



# Immuron Limited

## *Changing the Paradigms of Care*

August 2017

# 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.

Although Immuron believes the forward-looking statements are based on reasonable assumptions, they are subject to certain risks and uncertainties, some of which are beyond Immuron's control, including those risks or uncertainties inherent in the process of both developing and commercializing technology. As a result, actual results could materially differ from those expressed or forecasted in the forward-looking statements.

The forward-looking statements made in this presentation relate only to events as of the date on which the statements are made. Immuron will not undertake any obligation to release publicly any revisions or updates to these forward-looking statements to reflect events, circumstances or unanticipated events occurring after the date of this presentation except as required by law or by any appropriate regulatory authority.

# 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)**

# Experienced Management Team

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## **Jerry Kanellos, PhD**

*Chief Executive Officer*

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Dr. Kanellos has over 20 years of experience in the pharmaceutical and biotech industries including CMC, operations and BD. He has held senior roles at CSL and was CEO of Avipep Pty Ltd a privately owned oncology biotech company.

## **Travis Robins**

*US Sales Director*

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Mr. Robins is an accomplished, motivated leader with progressive years of proven success in dramatically increasing revenues and expanding market shares, while building key relationships.

## **Dan Peres, MD**

*Chief Medical Officer*

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Dr. Peres, a surgeon by training, has deep experience in liver diseases and clinical development including NASH, having worked for leading Medical Devices and Pharma companies since 2008.

## **Reza Moussakhani**

*Manufacturing Quality Director*

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Mr. Moussakhani has extensive experience in implementation of project/quality and process improvements, including with Hospira and Sigma Pharmaceuticals.

# Prominent Scientific Advisory Board and Leading Research Partners



## Advisory Board

### **Dr. Arun Sanyal (MD)**

*University of Virginia*

Former President of the AASLD. Current Chair of the Liver Study Section at the NIH. IMM-124E lead PI.

### **Dr. Stephen Harrison (MD)**

*San Antonio Military Medical Center  
Brooke US Army Medical Center*

Internationally renowned expert in NASH. Lead PI of Galectin's GR-MD-02's Phase II trial.

### **Dr. Manal Abdelmalek (MD)**

*Duke University Medical Center*

Dr. Abdelmalek is a leading investigator in the field of NASH.

### **Dr. Gerhard Rogler (MD, PhD)**

*Zurich University*

Professor Rogler is a leader in the field of Colitis and has authored more than 200 original peer-reviewed articles.

### **Dr. Miriam Vos (MD)**

*Emory University*

Dr. Vos specializes in the treatment of gastrointestinal disease in children as well as fatty liver disease and obesity.

### **Dr. Dena Lyras (PhD)**

*Monash University*

Dr. Lyras is one of the world's leading experts in *C. difficile*.

## Organizations



Universität  
Zürich<sup>UZH</sup>



Immuron



# Oral Immunoglobulins: Scalable, Disruptive Technology



1

## Vaccines Are Developed



2

## Antibodies Are Harvested from Colostrum



Antigen Specific  
Antibodies  
(IgG and IgG1)

+

Adjuvants

3

## Broad Therapeutic Effect

Induction of  
regulatory  
T-cells

+

Clearance of  
Targeted GUT  
Pathogens

- Reduced gut and blood pathogens responsible for initiating inflammation
- Reduces systemic inflammation
- Lowers organ injury
- Not associated with general immune suppression
- Generally Regarded as Safe (GRAS)

## Competitive Advantage

- **Platform capable of producing multiple drug candidates** → Long-term value creation
- **Regulated as biologics by the FDA** → 12 years exclusivity in the US for each approval
- **Unique technology offering protection from future generic biosimilar market erosion**
- **Safety established** → Generally Regarded As Safe (GRAS) by FDA, accelerated approval process
- **Low manufacturing costs** → ~ \$1 / gram compared with > \$100 / gram for MAb

# Immuron's Clinical Programs

## Multiple Near-Term Inflection Points



Program	Indications	Development Stage				Program Highlights
		Pre-Clinical	Phase 1	Phase 2	Phase 3	
Anti-Inflammatory Programs						
IMM-124E	NASH	<div></div>				- Interim data reported 2Q 2017 - Topline results expected 4Q 2017
IMM-124E	ASH	<div></div>				- NIH Funded; UVA - Topline results expected 2018
IMM-124E	Pediatric NAFLD	<div></div>				- NIH Funded; Emory University - Topline results expected 1H 2018
IMM-124E	Colitis	<div></div>				Collaboration with Dr. Rogler, Zurich University
IMM-124E	Autism	<div></div>				Murdoch Childrens Research Institue, La Trobe & RMIT Universities
Anti-Infective Programs						
IMM-529	C. difficile	<div></div>				Phase 1/2 Expected to start 3Q 2017
IMM-124E / Shigella Vaccine	Shigella Infections	<div></div>				Collaboration with US Army
IMM-124E	Campylobacter; ETEC Infections	<div></div>				Collaboration with US Navy

# IMM-124E

Revolutionary Treatment for NASH

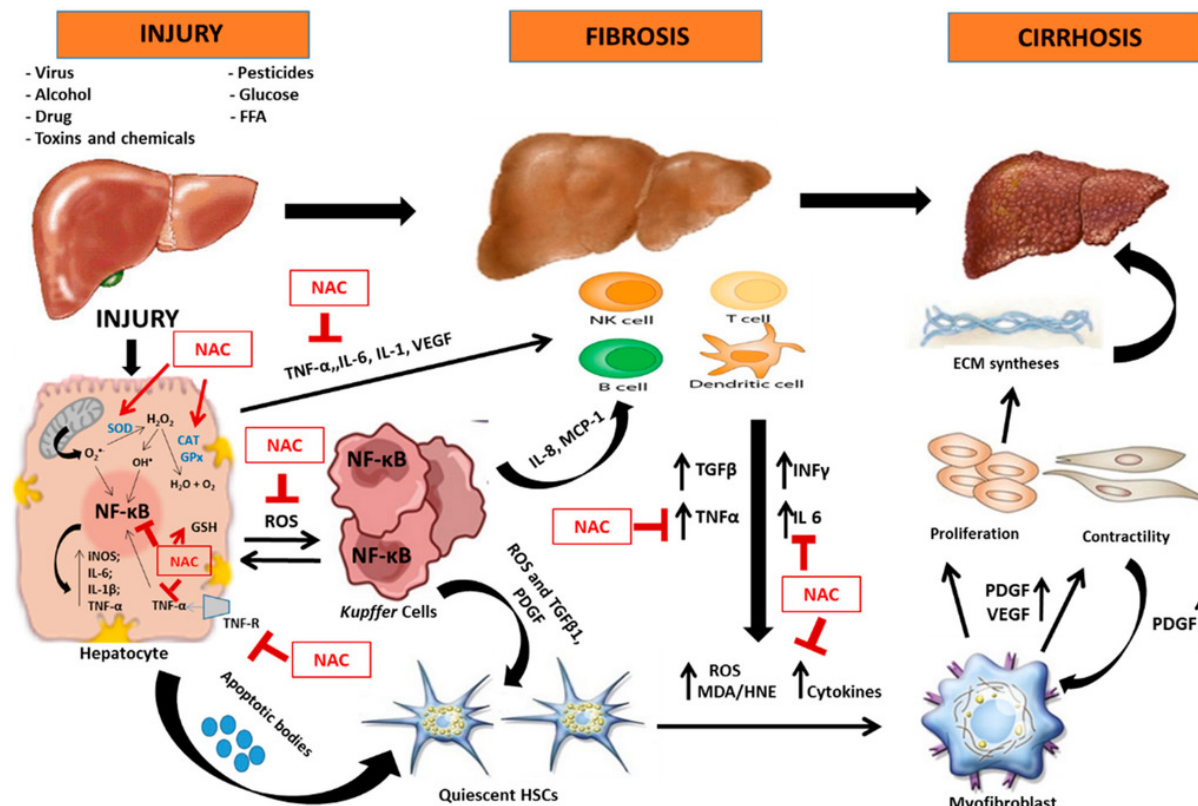
Immuron



# NASH (Non-Alcoholic Fatty Liver) Pathophysiology



## NASH – Pathophysiology



- Blood derived antigens (including circulating LPS) determines tolerance vs. inflammation
- Kupffer cells play a key role in liver inflammation and fibrosis
- Tregs hold a key role in tolerance (homeostasis)
- Much like hepatic tolerance the gut immune system can promote anti-inflammatory effect

