



Initiating Coverage Report

## **Immuron Limited**

Substantial Rerating in NASH

**immuron**

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<b>Name:</b>	<b>Immuron Ltd</b>
<b>Country:</b>	<b>Australia</b>
<b>Price:</b>	<b>AUD 0.30</b>
<b>ISIN Code:</b>	<b>AUU000000IMC7</b>
<b>Reuters Code:</b>	<b>IMC.AX</b>
<b>Market Cap (AUD m):</b>	<b>31.7</b>
<b>EV (AUD m):</b>	<b>22.1</b>
<b>Cash &amp; cash eq. (AUD m):</b>	<b>9.1</b>
<b>Shares outstanding (m):</b>	<b>103</b>
<b>Volume:</b>	<b>45,110</b>
<b>Free float:</b>	<b>100%</b>
<b>52-week Range:</b>	<b>0.22-0.43</b>

AUD m (30 June)	2014/15A	2015/16A	2016/17E
<b>Total Revenues</b>	1.959	4.164	4.200
<b>Net (Loss)/Profit</b>	(3.448)	(4.390)	(7.360)
<b>Net loss p.s. (cents)</b>	(4.60)	(5.71)	(7.15)
<b>R&amp;D costs</b>	3.018	3.624	5.000
<b>Cash increase/(decrease)</b>	(3.025)	(0.825)	15.00
<b>Cash and market sec.</b>	3.116	2.29	17.39



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## Executive Summary

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- Immuron Ltd is a publicly listed Australian biopharmaceutical company focused on oral immunotherapy utilizing polyclonal antibody products that target the human gut immune system. Its lead program is IMM-124E which is currently in Phase II for fatty liver-diseases NASH (non-alcoholic steatohepatitis) and ASH (alcoholic steatohepatitis). Its second program, IMM-529, is in development to target the *Clostridium difficile* bacterium. The company is currently preparing its clinical protocol for a phase I/II in patients with *Clostridium difficile* infections (CDI).
- Next to its development pipeline, Immuron markets an OTC product Travelan for the prevention of Travelers' Diarrhea and is sold in several countries (Australia, Canada, US and China). Travelan has been shown to be 90% effective in the prevention of diarrhoea in several E-coli challenge placebo controlled studies. Sales for 2016 were AUD 1.1 million.
- With IMM-124E and IMM-529, the company targets large markets with high unmet medical needs. NASH is a severe type of non-alcoholic fatty liver disease (NAFLD) and is the most common liver disease associated with obesity and type-2 diabetes. 10-20% of people with NAFLD will progress to NASH and has a prevalence of 24 million people in the US alone. The total market for NASH therapies is estimated to be more than USD 35 billion by 2025. CDI is one of top three most urgent antibiotic resistant bacterial threats in the US. It is the most common cause of hospital acquired infection and has overtaken Methicillin-resistant *Staphylococcus aureus* (MRSA) in prevalence.
- Last year, the company successfully raised AUD 6.3 million from a rights offering. The Company's current cash position is AUD 2.3 million, and we believe that this should be



sufficient to carry out the further development of its pipeline in the coming 12 months. The company also filed a S1 report to the SEC and is targeting a NASDAQ as well as a subsequent US capital raise. We anticipate the listing to be ready in 2017H1. Furthermore, we expect the company to be able to sign a lucrative partnering deal following positive topline Phase II data from IMM-124E given the increased interest from big pharma for NASH assets.

- There are a number of key milestones to focus on in the next 6-12 months which includes the publication of interim and topline results of the IMM-124E Phase II trial in NASH, granting Orphan Indication Status for IMM-529 in CDI and the initiation of a Phase I/II study in CDI.
- **Based on an NPV valuation, we believe that Immuron is substantially undervalued at the current share price of AUD 0.30. We have increased our valuation calculation following a rerating of both its programs in NASH and CDI. Especially in NASH, the potential deal size has increased following recent activity in the area. In our view, the company's current total value should be AUD 197 million, or AUD 1.92 per share compared to our previous calculation of AUD 75 million. This represents a substantial upside from the current share price.**



## Company Profile & Technology

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Immuron Limited is an international biopharmaceutical company with a focus on oral immunotherapy using polyclonal antibody products that target the human gut immune system and gut microbiome. Immuron's technology platform is capable of developing and producing an orally stable therapeutic for various immune mediated and inflammatory disorders among them: non-alcoholic steatohepatitis (NASH), diabetes, colitis, arthritis, inflammatory bowel diseases (IBD), irritable bowel syndrome (IBS), liver fibrosis and other chronic disorders. Its proprietary polyclonal antibody platform produces antibodies potentially suited to treat a wide range of diseases including chronic inflammatory diseases and infectious diseases.

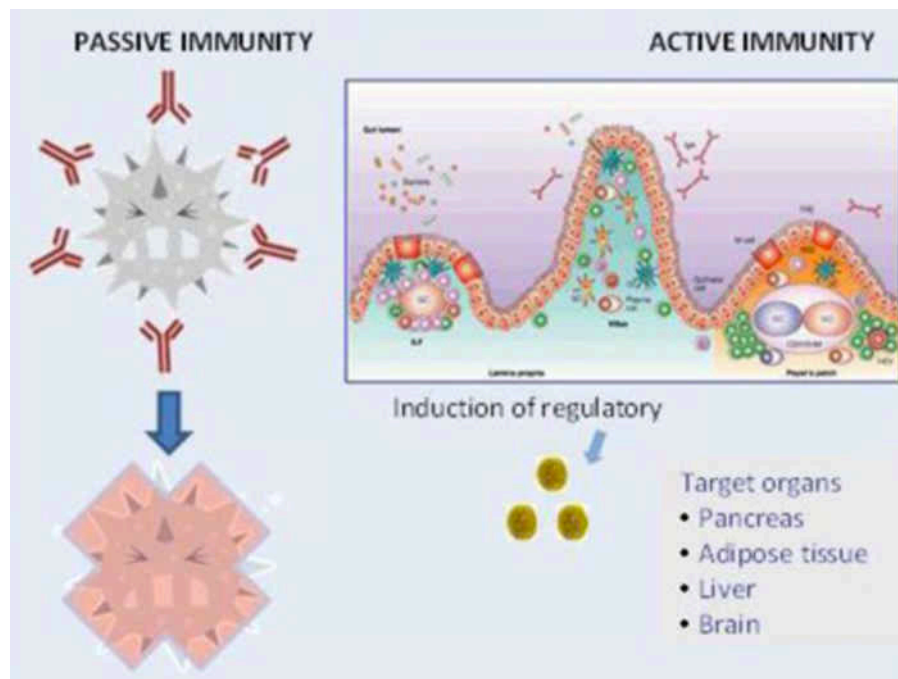
Immuron's platform technology is based on producing antigens targeted, hyper-immune bovine colostrum powder (BCP) suitable for pharmaceutical use. Polyclonal antibodies are derived from the first milking of a cow after calving. Prior to calving, cows are immunized with proprietary vaccines to ensure maximum immunogenicity. The milk is then harvested and purified. This proprietary process ensures that the colostrum contains a high concentration of antibodies and Immunoglobulin G1.

The antibodies have powerful anti inflammatory effect and work through two modes of actions:

- **Passive Immunity:** Immuron's active ingredient targets a specific antigen. When bound by polyclonal antibodies the antigens are prevented from infecting the cells of the patient.
- **Active Immunity:** Immuron's active ingredient modulates the body's own immune system by boosting T-Regulatory (Treg) cells, which are cells that are responsible for regulating the intensity of inflammatory processes in the body. The antibodies, once orally ingested, are



presented in the peyers patches to the lymph system's dendritic cells which sample the antibodies, thereby eliciting the immune response. This response is associated with increased differentiation to T regulatory lymphocytes and anti-inflammatory cytokines and decreased levels of pro-inflammatory cytokines.



Source: Immuron

The technology is classified as GRAS by the FDA and can be applied to a range of therapies, including infectious diseases and inflammatory mediated disorders. The platform can be used to impact the immune system through regulatory T cell populations or it can directly block viruses and bacteria at mucosal surfaces such as the GI tract. Additionally, the dairy origins of Immuron's antibodies enables the company to commercialize the platform through most regulatory pathways, including prescription, medical foods, OTCs and dietary supplements. The GRAS status of its



technology platform allows the company to advance its pre-clinical programs into clinical trials much faster compared to other companies as a result of the platform's proven safety profile.

### *Business Strategy & Partnerships*

Immuron strives to become one of the leading biotech companies in inflammation mediated diseases and anti-infectives. To reach this goal, the company set out a strategy consisting of:

- Rapidly advancing its two lead programs IMM-124E (NASH) and IMM-529 (CDI)
- Leveraging its proprietary technology platform to other indications like ASH, Pediatric NASH and other anti-infectives with the US Army and Navy
- Partnering its fatty-liver programs with commercially strong partners
- Investing in its growing Travelan business worldwide
- Investing in mechanism of action (MOA) studies to potentially identify new opportunities
- Protecting its IP portfolio and patents





## Pipeline: Focus on the Gut

With its platform technology that is based on polyclonal antibodies derived from hyper immune bovine colostrum powder (BCP), Immuron currently has two lead programs in development that are targeting high unmet medical needs in diseases that are associated with the human gut. These are (1) IMM-124E targeting NASH, which is currently in Phase II and (2) IMM-529 which is designed to prevent, treat and prevent recurrences of Clostridium Difficile Infection (CDI). Currently, the company markets two OTC products for Traveler’s Diarrhea (Travelan) and Gut dysbiosis (Protectyn). Travelan is marketed in Australia, US, China and Canada. The company plans to roll out Travelan in additional countries. Last year, Protectyn was launched in Australia targeting the LSP bacteria in the gut to prevent dysbiosis.

Program	MOA	Dosing Form	Indication	Development Status				Notes	Commercial Rights
				Pre-Clinical	Phase 1	Phase 2	Phase 3		
IMM-124E	Anti-LPS	Oral	NASH	[Progress bar: Pre-Clinical, Phase 1, Phase 2]				Top line results in mid-2017	Worldwide
IMM-124E	Anti-LPS	Oral	ASH	[Progress bar: Pre-Clinical, Phase 1, Phase 2]				NIH Funded; UVA	Worldwide
IMM-124E	Anti-LPS	Oral	Pediatric NASH	[Progress bar: Pre-Clinical, Phase 1, Phase 2]				NIH Funded; Emory University	Worldwide
IMM-529	ToxinB antagonist	Oral	C. difficile	[Progress bar: Pre-Clinical, Phase 1]				Start of Phase 1 in 2017	Worldwide
Several	Shigella vaccine	Oral	Shigella infections	[Progress bar: Pre-Clinical]				In collaboration with US Army	Worldwide
Several	Campylobacter; ETEC Vaccines	Oral	Campy/ETEC infections	[Progress bar: Pre-Clinical]				In collaboration with US Navy	Worldwide
TBD	Anti-LPS	Oral	Colitis	[Progress bar: Pre-Clinical]				In collaboration with Dr Rogler	Worldwide
TBD	Anti-LPS	Oral	Autism	[Progress bar: Pre-Clinical]				In collaboration with Melbourne University, Murdoch Children's University and La Trobe University	Worldwide

