Positive Results Support Travelan® progress to Phase 3 Clinical Trials in the US

Highlights:

- **Immuron proceeding to Phase 3 registration strategy with the FDA**
- **Travelan® topline clinical trial results demonstrate protective efficacy with single daily dose**
- **36.4% protective efficacy against Enterotoxigenic *Escherichia coli* (ETEC) induced moderate to severe diarrhea was observed in the Travelan® group compared to the placebo group (primary endpoint)**
- **66.7% protective efficacy against ETEC induced severe diarrhea was observed in the Travelan® group compared to the placebo group (secondary endpoint)**
- **83.3% statistically significant reduction in the number of subjects in the Travelan® group requiring early antibiotic treatment post challenge compared to the placebo (secondary endpoint)**
- **100% of the subjects requiring IV fluids post challenge were in the placebo (secondary endpoint)**
- **55.6% reduction in the number of subjects experiencing adverse events associated with the ETEC challenge observed in the Travelan® group compared to the placebo group (secondary endpoint)**
- **Phase 2 clinical study data supports the excellent safety and tolerability profile of Travelan®**

Melbourne, Australia, March 7, 2024: Immuron Limited (ASX: IMC; NASDAQ: IMRN), an Australian based and globally integrated biopharmaceutical company is pleased to announce the interim topline results confirming that a single daily dose of Travelan® is effective in prevention of moderate to severe diarrhea following challenge with enterotoxigenic *Escherichia coli* (ETEC).

Immuron was awarded AU $4.8 (USD $3.43) million funding by the U.S. Department of Defense (ASX Announcement 12 January 2022) to perform a randomized double-blind placebo-controlled phase 2 controlled human infection model (CHIM) study to assist with evaluating a dosing regimen that is most suited to deployed US troops visiting developing countries. Healthy volunteers were recruited and randomly assigned to receive a single daily oral dose of 1200 mg of Travelan® or placebo. Dosing commenced 2 days prior to challenge with ETEC strain H10407 and continued for 7 days. ClinicalTrials.gov Identifier: NCT05933525.

This interim analysis summarizes the data for a total of 60 subjects who have completed the inpatient challenge component of this current clinical study. Last patients last visits are anticipated to commence in April this year and final clinical study report will be completed in H2 2024.

Having demonstrated protective efficacy in two published clinical studies (Otto et al., 2011), this Phase 2 study was designed to compare the preventative effects of once daily dosing to the current standard recommended treatment of three times daily dosing. To learn more about Phase 2 study design, read: U.S. Food and Drug Administration Step 3: Clinical Research

IMM-124E (Travelan®) will be the first product developed with Immuron's platform technology to proceed into Phase 3 clinical trials. The underlying nature of Immuron's platform technology enables the development of medicines across a large range of infectious diseases. The platform can be used to block viruses or bacteria at mucosal surfaces such as

the Gastrointestinal tract and neutralize the toxins they produce. More information on Immuron's platform technology can be found below.

Travelan® demonstrated clinical efficacy in preventing ETEC-attributable diarrhea in two previous CHIM studies. These studies showed dosing 400 mg three times daily, resulted in 76.7% (p=0.007) to 90.9% (p=0.0005) protection (Otto et al., 2011).

This trial demonstrated protective efficacy* with once daily dosing even though the attack rate for this study was much lower than planned. The intended attack rate (percentage of subjects with ETEC-induced moderate- severe diarrhea) for this study was approximately 70%. The attack rate for the Placebo group of this study was only 37% (Table 2). Given the lower than planned attack rate, this current study is underpowered to appropriately detect a significant difference in moderate to severe ETEC attributed diarrhea in the Placebo group compared to the Treatment group. This makes the demonstration of protective efficacy and reduction in adverse events and diarrheal symptoms particularly noteworthy.

The company will now proceed to hold an end of Phase 2 meeting with the U.S Food and Drug Administration to discuss the pivotal Phase 3 registration strategy and planned clinical trials including recommended dosing to support a Biologics License Application (BLA) for Travelan® as a prophylactic medicine for Travelers' Diarrhea. A preventative treatment that defends against infectious enteric diseases is a high priority objective for the U.S. Military.

Immuron is in the process of exploring non-dilutive funding opportunities for these Phase 3 clinical trials.

Topline results:
Travelan®, a first-in-class, oral antibody therapy, dosed once daily resulted in a reduction ETEC-induced moderate-severe diarrhea compared to placebo.