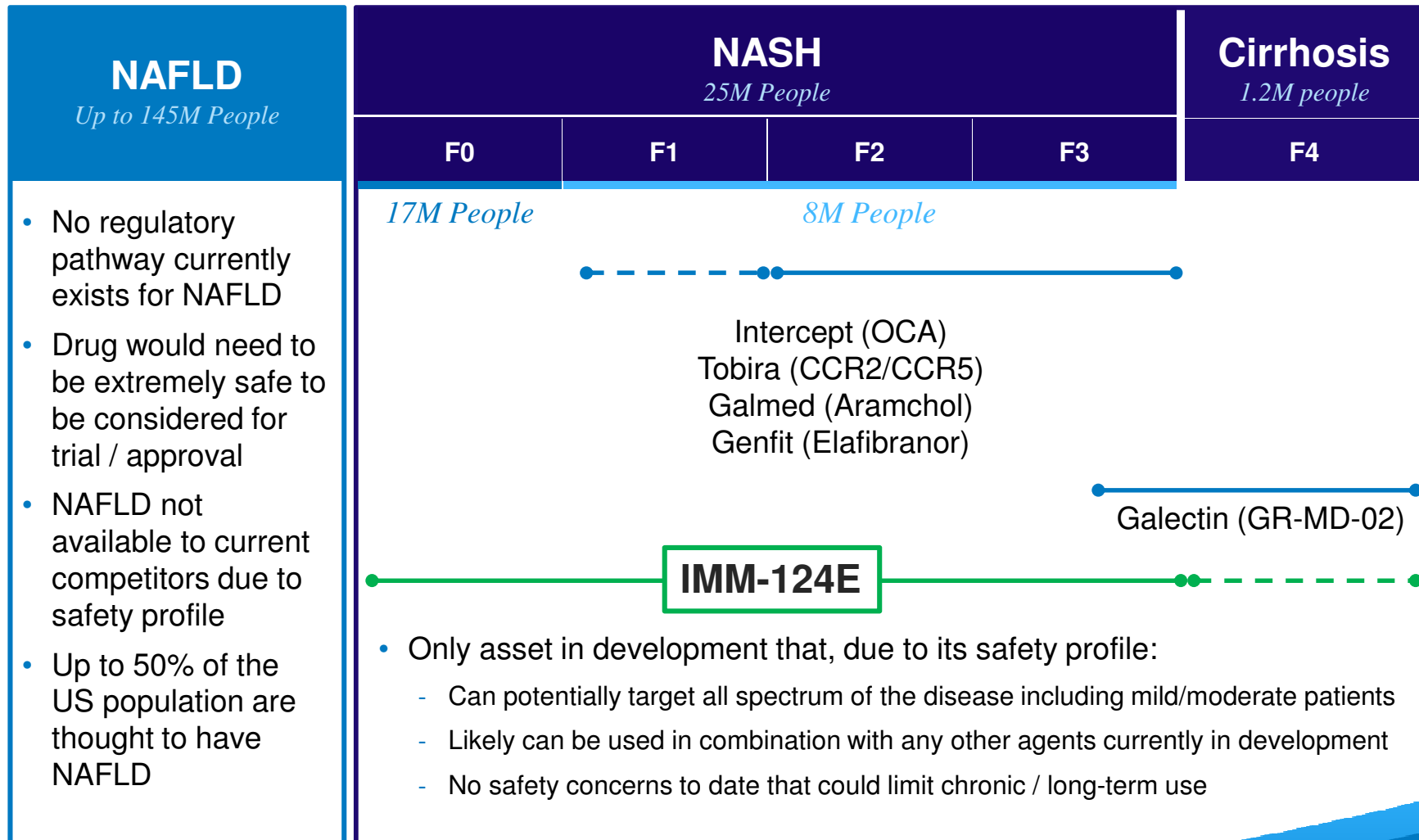
Source: Adapted from Cohen-Naftaly; Scott L. Friedman, 2011

# IMM-124E in NASH (Non-Alcoholic Fatty Liver)



- **Targeted antibodies mediate broad anti-inflammatory mechanism of action**
  - Upstream Effect: **LPS-TLR4 pathway**
  - Downstream: **Anti-inflammatory through both innate and adaptive immune systems** (e.g., the induction of regulatory T-cells to control and inhibit excess inflammation)
- Strong **anti-fibrotic effect** demonstrated with CCl4 model
- **Unique competitive profile due to safety/MOA:**
  - Addresses **multi-factorial** nature of NASH
  - Potential for **combination use**
  - Safety profile supporting of **long-term chronic use**
  - Potential to **expand to mild/moderate** populations
- **Market exclusivity** (biologics; High barriers to generic biosimilar entry)

# IMM-124E – Uniquely Positioned to Address Large Unmet Need of \$35B Market (2030)



# IMM-124E: Fatty-Liver Portfolio – 3 Phase II Trials



## Three Ongoing Phase 2 Programs: NASH, ASH and Pediatric NAFLD

### NASH

- Lead Principal Investigator: Arun Sanyal; Former President of AASLD (American Association for the Study of Liver Diseases) and current Chair of the Liver Study Section at the NIH (National Institute of Health)
- Multi-center, double-blinded, placebo controlled trial; 25 sites running in US, Australia and Israel
- Fully recruited: 133 patients with biopsy proven NASH
- Primary endpoint: changes in liver fat content confirmed by MRI; changes in ALT (liver enzymes)
- 3 arms: placebo, high dose and low dose
- Timing: topline results by 4Q 2017

### ASH

- NIH funded; sponsored by University of Virginia
- Expected enrollment: 66 patients
- Endpoint: ALT
- Timing: topline results in 2018

### Pediatric NAFLD

- NIH funded; sponsored by Emory University
- Expected enrollment: 40 patients
- Endpoint: ALT; 3 months treatment
- Timing: topline results in 1H 2018

# IMM-124E – Summary of Data

Prevention of Fibrosis and Improvement in Metabolic & Inflammatory Markers



## CCl4 Fibrosis Studies

- **Carbon-Tetrachloride (CCl4) a non-disease related fibrosis model**
- **Aim:** To demonstrate effects of IMM-124E on Fibrosis caused by Intraperitoneal CCl4
- **Results:**
  - Marked **reduction in Liver Fibrosis and Inflammation** on Histology
  - Marked reduction on Liver Damage markers (i.e. ALT, Bilirubin etc.)
  - Marked **reduction in Liver Activated Macrophages (F4/80 high)**