Source: Immuron Ltd

### IMM-124E: Phase II study in NASH

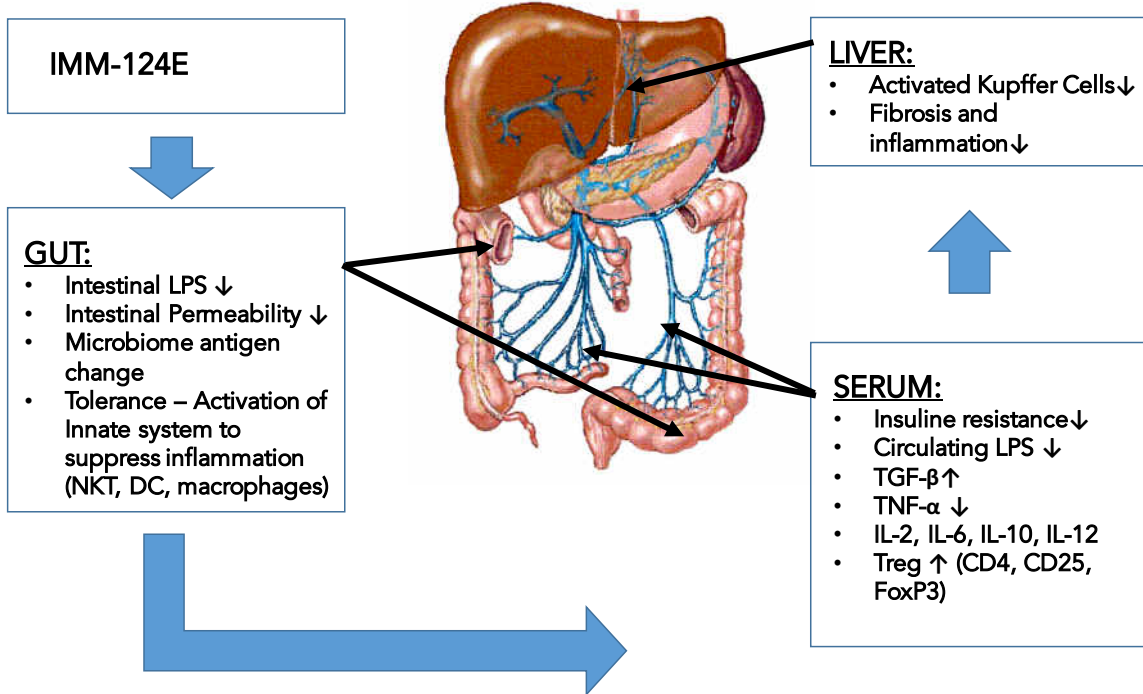
IMM-124E is a first in class oral, anti-LPS antibody, with strong anti-inflammatory and anti-fibrotic



properties, making NASH an ideal target for this compound. IMM-124E binds to the LPS of gram-negative bacteria and affects the peripheral inflammatory balance through regulatory T cell populations, creating a downstream decrease of liver inflammation. IMM-124E is also the investigational drug of two NIH-sponsored Phase II clinical trials in alcoholic steatohepatitis (ASH) and Pediatric NASH.

In December 2014, Immuron announced the launch of its NASH Phase II multicenter randomized double blind placebo controlled study with IMM-124E for the treatment of NASH. The trial's first patient was enrolled in February 2015. To date, 118 patients are enrolled out of 120. Top line results are expected to be available in 2017H2. The trial Principal Investigator is Dr. Arun Sanyal, one of the world's foremost leaders in NASH. Dr. Sanyal is Professor of Medicine and Former Chairman of the Division of Gastroenterology, Hepatology and Nutrition at VCU Medical Center, Virginia, U.S.A. Dr. Sanyal is an internationally renowned expert in liver diseases.

IMM-124E is made of anti-LPS polyclonal antibodies and manufactured from colostrum which is harvested from dairy cows that have been immunized against bacterial LPS from the most common strains of ETEC. IMM-124E contains at least 40% immunoglobulins composed mainly of IgG1. Studies have shown that these antibodies have high binding affinity to bacterial LPS specific sites. It was also demonstrated that these antibodies cross react with other types of bacteria such as shigella and salmonella.



Source: Immuron Ltd

There is strong support for the clinical benefit of IMM-124E in the treatment of fatty liver diseases. Ingested immunoglobulins are known to interact with the gut immune system to elicit a cell mediated anti inflammatory response recorded in the serum. This subsequently lowers inflammation throughout the body. In addition, IMM-124E has also been shown to bind to intestinal LPS. This is thought to restore the intestinal barrier function thereby reducing liver LPS related inflammation as well as lowering bacterial translocation and circulatory LPS levels. Since NASH is associated with changes in the gut microbiota, direct change in the disease associated gut flora is thought to reduce the bacterial strains that are associated with NASH.

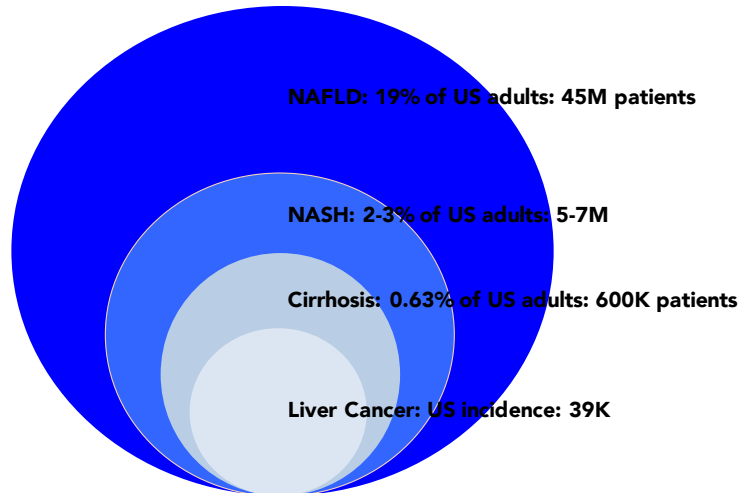


In addition to the company-funded Phase II study in NASH, the NIH is funding two fatty-liver disease Phase II trials utilizing IMM-124E as the investigational agent. The first is a Phase II study for the treatment of ASH. The trial is currently enrolling and aims to enrol 66 patients, randomized to the double blinded placebo controlled study. The study is expected to generate safety and preliminary efficacy data and should be completed in 2018. The second study is a Phase II study for the treatment of pediatric NASH. This study aims to enrol 40 pediatric patients for three months treatment and aims to determine safety and efficacy of IMM-124 in these patients. Pediatric NASH is a growing concern in many countries and similar to NASH, it is a progressive form of liver disease associated with excessive fat storage in the liver together with inflammation, which can lead to liver fibrosis and cirrhosis. Pediatric NASH is believed to affect up to 5-10% of the US pediatric population. There is currently no approved drug for pediatric NASH.

ASH is one of the hepatic manifestations of alcohol abuse and typically occurs in patients with long standing history of alcohol intake. Also in ASH, inflammation plays a key role in the development of the disease. More than 90% of heavy drinkers have steatosis, 10-35% have ASH and 8-20% have alcoholic cirrhosis. Besides alcohol consumption, other factors also contribute to the development of ASH including diet, age and ethnicity. It is estimated that the prevalence of alcoholism in the US is 8% of the total population or more than 15 million people. At least 20% of them have ASH.



## *Landscape Liver Diseases*



## *IMM124E in comparison with other assets in development against NASH*

IMM-124E has significant competitive advantages when compared to other assets in development:

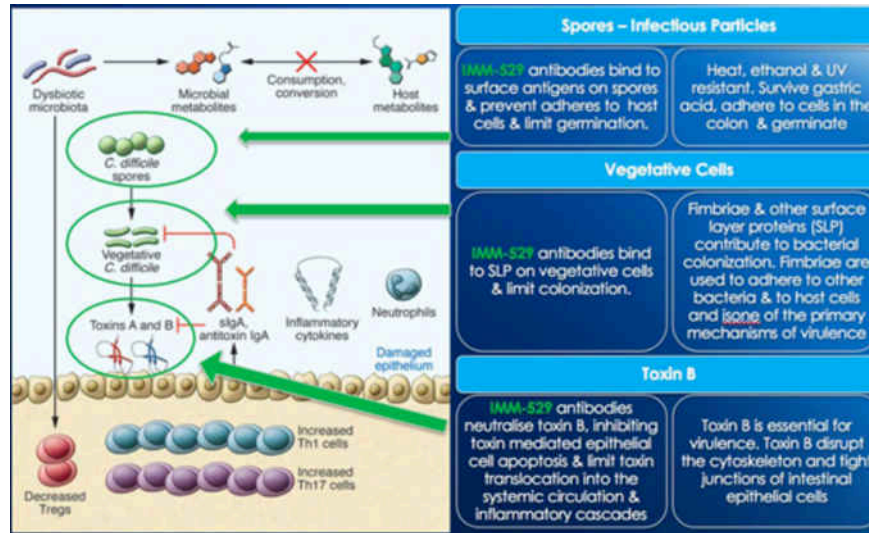
- **Multi-Factorial / Broad Anti-Inflammatory Upstream Effect** – It is acknowledged that NASH is a multi-factorial disease, and that targeting only one or two pathways is likely to only have a marginal effect on the disease. IMM-124E offers hope for long-lasting effects because of its broad upstream anti-inflammatory effects which induces the release of regulatory T-cells and anti-inflammatory cytokines while decreasing levels of pro-inflammatory cytokines.
- **Attractive Profile for Long-Term Chronic Use** – Because of its exceptional safety profile, which is derived from a GRAS (Generally Regarded as Safe) platform, we believe that data will support the use of IMM-124E as a chronic / long-term treatment, providing a unique advantage over other NASH therapies as some have already shown significant side effect profile (e.g., increased cholesterol).



- **Potential for Use as Backbone Agent for both Early and Severe Disease** – While other more toxic agents in development are likely to be confined to severe populations, we believe that IMM-124E will be able to be used in all NASH patients, including for those with mild fibrosis (F1)/no scarring (F0), and potentially in NAFLD patients as well, to reduce their elevated inflammation state. We do not believe that other agents will have the efficacy/safety profile to justify such broad use, hence putting nearly 15 million of mild NASH patients within reach of IMM-124E but out of reach of the competition.
- **Potential for Use in Combination Therapy** – Because of its delivery method and exceptional safety profile, it is likely that IMM-124E can not only be used as monotherapy, but also in combination with other NASH agents, if these are approved, and if physicians feel that this is warranted for their patients. We do not believe that other agents will have the efficacy / safety profile to justify being used in combination with other agents as readily as IMM-124E.

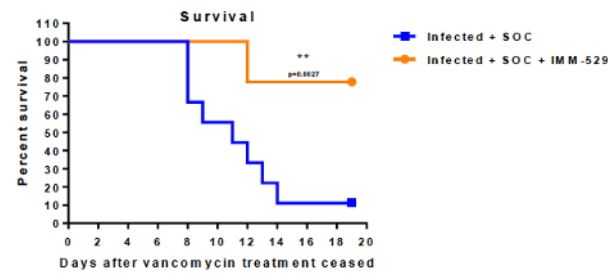
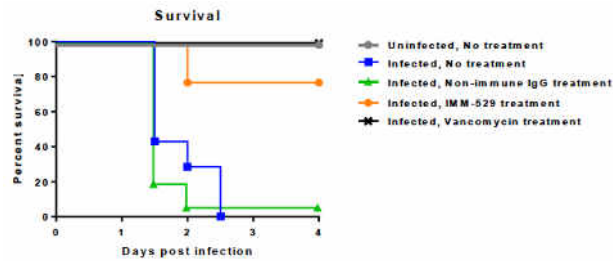
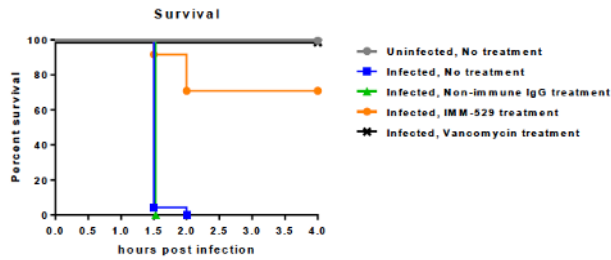
#### *IMM-529: Potential New Revolutionary Treatment for CDI*

IMM-529 is an oral biologic that targets the *C. difficile* bacteria, but also does not destroy the microbiome like antibiotic treatments. This allows the microbiome to return to a healthy state while treating CDI. The antibodies in IMM-529 have been generated against the essential *C. difficile* virulence components, specifically, spores, vegetative cells and toxin B and shown to bind and neutralise a variety of human and animal *C. difficile* isolates. IMM-529 is in the clinical stage and has successfully completed its preclinical program in CDI. Immuron is currently in the process of manufacturing clinical supplies for its Phase I/II and is finalizing the Phase I/II protocol. The company aims to start with the Phase I/II in 2017Q2.



