor of Gastroenterology and Hepatology from the Virginia Commonwealth University in Richmond, USA and the study lead Principle Investigator.

> *"The IMM-124E drug candidate has been developed to target LPS in the gut and prevent it translocating into the portal circulation.* ***The study results clearly demonstrate a statistically significant reduction of serum LPS levels*** *in the treatment groups when compared to placebo and provides us with a proof of concept that metabolic endotoxemia can indeed be decreased using this drug candidate (IMM-124E) which targets the endotoxin LPS.*
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> *We are encouraged that IMM-124E, a drug with an exceptional safety profile, can lower the LPS-associated inflammatory burden and improve liver enzymes. The potential clinical applications for this drug candidate are numerous and very exciting indeed"*

The primary objective of the study was to evaluate the safety and efficacy of IMM-124E, at two oral dosage levels as compared with a placebo and provide proof of concept in human subjects for its unique Mechanism of Action (MoA). No safety concerns or serious adverse events were associated with the study drug, as evident by serum biochemistry, haematology, vital signs, or physical examination for both treatment groups. Both doses of IMM-124E in the study (600mg and 1200mg) were well tolerated therefore supporting the use of even higher doses and extended treatment periods in future clinical trials.

The Significant Results Reported were as follows:

1. **LPS Reduction**

IMM-124E demonstrated a statistically significant reduction in serum lipopolysaccharide (LPS) levels, when compared to placebo. LPS, is a bacterial endotoxin implicated in numerous peer review publications to drive liver inflammation, and to play a role in the progression of NASH.

In the study 64.29% of patients treated with IMM-124E demonstrated a 15% or greater **decrease** in serum LPS levels compared with only 34.48% of patients showing a decrease for the placebo group, reaching statistical significance (p=0.01843). The opposite trend was observed in the placebo group with 58.62% of patients demonstrating a statistical significant 15% or greater **increase** in serum LPS levels by the end of the study, compared with only 25.0% in drug treated patients (p=0.0062). The MOA is consistent with the substantial peer review literature, in which LPS is thought to contribute to the progression of NASH. Overall, the distribution of

cases with > 15% decrease in serum LPS compared to no change (± 15%) compared to > 15% increase in circulating LPS levels were shifted in favor of IMM-124E treatment which decreased LPS in a significantly greater proportion of subjects compared to placebo (p=0.0302).

2. **Transaminases Reduction (ALT and AST)**

When comparing IMM-124E treated patients to placebo significantly more treated patients demonstrated a decrease in mean serum ALT by at least 30% (considered to be a clinically meaningful reduction), than placebo in patients with elevated pre-treatment ALT (p=0.048).

More than twice as many **patients in the high dose arm reached this endpoint compared with placebo** (36.36% and 13.64% for 1200mg vs. placebo respectively). IMM-124E also demonstrated a strong positive trend (p=0.107) in reducing ALT by 30% or more compared to the placebo group in all patients.

Similarly, treatment with IMM-124E showed a significant decrease in mean serum AST in the IMM-124E high dose compared to placebo (p=0.0446). Additionally, AST demonstrated a statistical trend to reduce serum levels by 30% or more (p=0.107).

3. **Reduction in CK-18**

IMM-124E also showed a statistical significance to reduce serum CK-18 levels compared to placebo. Serum CK-18 levels correlate with hepatocyte apoptosis (liver cell death) and liver damage. Reducing CK-18 levels in the context of NASH correlates with a reduction in liver damage.

In the study, twice as many subjects treated with high dose IMM-124E demonstrated a 15% or greater decrease in serum CK-18 levels when compared to placebo, 38.89% versus 18.18% respectively (p=0.0494).

4. **Pharmacokinetics - IMM-124E is not absorbed into the blood stream**

Furthermore, as anticipated, oral administration of IMM-124E did not lead to increased levels of bovine immunoglobulin in the serum. The results demonstrated that IMM-124E is retained within the gut lumen and not absorbed systemically. Such findings strengthen further IMM-124E's safety profile and support the potential use of the drug in combination with other medications. Given the increasing momentum for NASH for combination therapy.