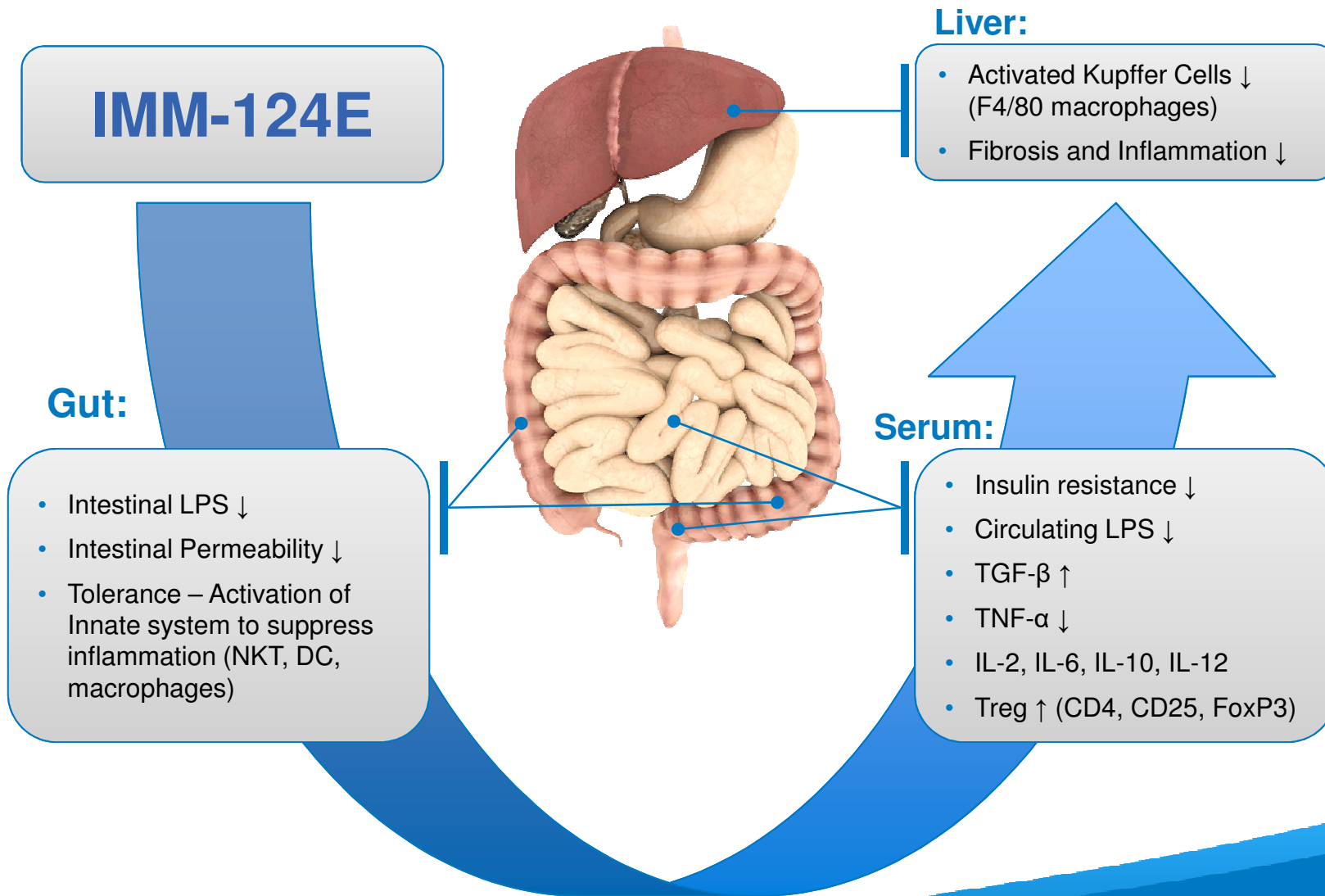
## Ob-Ob Mice

- **Model represents the Metabolic syndrome**
- **Aim:** To demonstrate the effect of IMM-124E or **anti-LPS IgG** (derived from IMM-124E)
- **Results:**
  - Anti-LPS IgG considerable reduces ALT level
  - Improved metabolic status for IG and IMM-124E treated mice (i.e. TG, Fasting Glucose and OGTT)
  - **Anti-inflammatory shift: Decreased TNF- $\alpha$  and increase splenic NKT cells**

## Phase 1/2 Clinical Studies

- **Aim: To show safety and efficacy of IMM-124E Biopsy Proven NASH Patients**
- **Population:** 10 subjects with biopsy proven NASH and Type 2 Diabetes
- **Results:**
  - Improved Metabolic status (e.g. HbA1c, HOMA OGTT) GLP1 and Adiponectin
  - Improved Liver status (e.g. ALT)
  - **Proof of concept: increase in Circulatory Regulatory T-Cell**

# IMM-124E in NASH (Non-Alcoholic Fatty Liver)

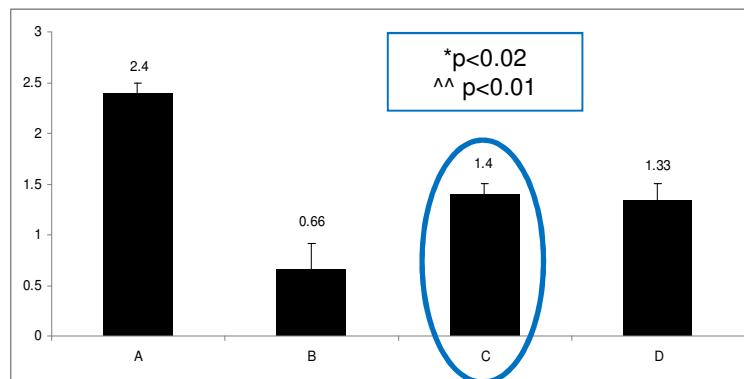
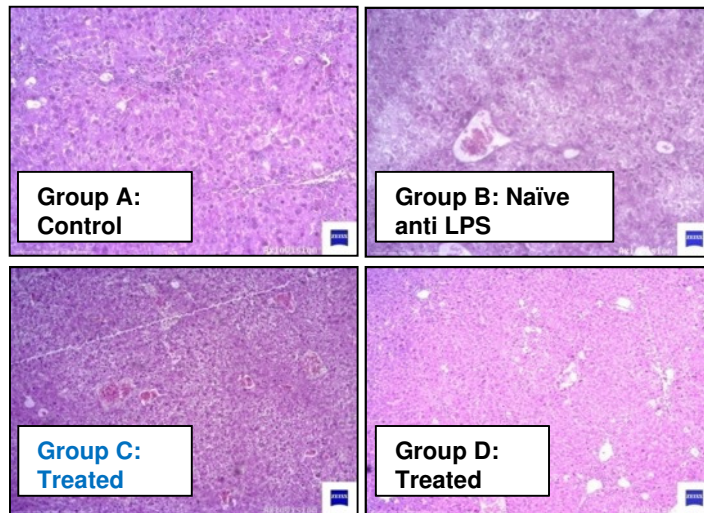




