Immuron Plans Phase 2 Trial for IMM-529 following FDA review

Key Points

- **Immuron completes pre-IND meeting with FDA on the development of IMM-529 as product to specifically prevent or treat *Clostridioides difficile* infection (CDI)**
- **Previous clinical trial data on IMM-529 provides support for continued development of IMM-529**
- **Investigational new drug (IND) application for IMM-529 planned for 1H 2025**

Melbourne, Australia, September 05, 2024: Immuron Limited (ASX: IMC; NASDAQ: IMRN), an Australian based and globally integrated biopharmaceutical company, is pleased to announce that it has received favourable feedback from the United States Food and Drug Administration (FDA) on the pre-IND (investigational new drug) information package to support the clinical development of IMM-529.

Following the FDA's guidance and feedback, the Company now plans to file an investigational new drug (IND) application for IMM-529 to prevent or treat *Clostridioides difficile* infection (CDI) during the first half of 2025, followed by a Phase 2 trial of IMM-529 in individuals with *Clostridioides difficile* infection.

The increased incidence of antibiotic resistant 'superbugs' has amplified the use of broad-spectrum antibiotics worldwide. An unintended consequence of antimicrobial treatment is disruption of the gastrointestinal microbiota, resulting in susceptibility to opportunistic pathogens, such as *Clostridioides difficile* (C. diff). Paradoxically, treatment of *Clostridioides difficile* infection (CDI) also involves antibiotic use, and the heavy reliance on antibiotics to control C. diff does not allow for the gut flora to regenerate and predisposes the patient to relapsing CDI. C. diff is currently the most common pathogen in healthcare-associated infections and was deemed an urgent threat in the Center for Disease Control and Prevention's report on antibiotic resistance threats in the United States (CDC, 2019). CDI affects over 400,000 people in the US on a yearly basis, contributing to over 30,000 deaths in the US alone annually. This serious health threat has led to an urgent call for the development of new therapeutics to reduce or replace the use of antibiotics to treat bacterial infections.

To address this need, Immuron is developing IMM-529 as an adjunctive therapy in combination with standard of care antibiotics for the prevention and/or treatment of recurrent CDI. IMM-529 antibodies targeting C. diff may help to clear CDI infection and promote a quicker re-establishment of normal gut flora, providing an attractive oral preventative for recurrent CDI.

Immuron is collaborating with Dr. Dena Lyras and her team at Monash University, Australia to develop vaccines to produce bovine colostrum-derived antibodies. Dairy cows were immunised to generate hyperimmune bovine colostrum (HBC) that contains antibodies targeting three essential C. diff virulence

components. IMM-529 targets Toxin B (TcB), the spores and the surface layer proteins of the vegetative cells (refer to MOA schematic - below).

This unique 3-target approach has yielded promising results in pre-clinical infection and relapse models, including **(1) Prevention of primary disease (80% *P* =0.0052); (2) Protection of disease recurrence (67%, *P* <0.01) and (3) Treatment of primary disease (78.6%, P<0.0001; TcB HBC).** Importantly IMM-529 antibodies cross-react with whole cell lysates of many different human strains of C. diff including hypervirulent strains.

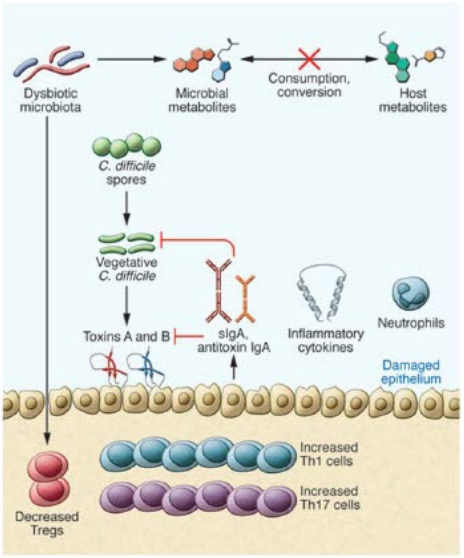
To our knowledge, IMM-529 is, to date, the only investigational drug that has shown therapeutic potential in all three phases of the disease. https://doi.org/10.1038/s41598-017-03982-5

IMM-529 MOA in CDI – Targets Spores, Vegetative Cells, and Toxin B

SPORES - Infectious particles – Heat, ethanol & UV resistant. Survive gastric acid, adhere to cells in the colon & germinate. Product X antibodies bind to surface antigens on spores & prevent adherence to host cells & limit germination.

VEGETATIVE CELLS – Fimbriae & other surface layer proteins (SLP) contribute to bacterial colonization. Fimbriae are used to adhere to other bacteria & to host cells. Fimbriae one of the primary mechanisms of virulence. Product X antibodies bind to SLP on vegetative cells & limit colonization.

TOXIN B – is essential for virulence. Toxin B disrupts the cytoskeleton and tight junctions of intestinal epithelial cells. Product X antibodies neutralise toxin B, inhibiting toxin mediated epithelial cell apoptosis & limit toxin translocation into the systemic circulation & inflammatory signal cascades.



Opportunity assessment by Lumanity indicates that if efficacious, IMM-529 will be positioned as early in treatment algorithm as payers will allow. Second recurrence appears to be most likely (after one course each of fidaxomicin and vancomycin) but some doctors who treat aggressively or see a patient as being especially high-risk may be willing to turn to IMM-529 even earlier. Up to ~31k patients would be eligible if IMM-529 is positioned at the second recurrence, and up to ~95k patients would be eligible if positioned at the first recurrence. Based on the estimated market size, anticipated payer restrictions, pricing, and competition, base case yearly revenue for IMM-529 is projected at US$93M. The estimate of $93M represents a conservative view of the target patient population (limited to 2nd recurrence and later by trial design and payer coverage) but likely aggressive use (75%) within that target patient population. Greater efficacy may lead to greater use in patients after their first recurrence, increasing the size of the patient population. Even capturing as few as 10% of first recurrence patients adds up to 9,500 patients to the treated pool (potential for some double counting), which could add up to US$48M in yearly revenue. Oral dosing of IMM-529 was viewed as a positive by infectious disease experts, particularly since current advanced CDI treatment approaches (e.g., bezlotoxumab, fecal microbiota transplantation) are expensive and complex in their administration.

This release has been authorised 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.

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.

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FORWARD-LOOKING STATEMENTS:

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