- ETEC- induced moderate to severe diarrhea was reduced by 36.4% in the Travelan® group compared to the placebo group
- Protective efficacy of once daily dosing shown to be approx. 50% as effective as the current recommended three times daily dosing regimen; this is a strong result given the lower than expected attack rate
- 66.7% protective efficacy against ETEC induced severe diarrhea was observed in the Travelan® group compared to the placebo group
- Statistically significant reduction of 83.3% in the subjects in the Travelan® group requiring early antibiotic treatment post challenge compared to the placebo
- For the subjects requiring intravenous rehydration post challenge 100% were in the placebo group and none were in the Travelan® group
- 55.6% reduction in the number of subjects experiencing adverse events post the ETEC challenge was observed in the Travelan® group compared to the Placebo group

Studies using the CHIM for a variety of different enteric pathogens suggest the greatest protection may be against more severe disease and in studies where the disease appears to be predominately mild, which appears to be the case in this study, the efficacy estimates can be lower than anticipated.

Table 2: Comparison of clinical study data attack rates

Event post challenge	Otto[3] Study 1 Placebo n = 15 n (%)	Otto[3] Study 2 Placebo n = 14 n (%)	Current Travelan® Study n = 30 n (%)
Number (n) of subjects with ETEC-induced moderate-severe diarrhea	11 (73%)	12 (86%)	11 (37%)

[3]Otto et al., 2011

Immuron is investigating the impact of the lower than expected attack rate.

Immuron has filed a provisional patent application with the U.S. Patent Office including results from this trial.

Table 1: Summary of current clinical study data

Event post challenge	Travelan® n = 30 n (%)	Placebo n = 30 n (%)	Reduction in AEs or Symptoms (%)	*P value*
Primary Endpoint				
Number (n) of subjects with ETEC-induced moderate-severe diarrhea	7 (23.3%)	11 (36.7%)	NA	0.399
Protective efficacy [%][1] 95% 2-sided Confidence Interval[2]	**36.4%* (-79.8%, 79.1%)**			
Secondary Endpoints - Safety and tolerability				
Number of subjects with an adverse event (AE) 95% 2-sided Confidence Interval[2]	4 (13.3%) (-3.8%, 37.1%)	9 (30.0%)	55.6%	0.1172
Number of subjects with (AEs) fever, nausea, anorexia, o abdominal pain/cramps rated as moderate to severe 95% 2-sided Confidence Interval[2]	3 (10.0%) (-5.2%, 31.9%)	7 (23.3%)	57.1%	0.1659
Secondary Endpoints – Degree to which a participant experiences diarrheal symptoms				
Number of subjects who experienced severe diarrhea 95% 2-sided Confidence Interval[2]	1 (3.3%) (-5.8%, 19.2%)	3 (10.0%)	66.7%	0.3006
Number of subjects requiring early antibiotic treatment 95% 2-sided Confidence Interval[2]	1 (3.3%) (1.0%, 32.4%)	6 (20.0%)	83.3%	**0.0444**
Number of subjects requiring IV fluids 95% 2-sided Confidence Interval[2]	0 (-0.7%, 20.7%)	3 (10.0%)	100.0%	0.0756

[1] Fishers exact test and binomial distribution [2] Chi-square test

AE = Adverse event associated with the ETEC challenge

* Intent-to-treat analysis set defined as randomized subjects who received study medication and were challenged

This release has been authorized by the directors of Immuron Limited.

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About Immuron

Immuron Limited (ASX: IMC, NASDAQ: IMRN), is an Australian biopharmaceutical company focused on developing and commercializing orally delivered targeted polyclonal antibodies for the treatment of infectious diseases.

About Phase 2 Clinical Trials

In Phase 2 studies, researchers administer the drug to a group of patients with the disease or condition for which the drug is being developed. Typically involving a few hundred patients, these studies aren't large enough to show whether the drug will be beneficial. Instead, Phase 2 studies provide researchers with additional safety data. Researchers use these data to refine research questions, develop research methods, and design new Phase 3 research protocols. https://www.fda.gov/patients/drug-development-process/step-3-clinical-research

About Travelan®

Travelan® is an orally administered passive immunotherapy that prophylactically reduces the likelihood of contracting travelers' diarrhea, a digestive tract disorder that is commonly caused by pathogenic bacteria and the toxins they produce. Travelan® is a highly purified tabletized preparation of hyper immune bovine antibodies and other factors, which when taken with meals bind to diarrhea-causing bacteria and prevent colonization and the pathology associated with travelers' diarrhea. In Australia, Travelan® is a listed medicine on the Australian Register for Therapeutic Goods (AUST L 106709) and is indicated to reduce the risk of Travelers' Diarrhea, reduce the risk of minor gastro-intestinal disorders and is antimicrobial. In Canada, Travelan® is a licensed natural health product (NPN 80046016) and is indicated to reduce the risk of Travelers' Diarrhea. In the U.S., Travelan® is sold as a dietary supplement for digestive tract protection.