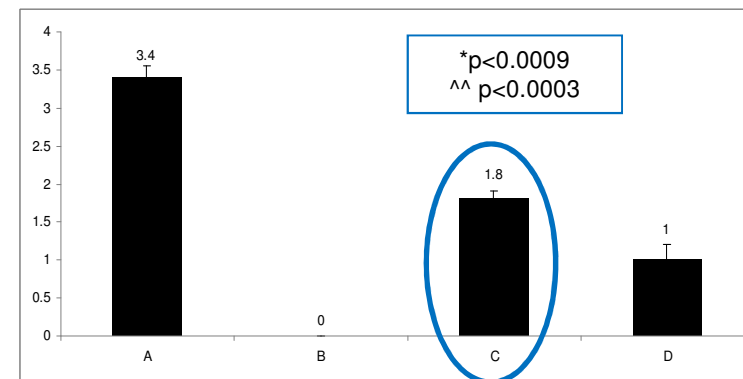
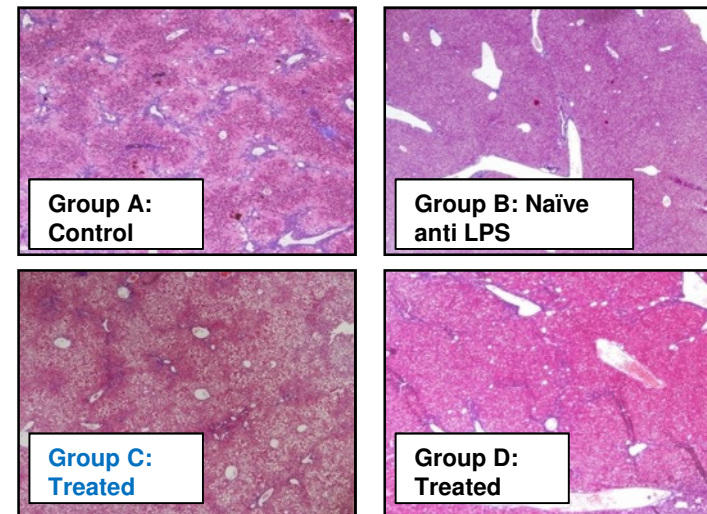
# Animal Models: IMM-124E Improves Fibrosis and Inflammatory Markers



## Decrease Portal Inflammation



## Improved Metavir Fibrosis Score



# Animal Models: Macroscopy – Prevents Fibrosis



## Fibrotic Liver

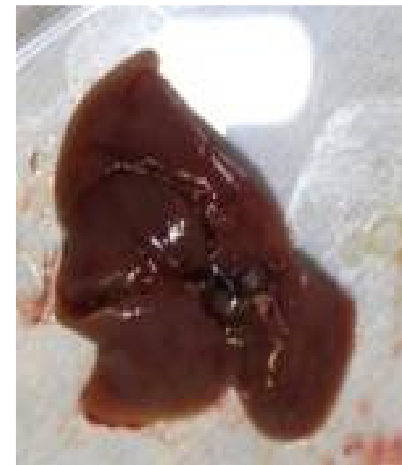
*CCl<sub>4</sub> (carbon tetrachloride)*



**IMM-124E**

## IMM-124E Treated Liver

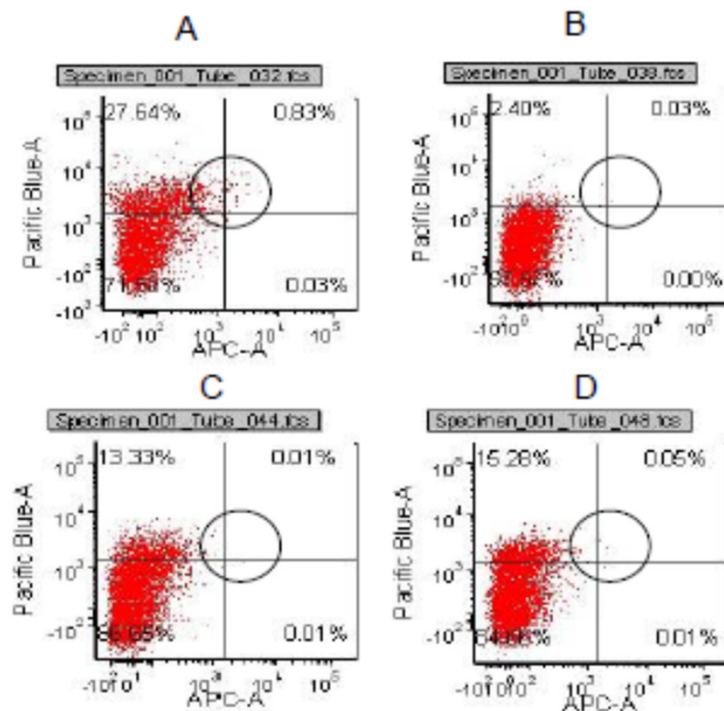
*CCl<sub>4</sub> (carbon tetrachloride)*



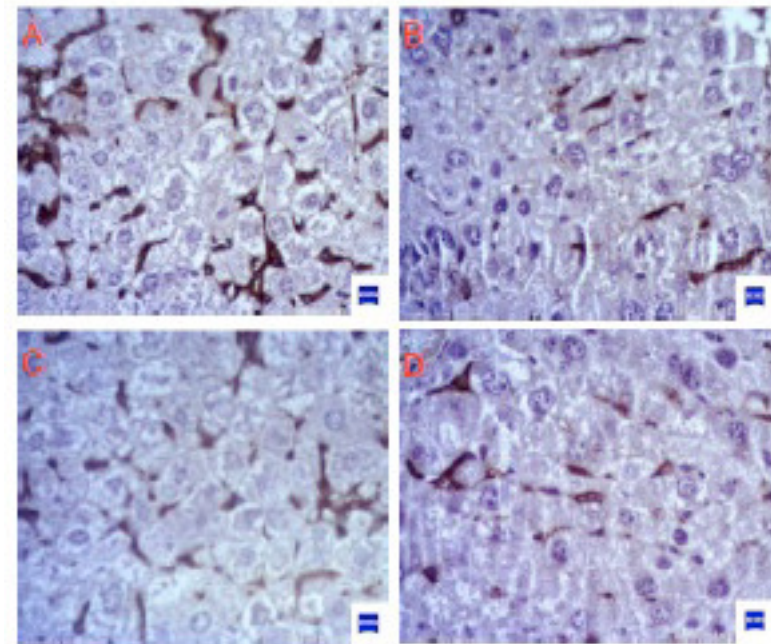
**Treatment with IMM-124E Prevents Fibrosis and Inflammation**

*Mizrahi M. 2013, AASLD; Hepatology 751A*

# Suppression of F4/80High Macrophages



Kupffer cells 4/80 Flow cytometry (FACS analysis) for F cells in group A vs. group C 4/80 showed higher F 0.05P<



Kupffer cells showed 4/80 Immunohistochemical staining for F 0.05 cells in group A vs. group C P<4/80 F rehgh

**Marked Reduction in Liver Activated Macrophages (F4/80 high)**

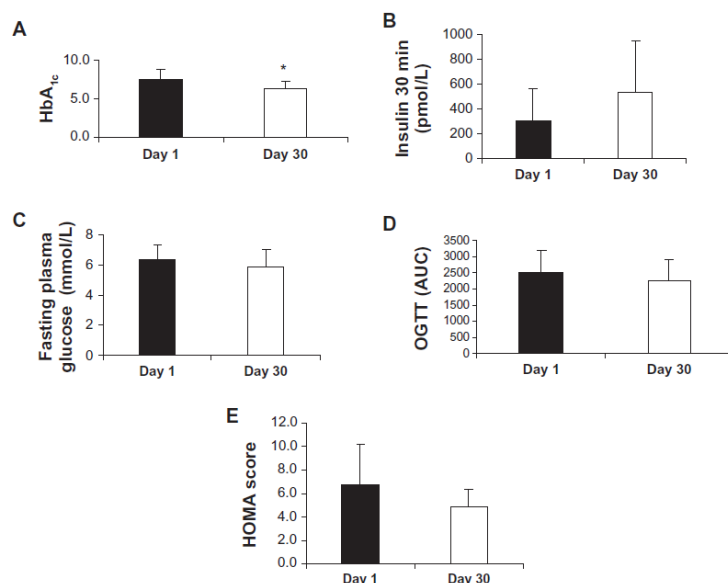
# Phase 1/2: Improves Liver Function and Reduces Insulin Resistance



