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# Immuron Limited Oral Immunoglobulins Changing the Paradigms of Care

March 2018

IMMUION ASX:IMC NASDAQ:IMRN

### **Forward Looking Statement**

Certain statements made in this presentation are forward-looking statements and are based on Immuron's current expectations, estimates and projections. Words such as "anticipates," "expects," "intends," "plans," "believes," "seeks," "estimates," "guidance" and similar expressions are intended to identify forward-looking statements.

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### **Company Highlights**



- Clinical stage biopharmaceutical company targeting inflammatory-mediated and infectious diseases with oral immunotherapies
- Validated technology platform with one registered asset generating revenue
- 2 Lead clinical assets in Phase 2 development for the treatment of multiple high value indications, Fat Liver Disease and CDI.
- Excellent safety profile, GRAS by FDA, expedited regulatory review and approval process
- Well positioned to address high unmet medical need in multiple blockbuster markets
- High-value peer licensing deals and M&A underscore potential upside
- Company listed on NASDAQ in 2Q 2017
- Experienced Management Team and strong support from leading KOLs and institutions (NIH, DoD)



#### **Platform Overview: Oral Immunoglobulins**





#### Competitive Advantage

- Platform capable of producing multiple drug candidates → Long-term value creation
- Bovine IgG possesses a unique ability to remain active in the human GI tract → delivering its full benefits to the bacteria found there
- Bovine IgG is capable of withstanding the acidic environment of the stomach and is resistant to proteolysis by the digestive enzymes in the GI tract
- Safety established → Not absorbed into the blood



### Immuron's Clinical Programs Multiple Near-Term Inflection Points



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Program	Indications	Pre-Clinical	Phase 1	Phase 2	Phase 3	Program Highlights
Anti-Inflammatory Programs						
IMM-124E	NASH					- Topline results Available
IMM-124E	ASH					- NIH Funded; UVA - Topline results expected 2019
IMM-124E	Pediatric NAFLD					- NIH Funded; Emory University - Topline results expected 4Q 2018
IMM-124E	Colitis					Collaboration with Dr. Rogler, Zurich University
IMM-124E	Autism					Murdoch Childrens Research Institue, La Trobe & RMIT Universities
			Anti-Infect	ive Programs		
IMM-529	C. difficile					- Phase 1/2 initiated 4Q 2017 - Topline results expected Q4 2018
IMM-124E / Shigella Vaccine	Shigella Infections					Collaboration with US Army
IMM-124E	Campylobacter; ETEC Infections					Collaboration with US Navy

#### **TRAVELAN**

- Hyperimmune bovine colostrum powder 200mg (30 caplets, 24 month shelf life)
- Reduces the risk of TD, reduces the symptoms of minor GI disorders





**US** Packaging

Regulatory Authority	Regulatory Pathway	Indications
TGA	Listed Medicine	<ul> <li>Reduces the risk of travellers' diarrhoea</li> <li>Reduces the symptoms of minor gastro-intestinal disorders</li> <li>Antimicrobial</li> </ul>
Medsafe (New Zealand)	Not marketed in New Zealand	Not marketed in New Zealand
FDA (USA)	Self-affirmed generally regarded as safe (GRAS) Dietary supplement. FDA does not review dietary supplements for safety and effectiveness	Hyperimmune colostrum dietary supplement
Health Canada	Natural Health Product	Travelan helps reduce the risk of traveller's diarrhea.
EMA (Europe)	Not marketed in Europe	Not marketed in Europe

ARTG Listing for Travelan

http://www.travelanusa.com/



#### Prominent immune-reactive bands of Campylobacter, ETEC and Shigella isolates



#### from Bhutan, Cambodia, Nepal and Thailand



#### Travelan immunoreactivity study:

- Armed Forces Research Institute of Medical Sciences (AFRIMS) •
- Walter Reed Army Institute of Research (WRAIR) •
- US Naval Medical Research Centre (NMRC) •

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# IMM-124E-2001 NASH Clinical Trial Top Line Results

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- IMM-124E demonstrated good safety and tolerability on both doses
- A statistically significant effect of IMM-124E to reduce serum levels of LPS
- A statistically significant and clinically meaningful effect to reduce ALT levels by 30% or more in patients with elevated ALT at enrollment
- Statistically significant reduction in mean AST compared to placebo.
- Statistically significant effect to reduce CK-18 compared to placebo
- IMM-124E was shown to remain in the gut and not cross into the bloodstream
- No effect on liver steatosis



### LPS ANTAGONISM FIRST IN CLASS MoA





# STUDY DESIGN IMM-124E-2001





120 patients, 3-arms, Randomized, double blind, Placebo – 2dose, balanced 1:1:1 design