IMM-529, which was developed in collaboration with world-leading *C. difficile* KOL Dr. Dena Lyras and her team at Monash University, has a unique Triple-Action MOA (antibodies to Toxin B + Spores + Vegetative Cells). It is a three pronged approach that is unique and which has yielded exceptional results in pre-clinical studies including (1) Prevention of primary disease, (2) Treatment of primary disease and (3) Suppression of recurrence. To date this is the only investigational drug that has showed positive therapeutic benefits in all three phases of the disease.

In the preclinical stage, prevention studies demonstrated an 80% efficacy without the use of antibiotics. Also in treatment studies an 80% efficacy was demonstrated without the use of antibiotics like vancomycin. In relapse studies a 90% survival rate was noticed vs 22% survival rate in the control group. See also the graphs on the next page.



### IMM-529 in comparison with other assets in development against CDI

We believe that IMM-529 has a unique competitive advantages:

- **Triple Mechanism of Action** – IMM-529 not only **targets the Toxin B**, but it also contains antibodies to the **spores and the vegetative cells**. This is unique among all assets currently in development.
- **Effective vs Virulent Strains** – As discussed above, IMM-529 has been shown to be effective vs both the normal strains as well as the virulent strains of CDI, providing a strong Proof-





of-Concept (POC) model that IMM-529 can be a front line agent in the battle vs hypervirulent and difficult to treat strains.

- **Effective in All phases of the Disease** – IMM-529 has shown that it can be an effective agent in all phases of the disease including prevention of infection, treatment of primary disease and recurrence. This is unique among all of the competition and indicate a much larger potential use than current development programs which primarily target recurrence.
- **Oral Therapy** – IMM-529 is an oral therapy lessening costs/burden on the patient, hospitals and the healthcare system overall.
- **Not an Antibiotic** – IMM-529 is not an antibiotic, and hence is only targeted at C. difficile its Toxin B, spores and vegetative cells. It therefore does not negatively impact the rest of the flora and allows the flora to return to normal, while fighting the primary infection/recurrence.

#### *Other Programs in Development*

Because of its flexibility, the Immuron platform is almost infinitely scalable, as antibodies can be made to target any pathogens in the gut. In that light, Immuron is developing several programs including the US Army and the US Navy that can potentially lead to additional value in the future (not included in the valuation).

- **U.S. Army** – In June 2016, Immuron signed an agreement with the Walter Reed Army Institute of Research (WRAIR) to develop a vaccine for shigellosis, a severe form of dysentery and ETEC. WRAIR aims to develop vaccines for both military and civilian use in



areas where endemic diseases such as shigellosis can compromise the health and readiness of the local community, travelers, contractors and defense personnel.

- **U.S. Navy** – In August 2016, Immuron signed an agreement with the U.S. Navy to test the reactivity and therapeutic effectiveness of Travelan against campylobacter and Enterotoxigenic Escherichia coli (EPEC), two common gram-negative bacterium. At least a dozen species of Campylobacter have been implicated in human disease, with *C. jejuni* and *C. coli* being the most common. *C. jejuni* is now recognized as one of the main causes of bacterial foodborne disease in many developed countries as well as developing countries where poultry is common.
- **Pre-Clinical - Colitis:** Professor Gerhard Rogler, The University of Zurich's world renowned inflammatory bowel diseases researcher, has teamed with Immuron to launch a pre-clinical development program in colitis to build on previously positive colitis program. The three stage program will use well-known acute and chronic colitis models and will take place throughout 2016/2017.
- **Pre-Clinical – Autism:** In July 2016, the company announced a strategic partnership with three leading Australian research institutes focused on understanding how the genetic basis underlying Autism Spectrum Disorder (ASD) relates to changes to the gut, and how Immuron's anti-LPS IMM-124E compound affects changes in mouse models for autism. This effort involves the University of Melbourne, La Trobe University and Murdoch Children's Hospital.

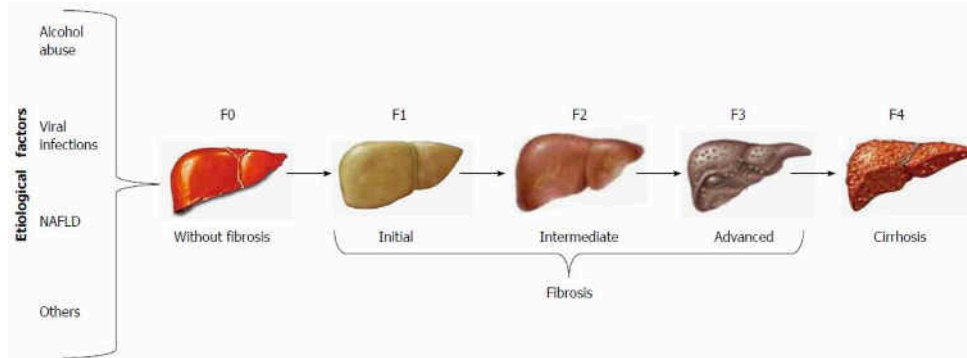


## Non Alcoholic Steatohepatitis (NASH): Next Holy Grail in Biotech?

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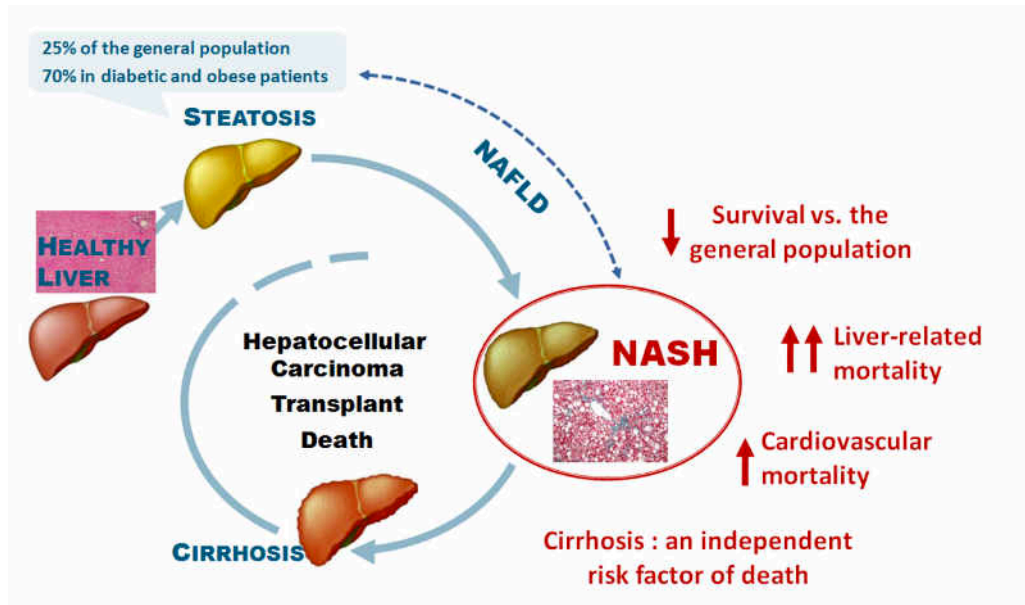
NASH stands for Non-alcoholic Steatohepatitis. It is often linked with NAFLD, or non-alcoholic fatty liver disease. NAFLD is a condition categorized by excessive fat in the liver of people who drink little to no alcohol. No direct cause has yet to be identified, but it is known that obesity and insulin resistance play strong roles. Most often, NAFLD goes relatively unnoticed, as a liver can remain fatty without disturbing function. However, NAFLD can progress into a far more serious condition known as non-alcoholic steatohepatitis (NASH), a disease characterized by inflammation and irreversible cell death. While most people are unfamiliar with NAFLD, the disease is actually incredibly common. In the US, NAFLD affects around 30% of the population or around 100 million people. Approximately 10-20% of people with NAFLD will progress to NASH. Current estimates place NASH prevalence at 24 million people in the US or 7% of the total population, with similar prevalence in other major developed markets. According to a recent Datamonitor report, in 2015 there were around 50 million patients with NASH and 139 million patients with NAFLD in the largest industrialized countries. By 2035, the number of cases of NAFLD in the US, Japan and five major EU markets will increase to 216 million, a 13.9% increase over the 20-year period, the report forecasts. That's just on the basis of their growing and ageing populations, from a total of 189.6m cases in 2015.

Much in the way a heart condition can worsen as years pass, NASH is a disease that progresses over time. It is estimated that 63% of all NASH patients or around 32 million people have either no scarring on the liver (F0) or mild fibrosis (F1). The other 18 million have either moderate (F2) or severe fibrosis (F3). Over a 10-year period up to 20% of patients with NASH will develop cirrhosis (healthy tissue being replaced with scar tissue) of the liver, and 10% will die from the disease.



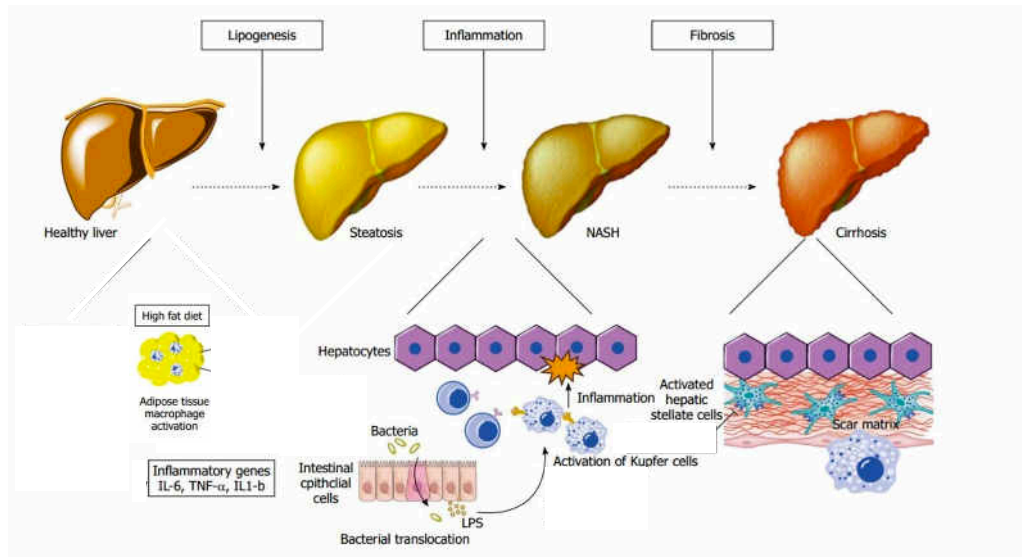
According to the leading hepatologists, NASH is considered a ticking time bomb and the regulatory authorities (FDA and EMA) have supported the need for the discovery of efficient treatments for this disease. The therapeutic needs are tremendous worldwide as the number of NASH cases is constantly expanding, together with the diabetes and obesity epidemic. Hence, in the US, NASH prevalence is estimated over 12% the adult population. For the diabetic population, the number rises up to 22%. It is noteworthy that between 15 to 25% of NASH patients will develop cirrhosis.