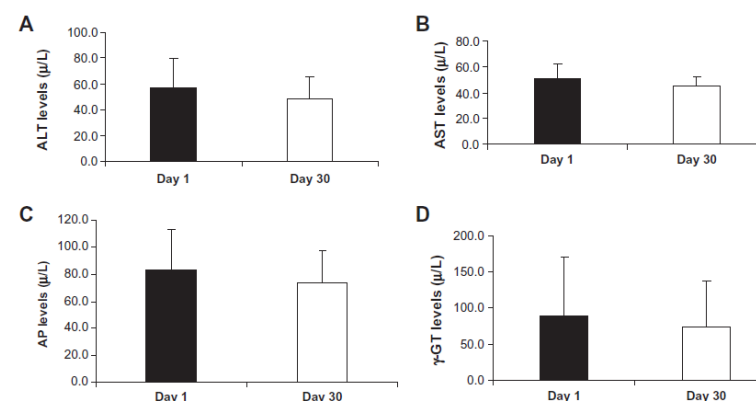
## Results of a Phase 1/2a clinical trial; N=10

30 Days Treatment Endpoint Met; NO SAFETY ISSUES REPORTED

### Improved HbA1c, OGTT and HOMA



### Improved Liver Enzymes

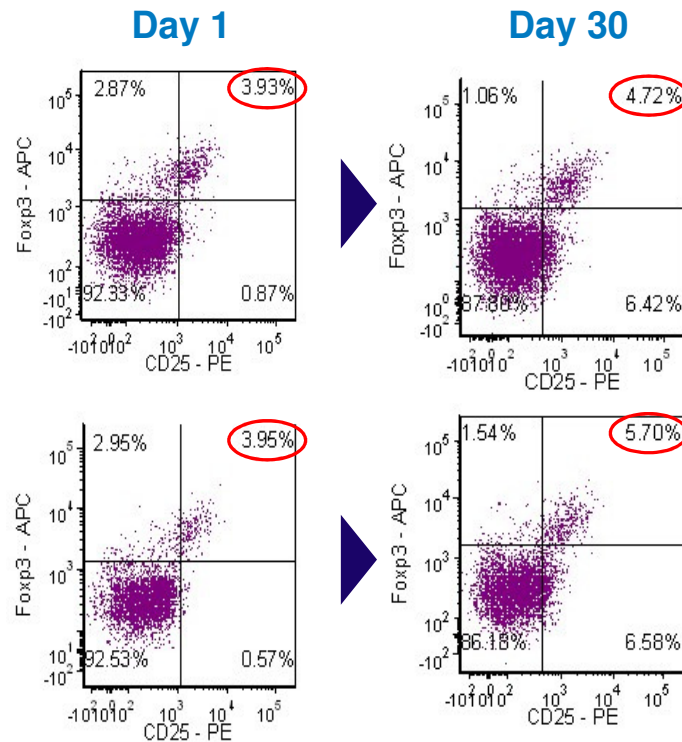


Improved Metabolic Status (e.g. HbA<sub>1c</sub>, HOMA OGTT) GLP1, and Adiponectin and Liver Function (e.g. ALT)

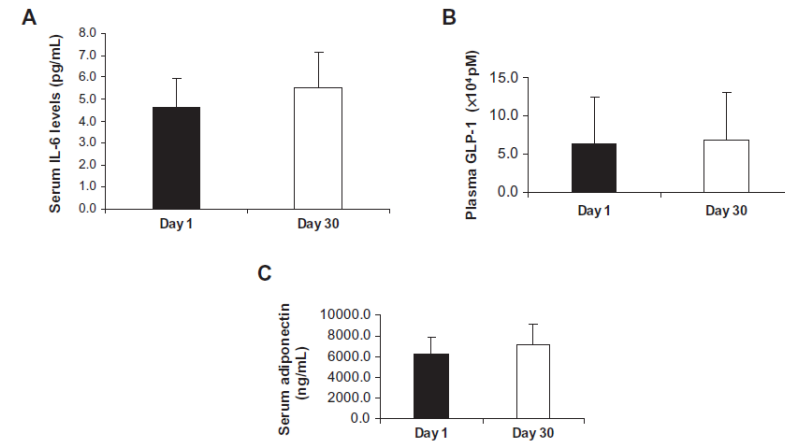
# Phase 1/2: Improves Inflammatory Biomarkers



## Increased CD4+CD25+FOXP3+ TREGS



## Increased GLP1 and Adiponectin



**Proof of Concept:**

**Increase in Circulatory  
Regulatory T-Cell**

# IMM-124E: NASH Phase II Trial



## IMM-124E-2001 Interim Analysis – No Safety Issues Reported

### NASH Study

- The study has 12 scheduled visits over the study duration of 28 weeks (24 weeks treatment and 4 weeks follow-up).
- The interim analysis was triggered when 80 patients (two thirds of the planned study population) had completed the entire 24-week treatment period and had verified Baseline and week 24 MRI data.
- The purpose of the interim analysis was to determine whether any signals exist regarding; safety of the study treatment and to search for signals of efficacy from primary, secondary and exploratory endpoints.

### Patient Populations

- A total of 133 patients have been randomized into the study.
- To be included in the interim analysis patients were required to have attended one post baseline visit.
- The Full Analysis Set population had 122 patients who met this criterion.
- To be included in the Per Protocol population patients had to complete the 24-week treatment period, have valid Baseline and Week 24 MRI values. A total of 69 patients met this criteria.

### Results

- Baseline participant characteristics across the 3 treatment groups are similar
- Baseline LPS 1000 – 10,000 times level reported for healthy blood donors
- Interim Analysis report achieves main goals – Safety, Tolerability and Futility
- There was a significant decrease in serum ALT and AST throughout 24 weeks, Changes in ALT values taking into account all time points by calculating area under the curve and correcting for baseline values demonstrated a dose-related effect.
- IMM-124E demonstrated a systemic effect decreasing liver injury and it's potential to treat NASH as a non-absorbable drug



# IMM-124E Interim analysis

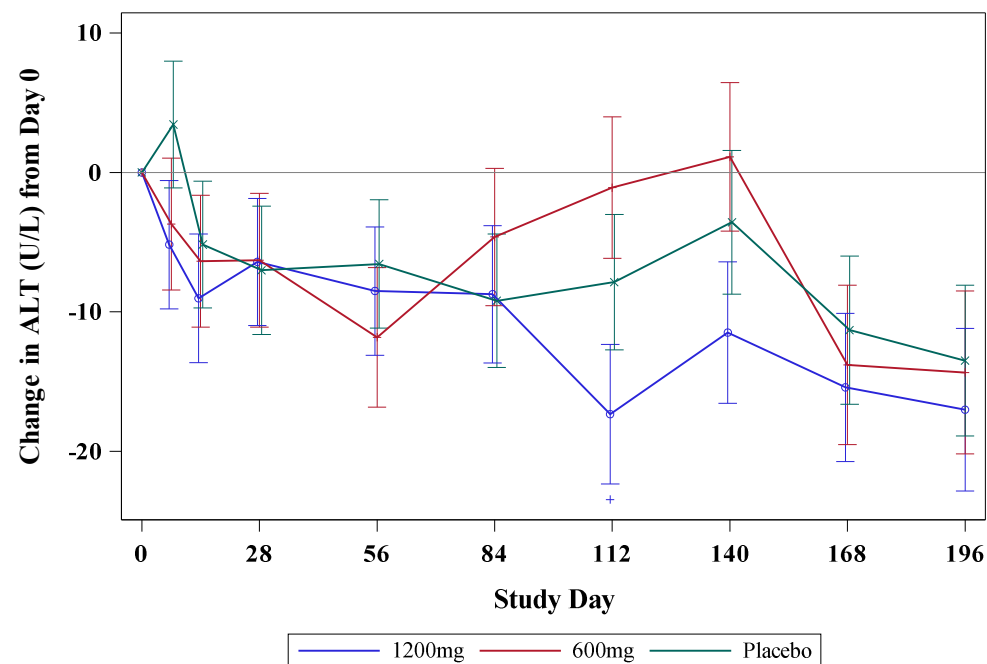


- **Goal:** Validate Safety and test for futility
- Analysis was not powered for efficacy due to sample size
- **Design:** interim analysis initiated when 80 patients reached 24W and have 2 MRI
- **Execution:** Performed by an independent Committee to keep Company Blinded
- **Results:**
  - **Excellent Safety**
  - **Treatment well tolerated at both doses**
  - **No Futility**
  - **Significant change in ALT and AST at 24W**
  - **Significant reduction in ALT and AST over time compared to placebo**
  - **Dose response**
  - **Non-absorbable**