#### Major Inclusion Criteria

Histologically proven NASH (≤12 months)

- NASH activity score (NAS) ≥4
- Cytologic ballooning score of at least 1
- 10% or more macrovesicular steatosis
- HBA1C of <u><</u>9.0



# STUDY ENDPOINTS



#### PRIMARY

- Safety
- Hepatic Fat Fraction

#### SECONDARY

- liver enzymes ALT, AST, GGT
- Glucose homeostasis and serum lipid profile
- Serum Bovine Ig Pharmacokinetics
- Establish recommended dose

#### MoA

- Lipopolysaccharides (LPS)
- CK-18
- Cytokines
- Adiponectin and GLP-1



#### **STUDY POPULATIONS**





<u>Definitions</u>: ITT = Intention to Treat FAS = Full analysis set PP = Per Protocol

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### SERUM ALANINE AMINO-TRANSFERASE (ALT) RATE OF SUBJECTS WITH ≥30% DECREASE \*



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### SERUM LIPOPOLYSACCHARIDES (LPS) RATE OF PATIENTS WITH ≥15% DECREASE\*



\* Baseline LPS>250



### SERUM LPS OVERALL RESPONSE TO TREATMENT TERTILE ANALYSIS

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- Analysis aimed at looking at the entire population
- Shows an overall beneficial effect across all patients
- Minimizes risk of cut-off selection bias
- p=0.0715 (1200mg vs. PLB)

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### SERUM CYTOKERATINE-18 (CK-18) RATE OF PATIENTS WITH ≥15% DECREASE\*



### SERUM CK-18 OVERALL RESPONSE TO TREATMENT TERTILE ANALYSIS





- Analysis aimed at looking at the entire population
- Shows an overall beneficial effect across all patients
- Minimizes risk of cut-off selection bias



### SERUM ASPARTATE-AMINOTRANSFERASE AST RATE OF SUBJECTS WITH AST DECREASE >30%



### ASPARTATE TRANSAMINASE (AST) LINEAR REGRESSION PREDICTED VALUES





#### **HEPATIC FAT FRACTION**





- No effect seen in any of the arms
- Since IMM-124E is no anti-steatotic

LS Mean ± Std Err



### PHARMACOKINETICS SERUM BOVINE Ig





- No significant change in any of the arm
- All curves remain essentially flat



### **Safety Results**



	Total	Placebo n=44 [n(%)]	600mg IMM124E n=43 [n(%)]	1200mg IMM124E n=46 [n(%)]
All Adverse Events	572	167	192	213
Grade 3-4 Subjects (events)	28	6 (6)	6 (12)	5 (10)
SAE <sub>1</sub> Events	6	3	1	2
Rx stopped due to AE	2	0	<i>1</i> <sub>2</sub>	13
Death	1	14	0	0

1 SAE - None determined related to study drug

2 Possibly related to study drug: Worsening of Arthraligia - Grade 2

3 Possibly related to study drug: Diarrhea - Grade 1

4 Road accident, Unrelated to study drug



#### **SUMMARY**



- IMM-124E demonstrates an outstanding safety profile
- IMM-124E shows a significant decrease in serum LPS making it the first ever LPS-antagonist drug candidate
- IMM-124E reduces Liver enzymes
- IMM-124E demonstrates a significant reduction in CK-18
- No change in Hepatic Fat Fraction was demonstrated in any study arm
- Pharmacokinetics shows no IMM-124E translocation into blood



# Neutralizing Clostridium *difficile*, while Sparing the Microbiome



IMM-529 in Clostridium difficile Infection (CDI)



- Biologic with unique triple mechanism of action
  - Targets and neutralizes the toxin B, the spores and the vegetative cells
- Potential to redefine the standard-of-care (SOC) therapy for CDI
  - Stops virulence, without impacting the microbiome
  - Compelling data in all three phases of the disease including (1) prevention of primary disease, (2) treatment of primary disease and (3) prevention of recurrence
  - Orally administrated, safe
- >70% survival rate in CDI mice treated with IMM-529 vs. <7% survival rate in control groups
- Potential orphan disease designation; Potential breakthrough / fast track designations
- Market exclusivity (biologics; High barriers to generic biosimilar entry)