Both NASH and NAFLD are becoming more common also because of the greater number of people with obesity. In the past 10 years, the rate of obesity has doubled in adults and tripled in children. Obesity also contributes to diabetes and high blood cholesterol, which can further complicate the health of someone with NASH due to insulin resistance. Diabetes and high blood cholesterol are also becoming more common among Americans. By 2020, NASH is projected to overtake hepatitis C as the leading cause of liver transplants in the U.S.



### *Pathophysiology of NASH*

Inflammation plays a key role in the pathogenesis of NASH as conditions like obesity are all associated with an elevated state of chronic inflammation that cause damage to organs such as the pancreas and the liver. In addition to the elevated state of inflammation suffered by NASH patients, it has also been shown that fatty diets, sugar and obesity are linked to an overgrowth of gram-negative bacteria within the gut. These bacteria produce LPS (LipoPolySaccharides) products that elicit strong innate and cell mediated immune responses in humans, both from within the gut and through circulating endotoxins, particularly via Toll-like Receptor 4 on cells. The importance of this LPS driven inflammatory process is often overlooked since there are no therapeutics that can effectively block gram-negative bacteria in the gut. Except for broad spectrum antibiotics which are not an option for long term use in NASH patients.



The immune and inflammatory response to liver cell damage is mediated through a well described signaling network of liver and immune cells. Kupffer cells, also known as resident liver macrophages, sense tissue injury and are the first responders to liver cell damage. Activated Kupffer cells initiate an inflammatory response to the liver injury and can activate HSCs (hematopoietic stem cells) to transdifferentiate into myofibroblasts, the primary collagen producing cell type responsible for liver fibrosis. The extent of this fibrosis can vary, and it is described in several stages (F0 to F4).

### *M&A Activity in NASH underscores big pharma's interest*

The field is consolidating, and we would not be surprised to see other big players making plays for smaller promising drug candidates going into 2017. Pharma giant Allergan already brought increased investor attention to the NASH market by buying two treatment developers, Tobira Therapeutics for a sum of USD 1.7 billion (**a premium of almost 500%**) and private company Akarna Therapeutics for USD 50 million. So far, Intercept Pharmaceuticals is one of the leaders in hoping to be the first to market in NASH, while Gilead Sciences splashed into the space with a USD 470



million deal for a Phase II NASH treatment with Phenex and more recently struck the potentially USD 1.2 billion deal with Nimbus and its early-stage NASH drug. With no treatments currently approved for this chronic disease, the market opportunity is significant. Several companies are working on developing treatments for NASH - the market could be worth billions of dollars and many companies are hoping to cash in on this opportunity. Analysts predict that the market for NASH therapies could reach USD 35 billion or more by 2025.

Company	Partner	Year	Total value	Program
Arresto	Gilead	2010	USD 225m	Phase I asset (LoxL2 antibody) targeting NASH and IPF
Regulus	AstraZeneca	2012	USD 125m	Preclinical
Lumena	Shire	2014	USD 260m	Two Phase II assets in NASH and cholestatic liver disease
Pharmaxis	Boehringer I.	2015	USD 600m	NASH asset in Phase I
Phenex	Gilead	2015	USD 470m	NASH asset in Phase II
Tobira	Allergan	2016	USD 1.7bn	Total pipeline of the company including Phase IIb asset in NASH
Akarna	Allergan	2016	USD 50m	Licensed preclinical NASH asset
Nimbus	Gilead	2016	USD 1.2bn	Phase I ACC inhibitor
Conatus	Novartis	2016	USD 700m	Worldwide rights to emricasan, a Phase IIb program in NASH Cirrhosis

Source: Van Leeuwenhoek Inc



## C-Difficile Infection: Underestimated Potential

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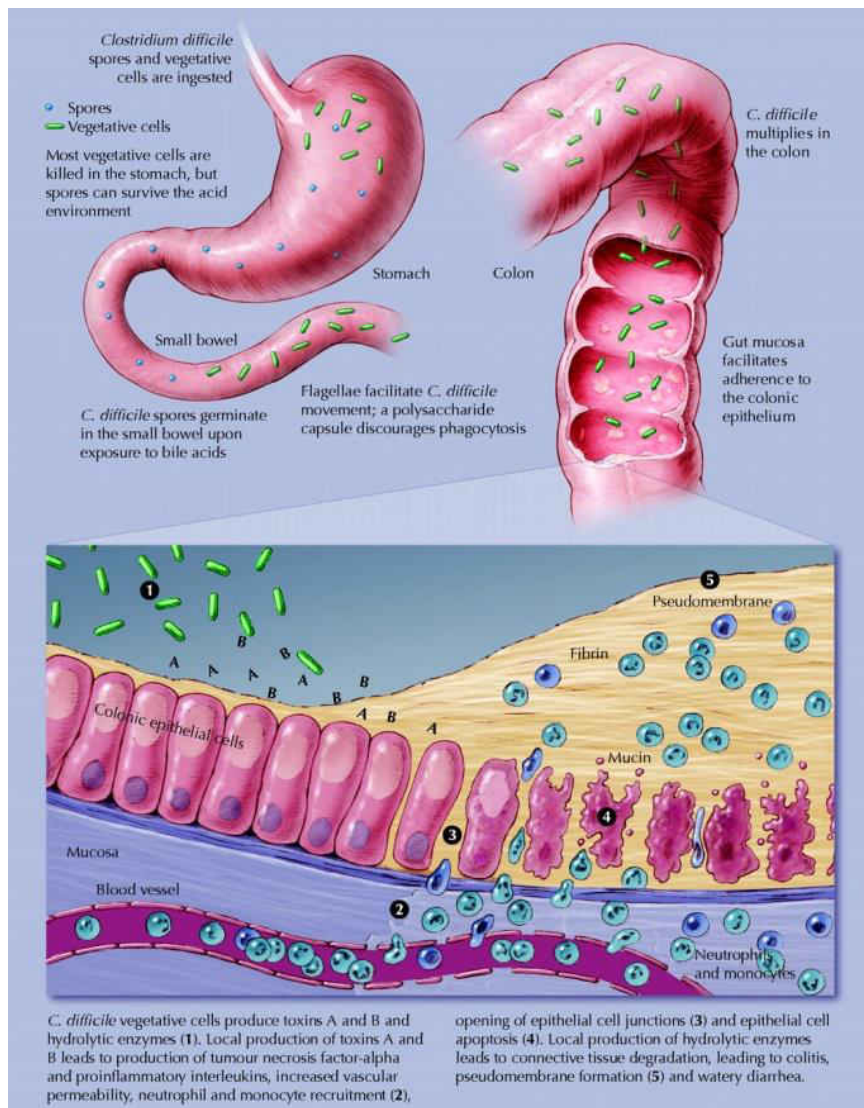
CDI is an infection of the colon caused by the bacteria *Clostridium difficile* that produces toxins that cause inflammation and severe diarrhea. CDI can also result in serious disease complications including bowel perforation, toxic megacolon and sepsis, and it can prove fatal in the most severe cases.

In recent years, increases in the frequency and severity of CDI have been observed worldwide, as well as an increased risk of community-associated CDI, and CDI in persons previously thought to be low risk. It is estimated that CDI affects up to 1.2% of hospitalized patients in the United States, representing an estimated cost of USD 4.8 billion per year (source: CDC). In Europe, the estimated cost is approximately 3 billion per year, which is likely to increase concomitantly with a more elderly society; more than 134 million Europeans will be >65 years by 2050. In addition to hospitalization, the most significant predisposing factors for CDI include advanced age (>65 years) and antibiotic therapy (disrupts the normal gut microbiota). The most common antibiotics implicated to date include broad-spectrum cephalosporins, fluoroquinolones and clindamycin. The only remaining effective therapeutic agents are metronidazole, vancomycin and fidaxomicin. Vancomycin and metronidazole are the current standard of care, accounting for 80% of patients share in the US. However, these two therapies are plagued by a 25% rate of CDI recurrences and each recurrence predisposes to further recurrence. After two or more episodes of recurrence, the risk of subsequent recurrence may reach 65%. This underscores the need for new treatments. Against this backdrop, the last decade has seen the emergence of a new epidemic of CDI characterized by increased frequency and severity of enteric disease and increased resistance to antibiotic therapy.



### Pathophysiology of CDI

*Clostridium difficile* (CD) is a spore-forming microorganism that releases toxins when in an anaerobic environment. The spore form allows the bacteria to remain dormant until the opportune conditions cause the bacteria to emerge. The CD spore, after ingested, is resistant to gastric acid





and can be passed into the intestines, where conditions are favorable. The spores then germinate and release two exotoxins, A and B, that contain properties of enterotoxins and cytotoxins. These toxins can open tight junctions between cells in the intestines that end with increased vascular permeability and hemorrhaging. The toxins also produce tumor necrosis factor-alpha and proinflammatory interleukins that cause an inflammatory response that leads to the development of pseudo membranes. Toxins A and B cause tissue damage in the gastrointestinal tract which results in diarrhea. CD is able to colonize in the gastrointestinal tract following a change in normal flora. The change in normal flora is typically caused by antibiotic use. Antibiotics kill off the body's normal flora in the intestines providing more nutrients and space for the remaining infectious microorganism like CD.

### *Potential Market for CDI expected to grow well above USD 1 billion*

The global therapeutics and prophylactics market for Clostridium difficile infections (CDIs) will expand more than fourfold from USD 356.3 million in 2014 to over USD 1.5 billion by 2024, representing an impressive Compound Annual Growth Rate (CAGR) of 15.8%, according to research and consulting firm GlobalData. The company's report states that this increase will be driven by the modest uptake of patent-protected, CDI-specific antibiotics and the arrival of novel non-antibiotic approaches to treat and prevent recurrent CDI. This bodes well for novel therapies against CDI like IMM-529. End of last year, Merck's antibody therapy bezlotoxumab (Zinplava) was approved by the FDA and will be available on the market as of 2017Q1. Compared to IMM-529, Zinplava neutralizes toxin B that has entered the blood stream, whereas IMM-529 not only targets toxin B but also spores and vegetative cells. Next to that, IMM-529 targets Toxin B in the gut, which is specific for CDI.



# SWOT Analysis

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## Strengths

Strong management with extensive relevant technical, commercial and financial expertise

Growing revenues from existing products provides source of cash flow

Direct product cost savings and work place cost efficiencies

## Weaknesses

Operating losses cumulating year-on-year

Relatively low market value makes its more challenging to be on investor's radar.

Competition with established players

## Opportunities

Nasdaq Listing will provide increased visibility and source of capital

Increasing interest from big Pharma following deal size in recent years

Large growing markets

## Threats

Delay in trials and filing with its programs in NASH and CDI

Increasing competition from larger companies

Failure to sign partnerships in key markets



## Patent Position

Immuron manages seven separate families of patent cases, requiring prosecution in each of the major global jurisdictions. All such cases are in different stages of development and prosecution. Worldwide, the company has issued 13 patents and 23 pending patent applications. These patents enhance the market exclusivity offered by the fact that Immuron’s compounds are classified as biologics by the FDA. The company further maintains a significant register of trademarks, particularly in association with the product Travelan.