# Phase II: Interim Analysis Report - Improves Liver Function



## Change in ALT by treatment group and visit (FAS population)



LS Mean  $\pm$  Std Err from RMMM on Change

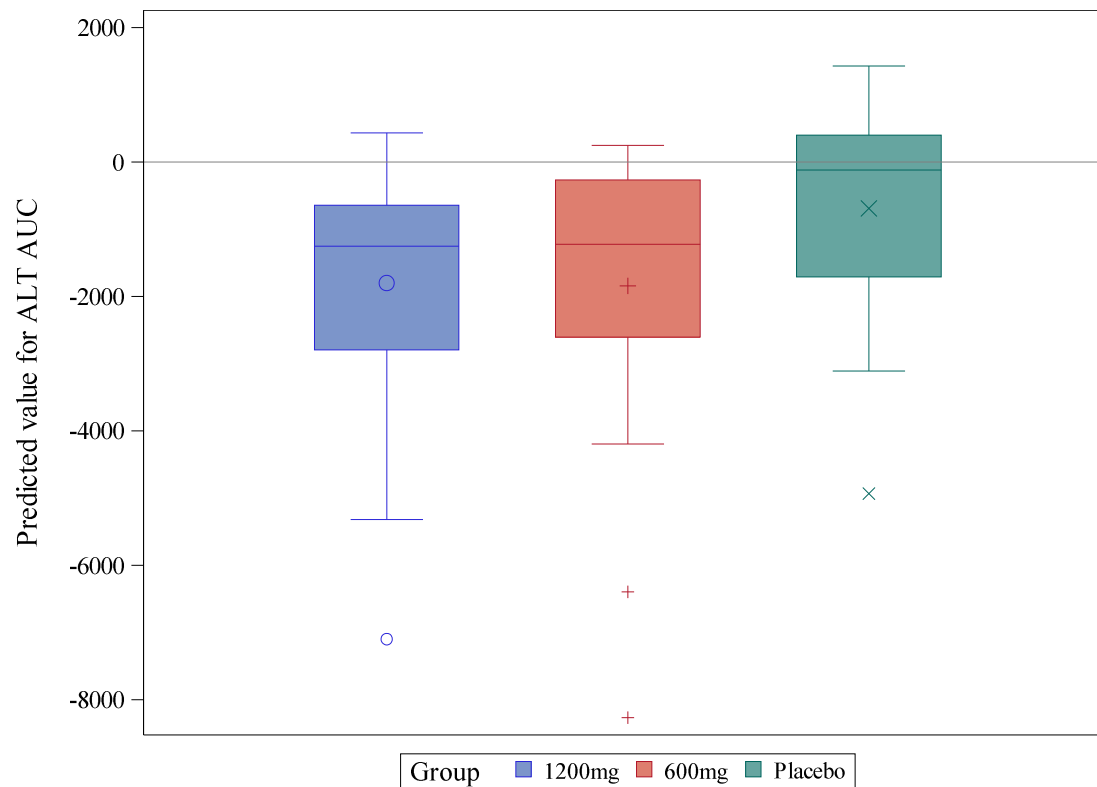
Differences ( $p < 0.05$ ): # Placebo v either active, + 600mg v 1200mg, \* 1200 v 600 and Placebo

- When comparing the 24W values of serum ALT to baseline all arms demonstrate a significant reduction
- However the change over time is different across the study arms

# Phase II: Interim Analysis Report - Improves Liver Function



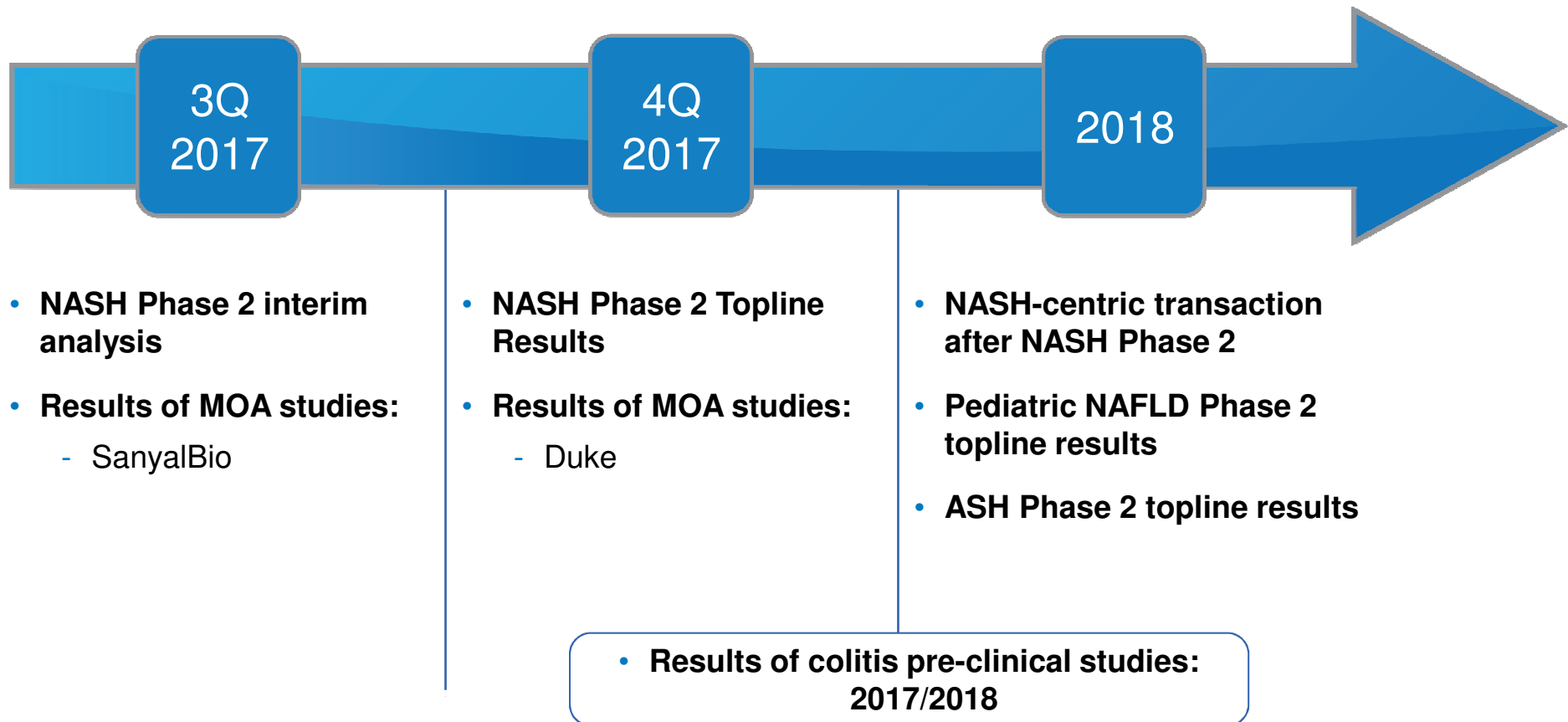
## Box plot for predicted ALT AUC from ANCOVA (FAS population) Improved Liver Enzymes