Travelers' diarrhea (TD)

TD is generally defined as the passage of ≥ 3 unformed stools per 24 hours plus at least one additional symptom (such as nausea, vomiting, abdominal cramps, fever, blood/mucus in the stools, or fecal urgency) that develop while abroad or within 10 days of returning from any resource-limited destinations (Leung et al., 2006). Diarrhea continues to be the most frequent health problem among travelers to destinations in lower- and middle-income regions (Steffen, 2017). Deployed US military personnel, essentially representing a long-term traveller population, are particularly affected given their population dynamics and the context in which they seek care and treatment (Connor et al., 2012). Diarrhea is the leading infectious disease threat to the overall health and preparedness of deployed US armed forces, with diarrheagenic E. coli, Campylobacter spp., and Shigella spp. among the most commonly reported etiologies (Riddle et al., 2006).

Immuron Platform Technology

Immuron's proprietary technology is based on polyclonal immunoglobulins (IgG) derived from engineered hyper-immune bovine colostrum. Immuron has the capability of producing highly specific immunoglobulins to any enteric pathogen and our products are orally active. Bovine IgG can withstand the acidic environment of the stomach and is resistant to proteolysis by the digestive enzymes found in the Gastrointestinal (GI) tract. Bovine IgG also possesses this unique ability to remain active in the human GI tract delivering its full benefits directly to the bacteria found there. The underlying nature of Immuron's platform technology enables the development of medicines across a large range of infectious diseases. The platform can be used to block viruses or bacteria at mucosal surfaces such as the Gastrointestinal tract and neutralize the toxins they produce.

IMM-124E

IMM-124E was developed using Immuron's platform technology. IMM-124E is produced from the colostrum of birthing cattle that have been immunised during pregnancy with a vaccine containing the outer antigens of multiple human derived ETEC. A total of 13 ETEC strains are used in the vaccine to produce high levels of antibodies against selected surface antigens from the most common strains of ETEC.

The resultant hyperimmune colostrum IMM-124E from ETEC vaccinated cows contains significant levels of polyclonal antibodies specific for ETEC antigens LPS, CFA-I and Flagellin (Sears et al., 2017).

The antibodies produced in IMM-124E have been found to have a stronger binding and neutralizing activity (than the antibodies of unvaccinated cattle) against a wide range of LPS antigens including both the variable O-polysaccharide region and the preserved oligosaccharide core 'R' region of LPS from the 13 serotypes used in the ETEC vaccine.

IMM-124E is manufactured into a tablet form referred to as Travelan®.

Pre-clinical studies

Pre-clinical studies have shown that IMM-124E contains a high level of IgGs which react with a wide range of ETEC species, including some strains of ETEC not present in the vaccine preparation used to generate IMM-124E. IMM-124E antibodies also cross-react with strains of other gram-negative bacteria such as Shigella, Salmonella, V. cholera, Campylobacter, Pneumoniae, Klebsiella aerogenes, Yersinia enterocolitica, and C. rodentium also causative agents of diarrhea. The strong binding and neutralisation activity of the polyclonal anti-ETEC antibodies present in IMM-124E bind to E. coli in the gastrointestinal tract preventing attachment to the intestinal wall and therefore neutralising their ability to cause diarrhea and its associated symptoms.

Other IMM-124E Clinical studies - Uniformed Services University Study

A concurrent field study, IDCRP-123, is in progress (Clinicaltrials.gov identifier: NCT04605783). To date approximately 50% of the target recruitment of 868 participants have been recruited and randomized to receive an oral dose of 600 mg of IMM-124E drug substance or placebo twice daily (total daily dose of 1200 mg) commencing 2 days prior to travel to overseas destinations, continuing in the overseas destination for a minimum of 10 days to a maximum of 20 days. To date, approximately 434 subjects have been dosed with either IMM-124E or placebo; there have been no reported serious adverse events (SAEs), adverse events (AEs), or new safety concerns.

References

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