5. **Hepatic Fat Fraction – no change**

Consistent with the IMM-124E mechanism of action to reduce serum LPS which is presumed to drive disease progression rather than the development of steatosis, IMM-124E did not have a significant effect on hepatic steatosis as measured by the hepatic fat fraction. The company and its medical advisory board believe that this

positions IMM-124E as a compound that can be used to decrease disease progression in those with NASH rather than resolve the steatosis.

Senior Vice President Head of Medical at Immuron Dan Peres MD, commented:

> ***"Immuron is pleased to report the first in-human clinical proof of IMM-124E decreasing serum LPS.*** *We are excited to show this world First-In Class drug effect achieved in conjunction with a reduction in serum ALT, AST, and CK-18. The proof for IMM-124E's non-absorbable nature and excellent safety profile as reported, will allow us to conduct further clinical research aimed at maximizing the effect with potentially higher doses and longer treatment times. Furthermore, these results support that IMM-124E offers potential as a standalone treatment or in combination with other classes of drugs."*

Immuron Interim CEO Dr. Jerry Kanellos commented:

> *"The Board of Immuron and Executive Management is very proud to have progressed our lead drug candidate IMM-124E to phase II proof of principle clinical trials. This has been a significant undertaking by the company and these results represent an opportunity for significant value creation for our loyal shareholders who have supported us over the journey. The Immuron team is extremely encouraged with these results, we have succeeded in demonstrating excellent safety and significant efficacy signals for our novel MoA in a relatively short treatment trial (24 weeks) and small numbers of patients (133 patients)"*
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> *"Our results offer evidence of a therapeutic mechanism of action and a clear direction for further NASH studies. The growing literature implicating LPS in many diseases offers the potential for a much wider scope for LPS antagonism as a treatment modality. With IMM-124E being the world's First-In Class Oral LPS Antagonist we are very confident, that when combined with its exceptional safety, there are substantial opportunities ahead across a broad range of diseases".*

The Company's Interim CEO, Dr Jerry Kanellos will host an investor teleconference event in the coming weeks for all shareholders to further explain the NASH trial results. Dr. Kanellos will also be embarking on a series of Australian and US Investor roadshow presentations to provide the market with a detailed explanation of the NASH trial results as well as other exciting developments at Immuron.

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ABOUT IMMURON:

Immuron Limited (ASX: IMC, NASDAQ: IMRN), is an Australian microbiome biopharmaceutical company focused on developing and commercializing orally delivered targeted polyclonal antibodies for the treatment of inflammatory mediated and infectious diseases.. Immuron has a unique and safe technology platform that enables a shorter development therapeutic cycle. The Company currently markets and sells Travelan® for the prevention of Travelers' Diarrhea and its lead clinical candidate, IMM-124E, is in Phase II clinical trials for **Non-Alcoholic Steatohepatitis** (NASH), **Severe Alcoholic Hepatitis** (SAH) and Pediatric **Nonalcoholic Fatty Liver Disease** (NAFLD). Immuron's second clinical stage asset, IMM-529, is targeting **Clostridium *difficile* Infections** (CDI). These products together with the Company's other preclinical immunotherapy pipeline products targeting immune-related diseases currently under development, will meet a large unmet need in the global immunotherapy market.