Predicted value adjusted for Baseline ALT

- Using logarithmic regression the predicted value was used
- Both 1200 mg and 600 mg arms demonstrated significant change over placebo ( $p=0.0036$  and  $p=0.0075$ )
- but were not different from one another ( $p=0.3589$ )

# IMM-124E Key Milestones



# IMM-529

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

- Therapeutic market is expected to grow from US\$356.3 million in 2014 to over \$1.5 billion by 2024 – CAGR 15%
- Nearly 30,000 patients die each year from *C. difficile* infections (US)
- Potential orphan disease (7 years market exclusivity and premium pricing)

## Unmet Need

- Vancomycin and metronidazole are the current standard of care, accounting for 80% of patient share (US)
- However, therapies are plagued by significant CDI recurrences (1st relapse: 25%; 2nd: 40%; 3rd: 50%) underscoring need for new treatments
- There is also growing resistance to vancomycin treatment

## IMM-529 Positioning

- Highly differentiated – Neutralizes *C. difficile* but does not impact microbiome
- Only asset that targets not only toxin B but also the spores and the vegetative cells responsible for recurrence
- Can be used in combination with standard of care
- Targets many isolates

Sources: GlobalData, Decision Resources, CDC

# 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

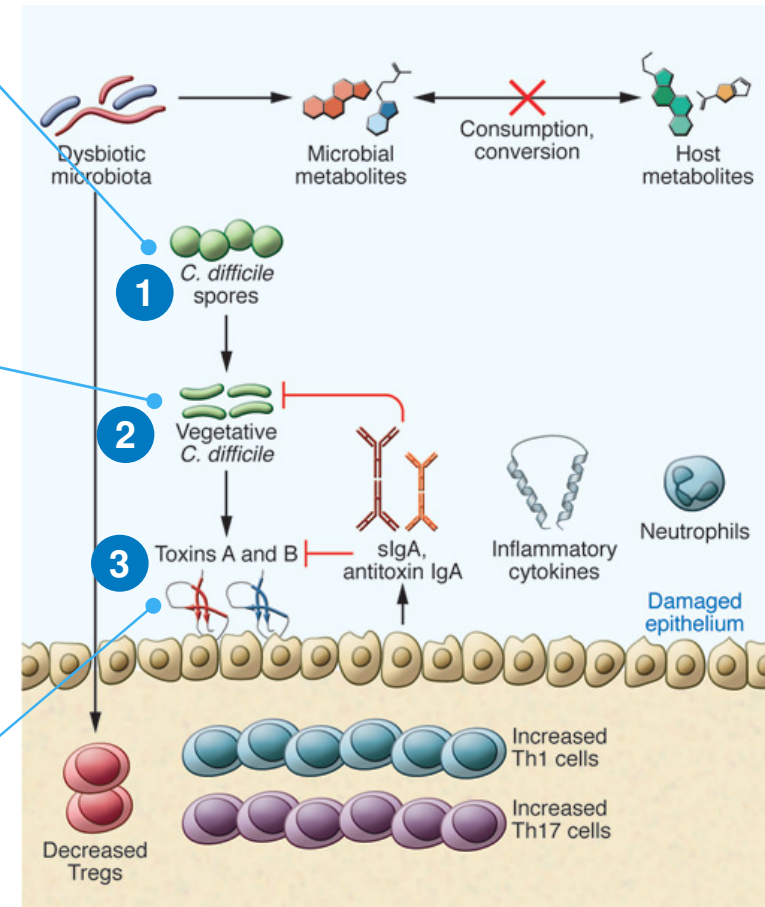
**IMM-529** antibodies bind to multiple epitopes on the surface layer proteins (SLP) on vegetative cells and limit colonization.

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.

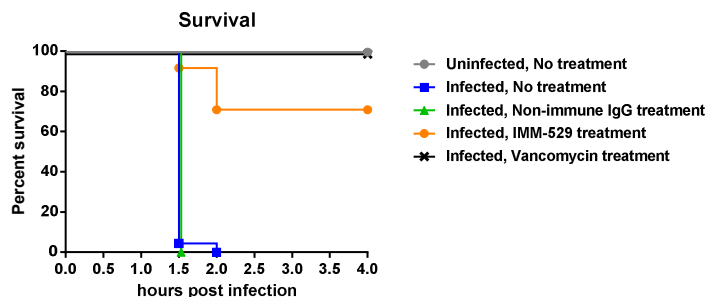
Toxin B is essential for virulence. Toxin B disrupt the cytoskeleton and tight junctions of intestinal epithelial cells.



# Results of Pre-Clinical Studies



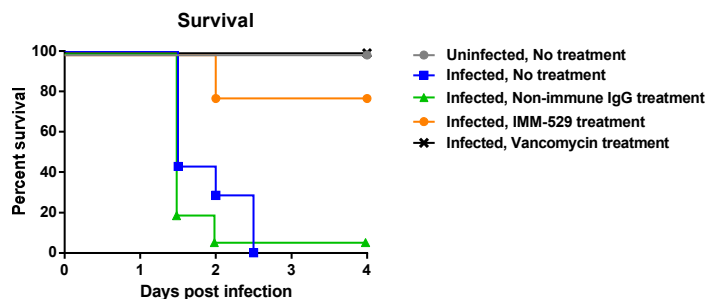
## Prevention Studies



Demonstrated ~70% survival rate without use of antibiotics vs. 0% for control group ( $P < 0.0001$ )

All studies statistically significant

## Treatment Studies

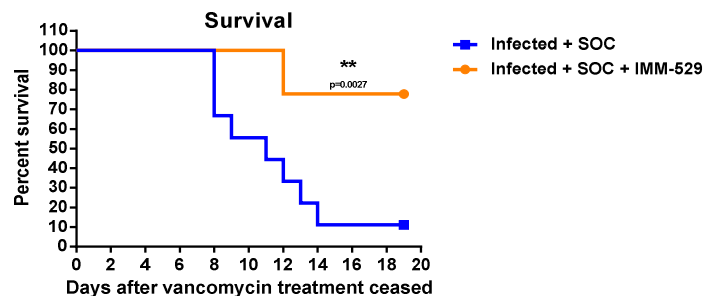


Demonstrated ~80% survival rate without use of antibiotics vs. <7% in control group ( $P < 0.0001$ )

Potentially only therapeutic (approved or in development) that can treat all phases of the disease:

1. Prophylaxis
2. Treatment
3. Recurrence

## Relapse Studies



Demonstrated ~20% relapse rate vs. ~89% relapse rate in control group ( $P < 0.0027$ )

# Phase 1/2 Study Design



## Phase 1/2 Study in CDI Expected to Commence 3Q 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

# IMM-529 Key Milestones



- Clinical supplies manufacturing
- Initiation of Phase 1/2 Trial in CDI
- Topline results expected from Phase 1/2 study in CDI

# Corporate and Financial Overview



# Robust IP and Extended Market Protection



## Strong Patent Portfolio

- 6 patent families offering composition and/or method of treatment claims
- Approved / pending in major geographies including US, Europe, Japan and China
- Granted patent terms ending between 2024 and 2030 with possible extensions

## Extended Market Exclusivity

- Immuron's drugs are considered "biologics" by the FDA
- In the US, this is expected to confer Immuron's new drugs 12 years of market exclusivity, offering investors a long revenue tail

## Generic Protection

- Immuron's drug not absorbed in the blood
- No baseline for PK studies
- This results in lengthy process for biosimilar manufacturers

# Recent High-Value NASH LM&A Highlights Potential for Significant Upside



- Focused on advancing IMM-124E and IMM-529 through key clinical inflection points while pursuing partnering opportunities
- Recent licensing and M&A partnerships in NASH **underscores potential of IMM-124E**