Due to the practical nature of the technology used to produce Travelan, the company also retains a significant amount of know-how and other unregistered intellectual property which presents significant hurdles to competitors in producing the same products. In its relationships with Hadasit and the Monash University, the company continues its policy of actively in-licensing and filing upon new technology that relates to all relevant business objectives. Immuron owns a number of patent families that have been filed to protect both the vaccine that is used to generate Immuron’s colostrum enriched with antibodies of choice, and methods of treating certain conditions with the resulting hyper immune colostrum.

### *Composition and Method for the Treatment and Prevention of Enteric Bacterial Infections*

Number	Country	Status	Expiry
2004216920	Australia	Granted	4 March 2024
0408085-8	Brazil	Pending	4 March 2024
2,517,911	Canada	Pending	4 March 2024
102698258	China	Pending	4 March 2024
EP 1605975	Europe	Pending	4 March 2024
230664 B	India	Granted	4 March 2024
542088	New Zealand	Granted	4 March 2024
9,402,902	USA	Granted	4 March 2024
8,637,025	USA	Granted	25 February 2028



*Immuno-Modulating Compositions for the Treatment of Immune-Mediated Disorders*

Number	Country	Status	Expiry
2009222965	Australia	Granted	11 March 2029
2,718,381	Canada	Pending	11 March 2029
EP 2268669	Europe	Pending	11 March 2029
587901	New Zealand	Granted	11 March 2029
13/715,371	USA	Pending	11 March 2029

*Anti LPS Enriched Immunoglobulin for the Treatment and/or Prophylaxis of a Pathologic Disorder*

Number	Country	Status	Expiry
2010243205	Australia	Granted	27 April 2030
2760096	Canada	Pending	27 April 2030
13/265,252	USA	Pending	27 April 2030
2424890	Europe	Pending	27 April 2030
12103554.8	Hong Kong	Granted	27 April 2030
315924	Israel	Pending	27 April 2030
5740390	Japan	Granted	27 April 2030
10-2011-7027634	Korea	Pending	27 April 2030
335793	Mexico	Pending	27 April 2030
201171304	Eurasia	Pending	27 April 2030

*Anti LPS Enriched Immunoglobulin Preparation For Use in Treatment and/or Prophylaxis of a Pathologic Disorder*

Number	Country	Status	Expiry
2011290478	Australia	Granted	27 April 2030
2808361	Canada	Pending	27 April 2030
2605791	Europe	Pending	27 April 2030
13/817,414	USA	Pending	27 April 2030
1185016	Hong Kong	Published	27 April 2030

*Methods and Compositions for the Treatment and/or Prophylaxis of Clostridium Difficile Associated Disease*

Number	Country	Status	Expiry
2014253685	Australia	Pending	17 April 2034
2,909,636	Canada	Pending	17 April 2034
2986316	Europe	Pending	17 April 2034
14/785,527	USA	Pending	17 April 2034
201480034857.3	China	Pending	17 April 2034
713233	New Zealand	Pending	17 April 2034



## Financials

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For the 12 months ended 30 June 2016, total revenues amounted to AUD 1.155 million, an increase of 3% compared to the same period last year. The company had set itself a sales target of AUD 1.3 million or 15% growth. That would have been reached if a large order from its Canadian partner, Endo Pharmaceuticals, had been shipped in this fiscal year, but it was received in August 2016, which will positively impact the FY2017 sales. Travelan registered strong growth in all of the markets including Australia (9%) and the US (1,077%). In the US, the reach of Travelan was expanded within travel clinics and with distributors. Immuron closed five large distribution agreements in the US including with Medique, one of the largest distributors in the US for OTC products. In August, Immuron announced that Travelan will be available in over 1,000 CVS stores, the largest pharmacy chain after Walgreens. We believe that Travelan has a great potential in the US and other countries as both an OTC and a prescription product. Sales in the 2017 could increase substantially, not only due to the agreements mentioned, but also because Immuron is increasing its marketing and sales spending in 2017 in the US, Australia and in China. In China for instance, the company made an agreement for both Travelan and Protectyn with QBID, a leading company in the Australia-China e-commerce trade. QBID is an official partner of JD.com, China's largest online sales company.

Expenses for the period totaled to AUD 8.3 million (2015: AUD 5.1 million) including R&D expenses of AUD 3.6 million. Net loss for this period increased by AUD 0.9 million to AUD 4.4 million. The company's current cash position after the recent capital raise (net proceeds: AUD 6.33 million) and the R&D tax refund of AUD 1.6 million amounts to AUD 9.2 million. The proceeds are used to fund continuation of the NASH Phase II/III studies, progression into a *C. difficile* Phase I trial, completion of the colitis preclinical studies and a further promotion of its OTC products (Travelan and Protectyn).



### *Profit & Loss Statement*

AUD mln	2014A	2015A	2016A	2017E
Revenues	0.981	1.124	1.156	2.200
COGS	(0.278)	(0.316)	(0.301)	(0.660)
Gross Profit	0.703	0.808-	0.854	1.540
Other Income	0.804	0.835	3.009	2.000
R&D Costs	(1.290)	(3.018)	(3.623)	(5.000)
Other	(2.283)	(1.452)	(4.581)	(5.000)
SG&A	(0.235)	(0.143)	(0.488)	(0.800)
Operating Profit/(Loss)	(2.495)	(3.448)	(4.390)	(7.260)
Income Taxes	0	0	0	0
Net Profit/(Loss)	(2.495)	(2.704)	(7.059)	(7.260)

### *Consolidated statement of cash flows*

AUD mln	June 30 <sup>th</sup> 2015A (12 months)	June 30 <sup>th</sup> 2016A (12 months)	June 30 <sup>th</sup> 2017E (12 months)
Cash flow from operating activities	(3.021)	(4.914)	(8.000)
Cash flow from investing activities	(0.003)	(0.002)	(0.0)
Cash flow from financing activities	(0.002)	4.091	25.000
Cash and cash equivalents at beginning of the period	6.142	3.116	2.291.
Net change in cash and cash equivalents	(3.026)	(0.825)	17.000



## Valuation

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We have increased our valuation on Immuron to AUD 197 million or AUD 1.92 per share from AUD 75 million or AUD 0.75 per share due to the fact that we see an increased interest from big pharma to partner in NASH. We also have altered our valuation model to incorporate both Europe and China as potential markets for Immuron's products in NASH and CDI. At this moment we do not address value to other programs in Immuron's pipeline. This is a potential upside for the company.

### *Phase Success and Likelihood of Approval (LOA)*

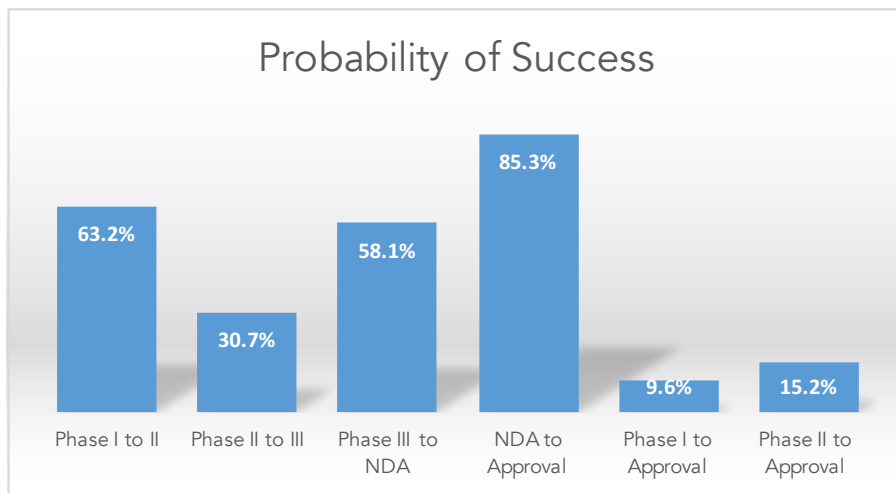
In estimating a value for each separate clinical program and products (Travelan and Protectyn) in Immuron's pipeline, we made use of several studies that were done on the clinical development success rates for investigational drugs to measure success rates for investigational drugs. We analyzed individual drug program phase transitions from January 1, 2006 to December 31, 2015. For the ten years studied, 9,985 transitions in the Biomedtracker database were analyzed. A phase transition is the movement out of a clinical phase – for example, advancing from Phase I to Phase II development, or being suspended after completion of Phase I development. These transitions occurred in 7,455 clinical drug development programs, across 1,103 companies (both large and small), making this the largest study of its kind. With this broad set of data, we aimed to capture the diversity in drug development across levels of novelty, molecular modalities, and disease indications. Only company-sponsored, FDA registration-enabling development programs were considered; investigator-sponsored studies were excluded from this analysis.

The Phase I transition success rate was 63.2% (n=3,582). As this Phase is typically conducted for safety testing and is not dependent on efficacy results for candidates to advance, it is common for this phase to have the highest success rate among the clinical phases across most categories analyzed in this report. Phase I success rates may also benefit from delayed reporting bias, as some larger companies may not deem failed Phase I programs as material and thereby not report them





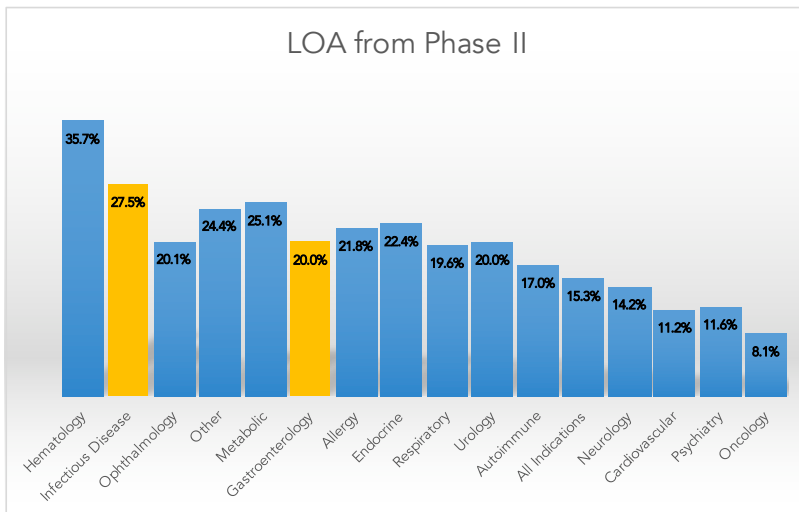
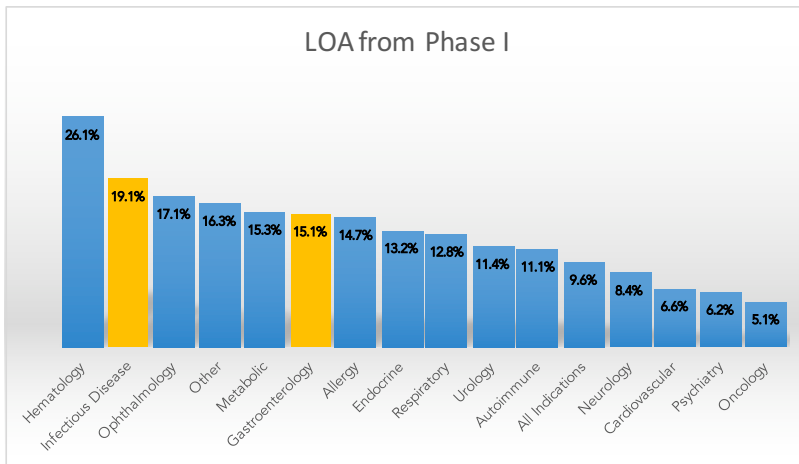
in the public domain. The Phase II transition success rate (30.7%, n=3,862) was substantially lower than Phase I, and the lowest of the four phases studied. As this is generally the first stage where proof-of-concept is deliberately tested in human subjects, Phase II consistently had the lowest success rate of all phases. This is also the point in development where industry must decide whether to pursue the large, expensive Phase III studies and may decide to terminate development for multiple reasons including commercial viability. The second-lowest phase transition success rate was found in Phase III (58.1%, n=1,491). This is significant as most company-sponsored Phase III trials are the longest and most expensive trials to conduct. The probability of FDA approval after submitting a New Drug Application (NDA) or Biologic License Application (BLA), taking into account re-submissions, was 85.3% (n=1,050). Multiplying these individual phase components to obtain the compound probability of progressing from Phase I to U.S. FDA approval (LOA) reveals that only 9.6% (n=9,985) of drug development programs successfully make it to market (see graph below)



Source: BIO Industry Analysis



Major disease areas were segmented according to the convention used by Biomedtracker, and categorized 21 major diseases and 558 indications for the 2006-2015 timeframe. As can be seen in the graphs below, there is a wide range of Likelihood of Approval (LOA) from Phase I, II and III.





we feel that each of the programs (NASH and CDI) in clinical development have blockbuster potential, catering to large markets that is also underscored by the sizable partnerships done in NASH. Analysts predict that the market for NASH therapies could reach USD 35 billion or more by 2025. The global therapeutics and prophylactics market for CDI will expand more than fourfold from USD 356.3 million in 2014 to over USD 1.5 billion by 2024, representing an impressive Compound Annual Growth Rate (CAGR) of 15.8%, according to research and consulting firm GlobalData.