For more information visit: http://www.immuron.com

About the IMM-124E Study

The IMM-124E study is a Phase II proof of concept multinational, randomized, double-blind study comparing 2 doses of IMM-124E to placebo for the treatment of NASH in adults with any stage biopsy-proven NASH. The trial enrolled 133 patients across 25 clinical sites in Australia (6), Israel (2) and the USA (17). The trial has 12 scheduled visits over a 28-week study duration, with 24 weeks of treatment and four weeks of follow-up and screened a total of 237 patients. It initially aimed to enroll 120 patients with biopsy-proven NASH, and was fully enrolled at 133 patients, which exceeds the original 120-patient target. The patients were randomized into three arms: placebo, high dose (1200mg), and low dose (600mg). The established primary endpoints of the study were improvement of liver steatosis, as assessed by magnetic resonance imaging (MRI) comparing the mean values. The key secondary endpoints are: change in ALT as well as other liver enzymes and metabolic markers. IMM-124E enrolled adults with all-stage biopsy proven NASH up to 12 months of randomization under an IND approved by the FDA.

About IMM-124E

IMM-124E is an oral, three-times-daily, non-absorbable compound containing poly-clonal anti-LPS immunoglobulins proposed to interact with the gut LPS and immune system to achieve an immunomodulatory effect reducing LPS-related inflammation and inducing tolerance. Because of this unique mechanism of action, targeting multiple pathways, IMM-124E has the potential to play a differentiated role in the management of NASH and may form the cornerstone of NASH combination treatment strategies, both as a single agent and in combination with other agents.

In addition to the adult NASH study, IMM-124E is also being evaluated in two NIH funded Phase II proof-of-concept studies of IMM-124E in children with Pediatric NAFLD and adults with Severe Alcoholic Hepatitis.

About Non-Alcoholic Steatohepatitis (NASH)

Nonalcoholic fatty liver disease (NAFLD) is characterized by a buildup of fat in the liver that is not attributable to excessive alcohol use, NASH is a severe type of NAFLD, which is characterized by the accumulation of fat in the liver with no other apparent causes. NASH occurs when the accumulation of liver fat is accompanied by inflammation and cellular damage. The inflammation can lead to fibrosis (scarring) of the liver and eventually progress to cirrhosis, portal hypertension, liver cancer, and eventual liver failure, requiring the patient to have a liver transplant.

NAFLD is one of the most common causes of liver disease in the U.S., with the majority of patients having simple fatty liver. It is estimated that between 30-40% of adults in the U.S. have NAFLD. Although the epidemiology of NAFLD is not fully understood, the condition is associated with certain conditions, including obesity and obesity related conditions (e.g., type 2 diabetes). Researchers have found NAFLD in 40-80% of people with type 2 diabetes and in 30-90% of people who are obese. Over 90% of severely obese people undergoing bariatric surgery had NAFLD in epidemiological studies. NAFLD is not

age-specific and has been shown to affect 10% of children ages 2-19, although the risk of developing NAFLD increases with age.

NASH is an emerging health crisis impacting 3% to 5% of the U.S. population and 2% to 4% globally, and is the fastest growing cause of liver cancer and liver transplant in the U.S. The increasing prevalence of NASH is attributed to the growing obesity epidemic and the disease is often diagnosed in patients who have diabetes, high cholesterol or high triglycerides. There is currently no approved treatment for NASH. NASH is projected to reach over $25B annually by 2026 with a compound annual growth rate (CAGR) averaging 45% in the 2018-2026 period. Research analysts believe that peak sales for IMM-124E could exceed $1.8B in the U.S. alone.

FORWARD-LOOKING STATEMENTS:

This press release may contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, each as amended. Such statements include, but are not limited to, any statements relating to our growth strategy and product development programs and any other statements that are not historical facts. Forward-looking statements are based on management's current expectations and are subject to risks and uncertainties that could negatively affect our business, operating results, financial condition and stock value. Factors that could cause actual results to differ materially from those currently anticipated include: risks relating to our growth strategy; our ability to obtain, perform under and maintain financing and strategic agreements and relationships; risks relating to the results of research and development activities; risks relating to the timing of starting and completing clinical trials; uncertainties relating to preclinical and clinical testing; our dependence on third-party suppliers; our ability to attract, integrate and retain key personnel; the early stage of products under development; our need for substantial additional funds; government regulation; patent and intellectual property matters; competition; as well as other risks described in our SEC filings. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law.