- 2016: Licensed preclinical NASH asset
- ~\$50M upfront + other undisclosed milestones



- 2016: Acquired Tobira
- ~\$530M (5x market cap at time of announcement), in a deal valued at up to \$1.7B



- 2015: Acquired Phenex
- NASH asset in Phase 2
- Total deal value \$470M



- 2014: Acquired Nimbus
- Preclinical assets and platform
- \$400M upfront in a deal valued at \$1.2B









- 2015: Acquired Pharmaxis
- NASH asset in Phase 1
- \$39M upfront – Total deal value \$600M



- 2014: Acquired Lumena
- 2 Phase 2 assets for NASH and cholestatic liver disease
- Total deal value \$260M

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



Company	Ticker	Program	Development Stage	Market Cap*
Program in NASH				
 <b>Intercept</b>	ICPT	Obeticholic acid	Phase 3	US\$2.9B
 <b>GENFIT</b> TOWARDS BETTER MEDICINE	GNFT	Elafibranor	Phase 3	US\$1.1B
 <b>Conatus</b> Pharmaceuticals	CNAT	ENCORE-LF	Phase 2	US\$195M
Program in <i>C. Difficile</i>				
 <b>SERES</b> THERAPEUTICS™	MCRB	SER-109; SER-262	Phase 2	US\$423M
 <b>summit</b>	SMMT	SMT19969	Phase 1	US\$143M
 <b>assembly</b> BioScience	ASMB	ABI-M101	Preclinical	US\$419M

\*As of May 4, 2017

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



## Current Top 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%
<b>TOTAL TOP 20 SHAREHOLDERS</b>		<b>55,798,238</b>	<b>42.76%</b>
BALANCE OF SHARES		74,642,224	57.24%
<b>TOTAL SHARE ON ISSUE</b>		<b>130,440,462</b>	<b>100.00%</b>

\* Denotes a Director Related Entity

## Current Company Market Capitalization

**AUD\$23.4M ≈ USD\$18.6M (8<sup>th</sup> Aug 2017)**

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



## Issued Capital

**130,440,462** Issue Shares (Fully Paid)

**25,289,894** Listed Options exercisable at AUD\$0.55 on or before 30 Nov 2019

**701,500** Warrants exercisable at USD\$10 on or before 13 June 2022 (40:1)

**9,937,629** Unlisted Options exercisable at various prices

## Recent Share Price Activity



immuron

# Travelan OTC/Business

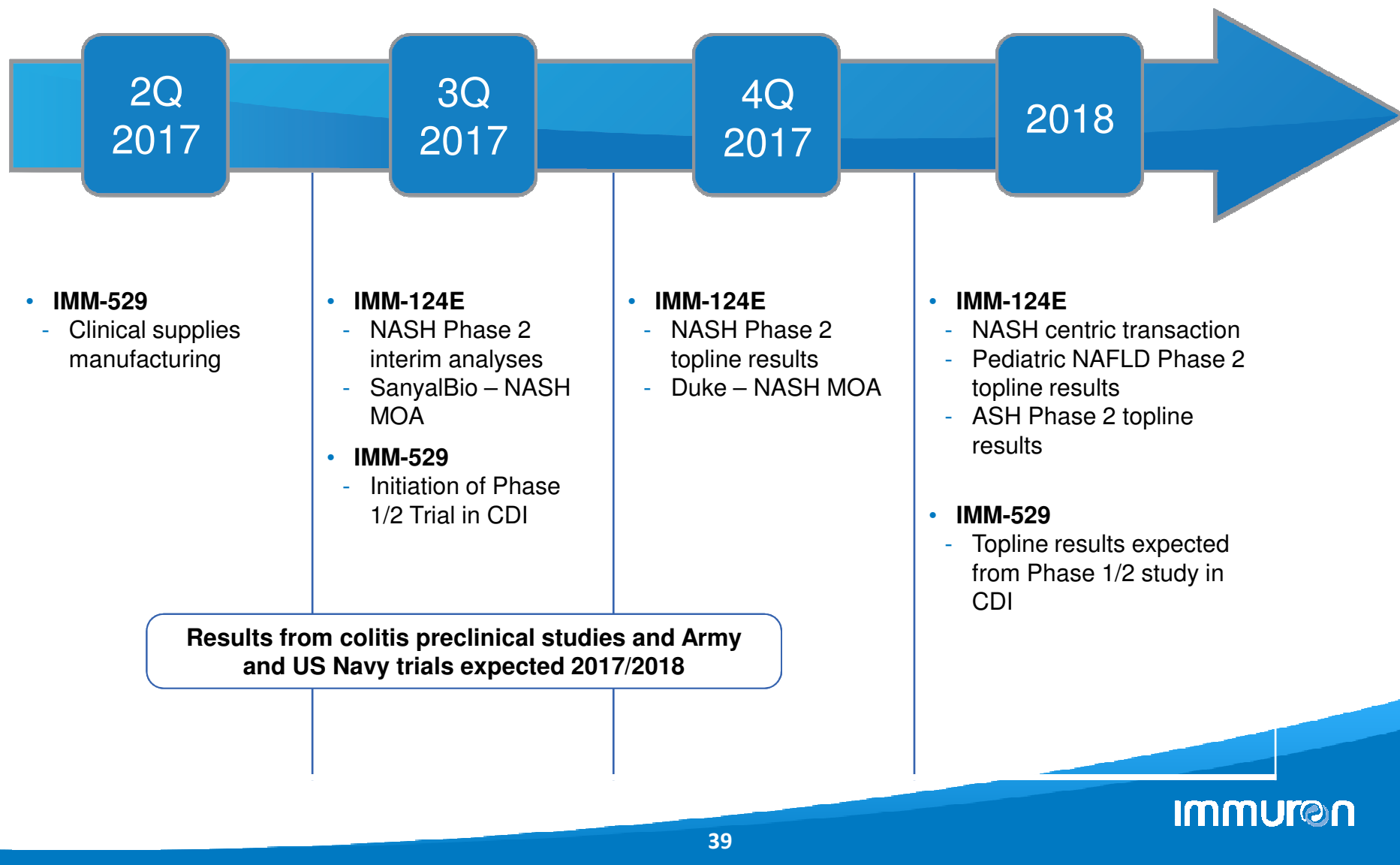
A unique OTC targeting Traveler's Diarrhea



- **Travelan/OTC: Unique value proposition that is valued by consumers and customers**
  - Significantly reduces the motility of ETEC strains
  - Binds to multiple epitopes and antigens on both the bacterial surface and flagella
  - Has substantially greater reactivity against purified ETEC flagella antigen than IgG purified from non-immune colostrum powder
- **Annual Revenues of AU\$1M+; Cash flow positive**
  - Net revenues: 1H2017 +41% vs 1H2016
  - Pursuing new geographies
  - Potential WW peak sales: \$20M+
- **Multiple ways to keep growing OTC business:**
  - Continued penetration of current markets
  - Geographic expansions
  - New products / New formulations (e.g., shigella)



# Key Milestones Expected to Drive Value





# Investment Highlights



- ✓ Well positioned to address high unmet medical need in multiple blockbuster markets
- ✓ Two clinical assets, 4 phase 2 clinical trials on going
- ✓ Robust R&D pipeline
- ✓ High-value peer licensing deals and M&A underscore potential upside ( Current Market Capitalization = USD\$18.6M, 6 August 2017)
- ✓ Validated technology platform – with one registered asset generating growing revenue
- ✓ Listed on NASDAQ in 2Q 2017
- ✓ Experienced Management Team with strong support from leading KOLs and institutions

**Thank You**