### *Valuation Travelan*

In estimating a value for Travelan, we made use of a potential growth in revenue up to AUD 45 million in the coming years with an increase of sales coming from Canada, China and the US. The global market of travel for Travelan is estimated to be USD 500 million. We calculate a Risk adjusted Discount Rate of 10% and a net margin of 25%.

Year	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Price	15	15	15	15	15	15	15	15	15	15
Travelers Australia (m)	8.1	8.1	8.1	8.1	8.1	8.1	8.1	8.1	8.1	8.1
Penetration	0.40%	0.70%	1.30%	1.60%	2.00%	2.50%	3.50%	4.00%	4.50%	5.00%
Travelers US (m)	61.5	61.5	61.5	61.5	61.5	61.5	61.5	61.5	61.5	61.5
Penetration	0.05%	0.10%	0.15%	0.25%	0.50%	0.80%	1.20%	1.50%	1.80%	2.00%
Travelers Canada (m)	5.2	5.2	5.2	5.2	5.2	5.2	5.2	5.2	5.2	5.2
Penetration	0.10%	0.30%	1.00%	1.30%	1.50%	1.80%	2.10%	2.30%	2.40%	2.50%
Travelers China (m)	81m	81m	81m	81m	81m	81m	81m	81m	81m	81m
Penetration	0.00%	0.01%	0.02%	0.03%	0.04%	0.04%	0.05%	0.06%	0.07%	0.08%
Total Revenues (\$m)	1.025	2.250	4.051	6.195	9.689	15.79	24.05	30.62	38.20	42.68
Margin 25%	0.256	0.563	1.013	1.549	2.422	3.948	6.012	7.654	9.549	10.67
WACC 10%	1.00	0.91	0.83	0.75	0.68	0.62	0.56	0.51	0.47	0.42
NPV (million)	0.256	0.512	0.837	1.163	1.654	2.451	3.394	3.928	4.455	4.525
<b>Total NPV (million)</b>										<b>23.18</b>
<b>Value per share (AUD)</b>										<b>0.30</b>



### Valuation IMM-124E in NASH

In estimating a value for IMM-124E in NASH, we took into account potential markets in the US, Europe and China with a total number of patients of 2.5 million in the US, 3.3 million in Europe and 6 million in China, with a market launch in the US in 2022 and 2023 in Europe. We calculate a Risk adjusted Discount Rate of 15%. Annual pricing per treatment is set at USD 15,000 which is comparable with pricing of cholesterol lowering drugs. In Europe we calculate a somewhat lower price of USD 12,000 and in China we estimate pricing of USD 3,000. Although we believe that Immuron will partner its program in NASH with a large pharmaceutical, in our model we have calculated its value by marketing the drug independently. We estimate that a peak market share of 5-6% is possible. In line with the report of BioMedTracker, we used a LOA of 20%. This leads to a total valuation of AUD 145 million or AUD 1.41 per share.

Year	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
No of patients treated US	674k	684k	694k	704k	715k	726k	737k	748k	759k	770k
Penetration	0.2%	0.4%	0.8%	1.5%	2.5%	3.5%	4.5%	5.5%	6.0%	6.0%
No of patients treated EU		897k	910k	924k	938k	952k	966k	981k	995k	1010k
Penetration		0.1%	0.2%	0.5%	1.0%	1.6%	2.2%	3.0%	3.8%	4.5%
No of patients treated China			970k	984k	999k	1014k	1029k	1045k	1061k	1076k
Penetration			0.3%	0.8%	1.5%	3.0%	5.0%	6.5%	8.0%	9.0%
Total Revenues (\$m)	20.2	51.8	105.8	215.9	384.4	571.3	765.0	986.7	1,157	1263
Margin 50%	10.1	25.9	52.9	107.9	192.2	285.6	382.5	493.4	579.0	631.4
WACC 15%	0.38	0.33	0.28	0.25	0.22	0.19	0.16	0.14	0.12	0.11
NPV (million)	3.8	8.5	15.0	26.7	41.3	53.4	62.2	69.7	71.2	67.5
<b>Total NPV (million)</b>										<b>144.9</b>
<b>Value per share (AUD)</b>										<b>1.41</b>



### Valuation IMM-529 in CDI

In estimating a value for IMM-529 in CDI, we took into account potential markets in the US and Europe with a total number of patients of 800,000 and 500,000 respectively. We expect market launch in 2022 with an estimated peak market share of 10%. We calculate a Risk adjusted Discount Rate of 15% to take into account the higher risk. Annual pricing is set at USD 50,000. Although we believe that Immuron will partner its program in CDI with a large pharmaceutical, in our model we have calculated its value by marketing the drug independently. In line with the report of BioMedTracker, we used a LOA of 20%. This leads to a total valuation of AUD 16 million or AUD 0.16 per share.

Year	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
No of patients US	525k	533k	541k	549k	557k	565k	574k	583k	591k	600k
No of patients treated EU	833k	846k	858k	871k	884k	898k	911k	925k	939k	953k
Recurrent CDI patients (20%)	272k	276k	280k	284k	288k	293k	297k	301k	306k	311k
Penetration	0.5%	0.8%	1.5%	2.5%	3.5%	5.0%	6.0%	7.0%	8.0%	9.0%
Total Revenues (\$m)	8.1	13.2	25.2	42.6	60.5	87.8	106.9	126.6	146.9	167.7
Margin 50%	4.1	6.6	12.6	21.3	30.3	43.9	53.5	63.3	73.4	83.9
WACC 15%	0.43	0.38	0.33	0.28	0.25	0.21	0.19	0.16	0.14	0.12
NPV (million)	1.8	2.5	4.1	6.1	7.5	9.4	10.0	10.3	10.4	10.3
<b>Total NPV (million)</b>										<b>16.5</b>
<b>Value per share (AUD)</b>										<b>0.16</b>



## Management Capabilities

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Immuron is being built by seasoned biotechnology innovators. The company is led by an experienced Board and management team, which has been responsible for the development of the business and has a long term track record of developing, protecting and commercializing innovative scientific products and processes. In the past several years, the company has been investing in developing a team of experts that have a focus on patient outcomes and can deliver results. Its board and senior management team are highly experienced in the early and late stage development and commercialization of therapeutics in gastroenterology.

### Management Team

#### Thomas Liquard, Chief Executive Officer

Mr. Liquard has held various product development and leadership roles with large pharma and biotech companies. From 2013 to 2014, Mr. Liquard was Chief Operating Officer and later Chief Executive Officer of Australian Biotech Company Alchemia. Prior to joining Alchemia from 2013 to 2014 Mr. Liquard was employed by Pfizer in New York for 7 years where he held various senior commercial positions in business and portfolio development. Mr Liquard spent three years as a key member of Pfizer's Established Products U.S. brands P&L Leadership Team where he engineered the groups \$700M acquisition of Next Wave Pharmaceuticals, Inc. (NextWave). Mr. Liquard led the pre and post-acquisition integration efforts of Next Wave into the existing Pfizer business. The development products acquired with the NextWave acquisition are now approved and generate more than \$250M in annual sales in the U.S. Mr. Liquard holds an MBA from Columbia Business School and a Bachelor of Science Degree from the University of Southern California.



## **Dr Jerry Kanellos, Chief Operating and Scientific Officer**

Dr. Jerry Kanellos has over twenty five years' experience in the pharmaceutical and biotechnology industry, and has held leadership roles in executive management, business development, project management, intellectual property portfolio management research and development. From 2008 until 2012, Dr. Kanellos was the Chief Operating Officer of TransBio Limited where he was responsible for the strategic identification, development and maintenance of commercial partnerships globally, along with development, management and maintenance responsibility for the intellectual property portfolio, research and development and technology transfer. Prior to this, Dr. Kanellos work for five years as a consultant to the biotechnology industry and has provided development and commercialization strategies for various bodies including academic institutes, private and publicly listed companies and government departments both national and international. He has also been involved in the establishment and management of several startup biotechnology companies. During his ten years tenure in research and development at CSL Limited, a global specialty biotherapeutics company that develops and delivers innovative biotherapies, Dr. Kanellos gained considerable experience in the international drug development process, formulation development through to pharmaceutical scale up and cGMP manufacture successfully leading the Chemistry Manufacturing and Controls (CMC) programs for the approval, manufacture and launch of several products. Dr. Kanellos holds a PhD in Medicine from the University of Melbourne.

## **Dan Peres, Chief Medical Officer**

Dr. Dan Peres (MD) has served in various clinical and medical managerial roles in pharmaceutical and medical device companies such as Exalenz Bioscience, CarboFix Orthopedics Ltd, NMB Medical Applications Ltd, ByPass Makafim Ltd, IOptima Ltd and NovoNordisk Israel. In addition, Dr. Peres has been responsible for operational, marketing and business development activities throughout his career in the life sciences industry. Dr. Peres began his career as a physician and



medical director in the Israel army. Dr. Peres' expertise lies with medical strategy, research and development, and the management of clinical studies and other laboratory processors. He has extensive knowledge of the leading International Centers for Liver Disease and established relationships with key Opinion leaders, including those currently participating in Immuron's NASH and ASH trials. Dr. Peres has been a certified physician since 2002 when he graduated from the Sackler School of Medicine at Tel-Aviv University.

### **Philip Hains & Peter Vaughan, Joint Chief Financial Officer**

Peter Vaughan and Philip Hains have been Immuron's joint Chief Financial Officer (CFO) and Company Secretary since April 2013. Mr Hains is a Chartered Accountant and specialist in the public company environment. He has served the needs of a number of public company boards of directors and related committees. He has over 20 years' experience in providing accounting, administration, compliance and general management services. He holds a Masters of Business Administration from RMIT and a Public Practice Certificate from the Institute of Chartered Accountants of Australia.

Mr Vaughan is a Chartered Accountant who has worked in the listed company environment for 13 years across a number of industries. He has served on, and provided accounting, administration, compliance and general management services to a number of private, not-for-profit, and listed public company boards of directors and related committees. Mr Vaughan is also currently studying a Senior Executive Masters of Business Administration at Melbourne University.





