

## Immuron Reports Significant Alleviation of Colitis Symptoms in Preclinical Program

### Results confirm LPS Antagonist action of IMM-124E offers a novel therapeutic approach to induce or maintain remission in IBD

**Melbourne, Australia, May 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 successful completion of its colitis preclinical program at the University of Zürich, Switzerland.

Immuron is pleased to report that oral administration of IMM-124E was successfully able to treat mice with immunologically induced colitis. The University of Zürich research revealed that IMM-124E offered a significant therapeutic benefit on clinically meaningful study parameters.

In contrast to the results reported in April 2017 using an acute colitis model the latest results were generated in the T cell transfer model which utilizes immunodeficient mice which are deficient in functional B and T lymphocytes. In this model chronic colitis is induced immunologically not chemically. IMM-124E was administered orally after the onset of colitis symptoms such as weight loss and macroscopically inflamed colon were confirmed by colonoscopy prior to the initiation of treatment.

The results reported clearly demonstrated that oral treatment with IMM-124E resulted in significant alleviation of colitis symptoms, including;

- **Reduced weight loss**
- **Reduced disease activity scores**
- **Reduced shortening of the colon**
- **Reduced levels of macroscopically detectable colitis**
- **Histology of the terminal and proximal colon also confirmed reduced colitis in the drug treatment arms.**

The research work has been submitted for presentation at the annual United European Gastroenterology Week conference which will be held on the 20<sup>th</sup> to 24<sup>th</sup> of October 2018 in Vienna, Austria.

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*"This study concludes our comprehensive preclinical program to evaluate the therapeutic potential of IMM-124E in our established colitis animal models."* said Gerhard Rogler, Professor of Gastroenterology and Hepatology from the University of Zürich, Switzerland and the study lead Principle Investigator.

*"Our results clearly demonstrate that treatment with IMM-124E significantly reduces intestinal inflammation via reducing the accumulation and differentiation of pathogenic T cells, while concomitantly enhancing the induction of regulatory cells. This indicates that IMM-124E inhibits lipopolysaccharide (LPS)-mediated effects on the mucosal immune system, resulting in reduced intestinal inflammation. Summarized, our findings indicate that IMM-124E administration represents a novel therapeutic strategy to induce or maintain remission in IBD patients".*

Immuron Interim CEO Dr. Jerry Kanellos commented:

*"The IMM-124E drug candidate has been developed to target the endotoxin, LPS in the gut and prevent it translocating into the portal circulation. This first in class mechanism of action was recently confirmed in our **Non-Alcoholic Steatohepatitis (NASH)** clinical study, where IMM-124E demonstrated a statistically significant reduction in serum LPS levels, when compared to placebo in patients with biopsy confirmed NASH.*

*The University of Zürich research program adds to our published preclinical and clinical data which has repeatedly shown that IMM-124E delivers a significant reduction in liver and mucosal inflammation. LPS endotoxins have been widely implicated as a major driver of inflammation in Colitis, Inflammatory bowel disease (IBD), NASH as well as numerous Auto-Immune Diseases".*

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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 **Non-Alcoholic Fatty Liver Disease (NAFLD)**. Immuron's second clinical stage asset, IMM-529,

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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

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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.

### About Lipopolysaccharide (LPS)

Lipopolysaccharide (LPS) also known as bacterial endotoxin is the major component of the outer membrane of Gram-negative bacteria which are natural inhabitants of the mammalian intestinal tract. These enteric bacteria serve as the source for systemic endotoxin exposure. There is a continuous release of endotoxin (LPS) in the host intestine with no consequence to the individual and if a small amount of endotoxin leaks into the portal vein, it is cleared by the liver, therefore, never entering the circulatory system. However, conditions that interfere with the integrity of the protective intestinal mucosal epithelium, such as our high fat, high sugar, western diets, chronic alcohol consumption or ischemia, increased LPS absorption into the hepatic portal system occurs. If the resulting endotoxemia overwhelms the liver's capability to metabolize absorbed LPS, an intense hepatic inflammatory response ensues. When bacterial cells are lysed by the immune system, bacterial fragments containing LPS are released into the circulation, causing fever, diarrhea, and possible fatal endotoxic shock (also called septic shock). Physiological response to inflammatory mediators can lead to hepatic damage. Elevated serum LPS is associated with increased risk for developing, Alcoholic Hepatitis, Alzheimer's disease, Auto-immune diseases, Cancer, Diabetes, Heart Disease, Inflammatory Bowel Disease (Crohn's Disease, Ulcerative Colitis), Metabolic Syndrome, Non-Alcoholic Fatty Liver Disease and many others.

### 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.

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