#### **IMM-529 for the Treatment of CDI**



Market Opportunity	<ul> <li>Therapeutic market is expected to grow from US\$356.3 million in 2014 to over \$1.5 billion by 2024 – CAGR 15%</li> <li>Nearly 30,000 patients die each year from C. <i>difficile</i> infections (US)</li> <li>Potential orphan disease (7 years market exclusivity and premium pricing)</li> </ul>
Unmet Need	<ul> <li>Vancomycin and metronidazole are the current standard of care, accounting for 80% of patient share (US)</li> <li>However, therapies are plagued by significant CDI recurrences (1st relapse: 25%; 2nd: 40%; 3rd: 50%) underscoring need for new treatments</li> <li>There is also growing resistance to vancomycin treatment</li> </ul>
IMM-529 Positioning	<ul> <li>Highly differentiated – Neutralizes C. <i>difficile</i> but does not impact microbiome</li> <li>Only asset that targets not only toxin B but also the spores and the vegetative cells responsible for recurrence</li> <li>Can be used in combination with standard of care</li> <li>Targets many isolates</li> </ul>



#### **Triple Action MOA** Neutralizing C. difficile; Sparing the Microbiome



#### **Spores – Infectious Particles**

**IMM-529** antibodies bind to multiple epitopes on surface antigens on spores and prevent adheres to host cells and limit germination.

Heat, ethanol and UV resistant. Survive gastric acid, adhere to cells in the colon and germinate.

#### **Vegetative Cells**

**IMM-529** antibodies bind to multiple epitopes on the surface layer proteins (SLP) on vegetative cells and limit colonization.

Fimbriae and other surface layer proteins (SLP) contribute to bacterial colonization. Fimbriae are used to adhere to other bacteria and to host cells and is one of the primary mechanisms of virulence

#### **Toxin B**

**IMM-529** antibodies bind to multiple epitopes effectively neutralize toxin B, inhibiting toxin mediated epithelial cell apoptosis and limit toxin translocation into the systemic circulation and inflammatory cascades.

Toxin B is essential for virulence. Toxin B disrupt the cytoskeleton and tight junctions of intestinal epithelial cells.



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#### **Results of Pre-Clinical Studies**





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#### Phase 1/2 Study Design



#### Phase 1/2 Study in CDI Initiated 4Q 2017

- Phase 1/2, randomized, double blind, placebo-controlled clinical study of IMM-529 for the treatment of CDI
- **60 subjects** to be enrolled up to 3 weeks of definitive diagnosis of CDI (at least 20 subjects to be enrolled within the first 72 hours)
- Subjects randomized to IMM-529 or placebo in a 2:1 ratio
- **Treatment duration:** 28 days on top of SOC (vancomycin / metronidazole)
- Follow-up: 3 months overall
- **Primary objective:** To evaluate the safety and tolerability of IMM-529 together with standard of care (SOC) in patients with CDI
- Secondary objective: To evaluate the effectiveness of IMM-529 together with SOC to treat patients with CDI



### NASH and C. *difficile* Comps Indicate Potential for Substantial Growth



Company	Ticker	Program	Development Stage	Market Cap*	
	Program in NASH				
Intercept	ICPT	Obeticholic acid	Phase 3	US\$2.9B	
GENFIT	GNFT	Elafibranor	Phase 3	US\$1.1B	
	CNAT	ENCORE-LF	Phase 2	US\$195M	
		Program in C. D	ifficile		
SERES THERAPEUTICS <sup>®</sup>	MCRB	SER-109; SER-262	Phase 2	US\$423M	
summit	SMMT	SMT19969	Phase 1	US\$143M	
	ASMB	ABI-M101	Preclinical	US\$419M	

\*As of May 4, 2017

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#### Capital Profile Immuron Limited (ASX:IMC NASDAQ:IMRN)



Current To	o 10 Shareholders

Rank	Holder Name	Current Qty	%
1	HSBC CUSTODY NOM AUST LTD (ADR Program)	19,531,706	14.97%
2	* GRANDLODGE PL	9,056,682	6.94%
3	AUTHENTICS AUST PL	8,624,999	6.61%
4	RETZOS EXECUTIVE PL	3,800,000	2.91%
5	* ANASTASIOU PETER + K P	2,907,236	2.23%
6	INVERAREY PL	2,731,632	2.09%
7	* FIFTY-FIFTH LEPRECHAUN PL	2,645,983	2.03%
8	INSYNC INV PL	2,500,000	1.92%
9	SBI INV PR LLC	2,000,000	1.53%
10	ADVANCE PUBLICITY PL	2,000,000	1.53%
	TOTAL TOP 20 SHAREHOLDERS	55,798,238	42.76%
	BALANCE OF SHARES	74,642,224	57.24%
	TOTAL SHARE ON ISSUE	130,440,462	100.00%
	* Denotes a Director Related Entity		

Current Company

Market Capitalization

AUD\$51.2M ≈ USD\$39.5M (9<sup>th</sup> Mar 2018)



## **Key Milestones Expected to Drive Value**





# **Thank You**