## Near Term Milestones

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In the past year, Immuron has already reached a number of important milestones with the development of both its lead programs and the increasing sales of Travelan. In the next 6-12 months, we expect a number of important milestones to drive the stock price upwards. These are:

- Ongoing: OTC Products Travelan and Protectyn: Continued Expansion
- 2017-Feb: NASH Phase II, Fully enrolled
- 2017H1: Nasdaq listing and US Capital Raise
- 2017H1: NASH Phase II Interim Results
- 2017Q2: C. difficile – Manufacturing of Clinical Supplies Completed
- 2017Q2: C. difficile – Initiation of Phase I/II
- 2017H2: NASH Top line data Phase II
- 2018: ASH – Top line data Phase II
- 2018: C. difficile – Phase I/II results



## Competitive Landscape

During examination of comparable companies, we looked separately at companies that are developing therapies in NASH and CDI. On page 20, we gave an overview of companies that are developing therapies in NASH and that have a made an agreement with a partner. This overview gives some additional insight in the size of the deals done and at what stages they were made. The tables provide an overview of the later stage programs in NASH and CDI followed by a brief profile per company/program.

### *Selected Investigational NASH Therapies in Advanced Clinical Studies*

Product	Company	Activity	Stage	Partnership
Ocaliva	Intercept	Farnesoid X receptor agonist	Phase III	NA
Elafibranor	Genfit SA	PPAR alpha, delta modulator	Phase III	NA
Aramchol	Galmed Pharma	ATP binding cassette transporter 1 inhibitor	Phase IIb	NA
Centicriviroc	Tobira/Allergan	Chemokine receptor 5 antagonist	Phase IIb	USD 1.7bn total pipeline
Emricasan	Conatus Pharma	Caspase inhibitor	Phase IIb	USD 700m with Novartis
GRI-0621	GRI Bio	NKT 1 inhibitor	Phase II	NA
GR-MD-02	Galectin Ther.	Galectin-3 protein inhibitor	Phase II	NA
Selonsertib	Gilead	Apoptosis signal regulating kinase 1	Phase II	NA
Tipelukast	MediciNova/Kyorin	Leukotriene inhibitor	Phase II	
MSDC-0602K	Octeta Ther.	mTOT (mitochondrial target of thiazolidinediones)	Phase II	NA
GS-9674	Phenix/Gilead	Farnesoid X Receptor (FXR)	Phase I	Total value USD 470m
PXS-4728A	Pharmaxis/B-I	SSAO inhibitor (VAP-1)	Phase I	Total value AUD 600m

Source: Van Leeuwenhoek Inc, Company Reports



### *Intercept Pharmaceuticals (ICPT)*

Intercept is a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat progressive non-viral liver diseases. Intercept's lead product, Ocaliva (obeticholic acid), was granted accelerated approval by U.S. Food and Drug Administration (FDA) in May of 2016 for the treatment of primary biliary cholangitis, previously known as primary biliary cirrhosis (PBC). Ocaliva is also being evaluated for potential indications across a variety of additional chronic liver diseases, including NASH. The FDA has granted OCA breakthrough therapy designation for the treatment of NASH with liver fibrosis. Ocaliva is currently being evaluated in an international Phase III for the treatment of NASH. In accordance with advice of the FDA and EMA, the Phase III trial (REGENERATE) is designated as a double blind placebo controlled Phase III trial. REGENERATE will assess the potential benefit of Ocaliva on liver-related clinical outcomes.

### *Genfit SA (GNFT.PA)*

Genfit is a French biopharmaceutical company focused on the discovery and development of drug candidates in areas of high unmet medical needs. GENFIT's R&D efforts are focused on bringing new medicines to market for patients with metabolic, inflammatory, autoimmune and fibrotic diseases, that affect the liver (such as NASH – Nonalcoholic steatohepatitis) and more generally the gastrointestinal arena. Its lead product is Elafibranor that is currently in Phase III (RESOLVE-IT) for the treatment of NASH. Elafibranor is an oral once daily treatment positioned as a first in class drug to treat NASH. RESOLVE-IT is a randomized pivotal trial, double-blind, placebo-controlled (2:1), conducted in approximately 2000 patients, at 250 centers worldwide. The study population is NASH patients (NAS $\geq$ 4) with F2 or F3 fibrosis. Elafibranor 120 mg or placebo are administered once daily. An interim analysis, for initial market approval under Subpart H, will be performed after 72 weeks of treatment in order to evaluate the beneficial effect of Elafibranor on the liver histology of the first 1000 patients.



### *Galmed Pharma (GLMD)*

Galmed is a clinical-stage biopharmaceutical company focused on the development of a novel, once-daily, oral therapy for the treatment of NASH and liver diseases utilizing its proprietary first-in-class family of synthetic fatty-acid/bile-acid conjugates, or FABACs. Galmed is currently conducting the ARREST Study, a multicenter, randomized, double blind, placebo-controlled Phase IIb clinical study designed to evaluate the efficacy and safety of Aramchol in subjects with NASH, who are overweight or obese, and who are pre-diabetic or type-II-diabetic. Galmed recently completed enrollment for its Phase IIb ARREST study. The ARREST Study is a global, multi-center, randomized, double blind, placebo-controlled, Phase IIb clinical trial evaluating the treatment effects and safety of Aramchol in 240 patients with biopsy proven NASH who are overweight or obese, and who are pre-diabetic or type-II-diabetic. The ARREST Study duration is 52 weeks with 12 weeks' follow-up period. Results are anticipated to be announced in 2018Q2. The ARREST Study primary endpoint, previously demonstrated in a Phase IIa study, is reduction in liver fat content measured by magnetic resonance spectroscopy (MRS). The secondary histological endpoints include improvement of fibrosis, two-point improvement in NAS (NAFLD Activity Score) and resolution of NASH. The ARREST Study will also evaluate surrogate metabolic endpoints. Patients enrolled in the ARREST Study have advanced NASH with more than 60% having fibrosis in stages 2 (19%) and 3 (42%) and a mean NAS score of 5.

### *Tobira Therapeutics (recently acquired by Allergan)*

Tobira is a clinical-stage biopharmaceutical company focused on developing and commercializing therapies to treat NASH and other liver diseases, inflammation, fibrosis and HIV. Its lead product candidate, cenicriviroc, or CVC, is a first-in-class immunomodulator and dual inhibitor of CCR2 and CCR5 being evaluated for the treatment of NASH, primary sclerosing cholangitis (PSC), and as an adjunctive therapy to standard of care in HIV. In September 2016 Allergan announced that it will acquire Tobira for an upfront payment of USD 28.35 per share in



cash an up to USD 49.84 per share in CVRs that may be payable based on the successful completion of certain development, regulatory and commercial milestones, for a total potential consideration of up to USD 1.695 billion. CVC is an oral, once-daily, potent immunomodulator with a high binding affinity that blocks two chemokine receptors, CCR2 and CCR5, which are intricately involved in the inflammatory and fibrogenic pathways in NASH and PSC that cause liver damage and can lead to cirrhosis, liver cancer or liver failure. The safety and efficacy of CVC for NASH with liver fibrosis is being investigated in the CENTAUR study. CENTAUR is a Phase IIb multinational, randomized, double-blind study comparing CVC to placebo in 289 adults with NASH and liver fibrosis. In July 2016, Tobira announced that CENTAUR met the key secondary endpoint of improvement in liver fibrosis by at least one stage with no worsening of steatohepatitis after one year of treatment, which was recommended by regulators as an endpoint for Phase III studies to support a marketing application. The CENTAUR study continues for a second year analysis of endpoints, which is expected in 2017Q3. The company plans to initiate a Phase III program in 2017.

### *Conatus Pharmaceuticals (CNAT)*

Conatus Pharmaceuticals is a biotechnology company focused on the development and commercialization of novel medicines to treat liver disease. Conatus' lead compound, emricasan, is a first-in-class, orally active pan-caspase protease inhibitor designed to reduce the activity of human caspases, which are enzymes that mediate inflammation and apoptosis. To date, emricasan has been administered to over 600 subjects in eight Phase I and seven Phase II clinical trials, and has been generally well-tolerated in both healthy volunteers and patients with liver disease. Recent emricasan clinical trial results have demonstrated emricasan's ability to provide statistically significant improvements in clinically important validated surrogate endpoints of portal hypertension and liver function across a variety of etiologies in the subgroups of liver cirrhosis patients with highest medical need. The parallel Emricasan, a Caspase inhibitor, for Evaluation (ENCORE) clinical trials are designed to provide clinically relevant efficacy, dosing, and safety data



from chronic administration in patients with NASH cirrhosis and fibrosis to support the design of Phase III efficacy and safety trials in these indications. In December 2016 Conatus signed a global partnership with Novartis on Emricasan. Under the terms of the agreement with Novartis, Conatus will receive USD 50 million upfront, and is eligible to receive USD 7 million following the exercise of the license option. Conatus can borrow up to USD 15 million in the form of convertible promissory notes under an investment agreement with Novartis. In addition, Novartis will pay 50% of Conatus' Phase IIb emricasan development costs after the option exercise, including the planned ENCORE-LF trial in decompensated NASH cirrhosis which, under the current development plan consistent with recent regulatory agency recommendations, will be conducted as Phase IIb rather than Phase IIb/III. Phase IIb emricasan development costs also encompass the ongoing ENCORE-PH trial in primarily compensated NASH cirrhosis, POLT-HCV-SVR trial in post-transplant HCV fibrosis and cirrhosis, and ENCORE-NF trial in NASH fibrosis. Novartis will assume full responsibility for emricasan's Phase III development and all combination product development.

### *Gilead*

Gilead's portfolio of products and pipeline of investigational drugs includes treatments for HIV/AIDS, liver diseases, cancer, inflammatory and respiratory diseases, and cardiovascular conditions. Gilead is currently planning or conducting Phase II and Phase III clinical trials evaluating single-agent and combination therapy approaches against multiple core pathways associated with NASH – metabolic dysfunction, inflammation and fibrosis. In 2010 it acquired the company Arresto and with it, the AB0024 program (later named simtuzumab). **Simtuzumab** is a humanized monoclonal antibody designed for the treatment of fibrosis. It binds to LOXL2 and acts as an immunomodulator. In January 2016, Gilead Sciences terminated its Phase II clinical study in patients with idiopathic pulmonary fibrosis (IPF) due to lack of efficacy. End of 2016 it also decided to discontinue the other programs under simtuzumab including NASH and to focus on its other Phase II program in NASH, selonsertib.



Selonsertib (formally known as GS-4997) is an investigational small molecule inhibitor of apoptosis signal-regulating kinase 1 (ASK1), a protein that promotes inflammation, apoptosis (cell death) and fibrosis in settings of oxidative stress. Oxidative stress normally occurs at low levels in healthy states, but can be increased in many pathological conditions such as NASH. Selonsertib demonstrated anti-fibrotic activity in an open-label Phase II clinical trial that included 72 patients with NASH and moderate to severe (F2-F3) liver fibrosis, who received treatment with selonsertib (18 mg or 6 mg orally once daily) alone or in combination with simtuzumab (SIM) or SIM alone (125 mg administered via weekly subcutaneous injections) for 24 weeks.

### *Galectin Therapeutics (GALT)*

Galectin Therapeutics is a biotechnology company focused on discovery and development of new therapies for fibrotic disease and cancer. Its lead program is GR-MD-02 that is in Phase II development for NASH cirrhosis and NASH advanced fibrosis. GR-MD-02 is a complex carbohydrate drug that targets galectin-3, a critical protein in the pathogenesis of fatty liver disease and fibrosis. Galectin-3 plays a major role in diseases that involve scarring of organs including fibrotic disorders of the liver, lung, kidney, heart and vascular system. The drug binds to galectin proteins and disrupts their function.

Galectin announced in August 2016 the completion of patient recruitment ahead of original expectations in the NASH-CX trial, its Phase IIb clinical trial with GR-MD-02 in patients with NASH with cirrhosis. The Company has enrolled 162 liver biopsy-confirmed NASH cirrhosis patients into the treatment phase, with the original goal to enter 156 patients. Enrolled patients are receiving either 8 mg/kg or 2 mg/kg of GR-MD-02 or placebo every other week for 52 weeks, for a total of 26 doses. The primary study endpoint is a reduction of hepatic venous pressure gradient (HVPG). Patients treated with GR-MD-02 will be evaluated to determine the change in HVPG as compared to patients treated with placebo. HVPG will be correlated with secondary endpoints of liver biopsy fibrosis staging at baseline and the end of the trial, measurement of liver stiffness (FibroScan®), and



assessment of liver metabolism ( $^{13}\text{C}$ -methacetin breath test, Exalenz). The Company projects topline results of this trial will be available in December 2017.

### *GRI Bio (private)*

GRI is a development stage biotech company with a focus on liver disease and autoimmunity. GRI's technologies target the regulation of NKT cells. NKT cells share properties of both NK and T cells and are a functional link between the innate and adaptive immune responses. Type 1 NKT cells play a role in initiating and propagating the inflammatory response and hepatic injury in liver disease. GRI's lead program is GRI-0621, an inhibitor of type I NKT cells and is being developed as an oral therapeutic for NASH, ALD and certain orphan diseases. A Phase IIb study in NASH patients with fibrosis is anticipated to start in 2017.

### *MediciNova (MNOV)*

MediciNova, Inc. is a biopharmaceutical company founded upon acquiring and developing novel, small-molecule therapeutics for the treatment of diseases with unmet medical needs with a commercial focus on the U.S. market. One of its lead programs is MN-001 or tipelukast, an orally bioavailable small molecule compound which exerts its effects through several mechanisms to produce its anti-fibrotic and anti-inflammatory activity in preclinical models, including leukotriene (LT) receptor antagonism, inhibition of phosphodiesterases (PDE) (mainly 3 and 4), and inhibition of 5-lipoxygenase (5-LO). The 5-LO/LT pathway has been postulated as a pathogenic factor in fibrosis development and MN-001's inhibitory effect on 5-LO and the 5-LO/LT pathway is considered to be a novel approach to treat fibrosis. MN-001 has been shown to down-regulate expression of genes that promote fibrosis including LOXL2, Collagen Type 1 and TIMP-1. MN-001 has also been shown to down-regulate expression of genes that promote inflammation including CCR2 and MCP-1. In addition, histopathological data shows that MN-001 reduces fibrosis in multiple animal models.





Previously, MediciNova evaluated MN-001 for its potential clinical efficacy in asthma and had positive Phase 2 results. MN-001 has been exposed to more than 600 subjects and considered generally safe and well-tolerated. MediciNova is collaborating with Kyorin Pharmaceutical in the global development of MN-001

### *Octeta Therapeutics (private)*

Octeta Therapeutics is engaged in the development of MSDC-0602K, a first-in-class mTOT modulating insulin sensitizer. It was formed in 2016. Octeta's MSDC-0602K is used for the treatment of NASH. mTOT insulin sensitizers are a new class of drugs that work by modifying metabolism. Unlike most therapeutic agents, which target specific enzymes or receptors that regulate some symptoms of disease, mTOT modulators affect a newly identified mitochondrial target of thiazolidinediones. MSDC-0602K is currently in a Phase II randomized double-blind placebo-controlled 12-month, multiple dose study to evaluate the safety, tolerability and efficacy of three dose levels of MSDC 0602K in patients with NASH (EMMINENCE). The primary endpoint of this clinical trial is reduction in the NASH pathology as assessed in direct examination of liver biopsies by an expert pathologist.

### *Phenex Pharmaceuticals (private)*

Phenex Pharmaceuticals AG is a drug discovery and development company focused on small-molecule drug discovery with a special emphasis on the target class of nuclear receptors. It was founded in 2002 with an aim to utilize its special know how & technology platform to develop novel innovative therapies i.e. for liver and gastrointestinal diseases, chronic inflammatory diseases and cancer - indications with a high unmet medical need and a significant market potential. Phenex is developing two proprietary R&D programs that target nuclear receptors which have emerged as very promising approaches for the treatment of liver diseases (FXR) or chronic inflammatory autoimmune diseases (ROR $\gamma$ t). Its lead program is FXR agonist Px-104 for the treatment of NASH



and acute complications of liver cirrhosis. FXR (Farnesoid X Receptor) functions as a receptor for bile acids. Regulation of FXR leads to a series of transcriptional responses that regulate triglyceride, cholesterol and bile acid metabolism. Selective synthetic FXR agonists have the potential to lower triglycerides and improve the cholesterol profile. The FXR program has been acquired by Gilead Sciences in late 2014 in a USD 465 million deal. The program is renamed GS-9674 is now being evaluated for its safety and efficacy in Phase 2 studies in NASH, primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC)

### *Pharmaxis (PXS.AX)*

Pharmaxis is an Australian based pharmaceutical company with a portfolio of products at various stages of development and approval. The pipeline is centered on its expertise in amine oxidase chemistry and includes semicarbazide Sensitive Amine Oxidase Inhibitors (SSAO) for NASH and inflammatory diseases including COPD. In March 2015, Pharmaxis signed an agreement with Boehringer Ingelheim for its inhibitor PXS4728A. Boehringer's primary interest in PXS4728A was directed at NASH and it acquired the program in May 2015 with an upfront of AUD 39 million. The total deal has a potential value of more than AUD 750 million including mile stone payments and royalties. The company expects to get a Phase II initiating milestone of AUD 25 million in 2017H1



### *Selected Investigational CDI Therapies in Advanced Clinical Studies*

<b>Product</b>	<b>Company</b>	<b>Activity</b>	<b>Stage</b>	<b>Partnership</b>
<b>Zinplava</b>	Merck & Co	Mab targeting C.difficile toxin B	Approved	NA
<b>Cadazolid</b>	Actelion	Bacterial Ribosome	Phase III	NA
<b>ACAM-CDIFF</b>	Sanofi	Vaccine	Phase III	NA
<b>Ribaxamase</b>	Synthetic Biologics	enzyme, targets beta- lactam antibiotics	Phase IIb	NA
<b>RBX2660</b>	Rebiotix	Microbiota intestinal	Phase IIb	NA
<b>SER-109</b>	Seres Health	Microbiota intestinal	Phase II	NA
<b>Ridinilazole</b>	Summit Ther.	Microtubules (Tubulin)	Phase II	NA
<b>DAV132</b>	DaVolterra	Antibacterial drug	Phase II	NA

### *Merck & CO*

In October 2016, Merck received approval for Zinplava (bezlotoxumab) and will be available as of 2017Q1. Zinplava is a human monoclonal antibody that binds to Clostridium difficile toxin B, indicated to reduce recurrence of Clostridium difficile infection (CDI) in adult patients who are receiving antibacterial drug treatment of CDI and are at a high risk for CDI recurrence. Zinplava is not indicated for the treatment of CDI. ZINPLAVA is not an antibacterial drug. Zinplava should only be used in conjunction with antibacterial drug treatment of CDI.



### *Actelion (ATLN.SW)*

Actelion initiated a Phase III trial with its antibiotic Cadazolid in patients suffering from *C. difficile* associated diarrhea. The Phase III program consists of two identical multi-center, randomized, double-blind studies comparing the efficacy and safety of cadazolid, (250 mg administered orally twice daily for 10 days) versus vancomycin, (125 mg administered orally four times daily for 10 days) in subjects with *Clostridium difficile*-associated diarrhea (CDAD). The program called IMPACT is expected to enroll more than 1,250 patients worldwide. Cadazolid was studied in a Phase II multi-center, double-blind, randomized, active reference, parallel group, therapeutic exploratory study. The study evaluated the efficacy, safety and tolerability of a 10-day, twice daily oral administration of 3 doses (250 mg, 500 mg or 1,000 mg b.i.d.) of cadazolid in subjects with *Clostridium difficile*-associated diarrhea (CDAD). As the current standard of care for CDAD, oral vancomycin (125 mg qid for 10 days) was used as the active reference. The study was completed in December of 2012, after having enrolled 84 subjects with CDAD. The results of the Phase II study indicate that the effect of all doses of cadazolid were numerically similar to, or better than vancomycin on key endpoints including CDAD clinical cure rates as well as sustained cure rates. Recurrence rates were numerically lower for all doses of cadazolid as compared to vancomycin.

### *Sanofi (SAN.PA)*

Sanofi Pasteur's candidate vaccine against *Clostridium difficile* takes a toxoid-based approach, which has been used extensively in Sanofi Pasteur's licensed vaccines against tetanus, diphtheria and pertussis (whooping cough). In August 2013, the company initiated a Phase III clinical program called *Cdiffense* to evaluate the safety, immunogenicity and efficacy of its investigational vaccine for the prevention of primary symptomatic *Clostridium difficile* infection (CDI). The *Cdiffense* Phase III clinical program will include up to 15,000 adults at 200 sites across 17 countries. A Phase II study of the vaccine against *Clostridium difficile* was done in the United States. The U.S. FDA has granted fast-track designation to Sanofi Pasteur's investigational *Clostridium difficile* vaccine.



### *Synthetic Biologics (SYN)*

Synthetic Biologics, Inc. (NYSE MKT: SYN) is a late-stage clinical company developing therapeutics focused on the gut microbiome. Its lead program is ribaxamase (SYN-004) that earlier this year concluded a Phase IIb study for CDI. Ribaxamase is a first-in-class oral enzyme designed to protect the gut microbiome from disruption caused by certain intravenous (IV) beta-lactam antibiotics. The study, a randomized, double-blind, placebo controlled trial of 412 patients, met its primary endpoint of significantly reducing CDI. Preliminary analysis of the data indicated seven confirmed cases of CDI in the placebo group compared to two cases in the ribaxamase treatment group. Patients receiving ribaxamase achieved a 71.4% relative risk reduction ( $p$ -value=0.045) in CDI rates compared to patients receiving placebo. Adverse events reported during this trial were comparable between treatment and placebo arms. Synthetic Biologics is in the process of analyzing data from several exploratory endpoints that were designed to evaluate ribaxamase's ability to protect the gut microbiome from colonization by opportunistic bacteria such as *C. difficile* and other antibiotic-resistant pathogens. Preliminary analysis of the data demonstrated a significant reduction in new colonization by vancomycin-resistant enterococci (VRE) for patients receiving ribaxamase compared to placebo ( $p$ -value=0.0002). With agreement from the FDA, the study included a secondary endpoint to assess ribaxamase's capacity to decrease the incidence of antibiotic-associated diarrhea from all causes. Preliminary analysis of the data suggested a trend towards such a reduction ( $p$ -value=0.13), which was due, for the most part, to the reduction of CDI.

### *Rebiotix (private)*

Rebiotix Inc. is a biotechnology company aimed at developing treatments for challenging gastrointestinal diseases by harnessing the power of the human microbiome. Rebiotix' Microbiota Restoration Therapy (MRT) is the drug platform for delivering healthy, live, human-derived microbes into a sick patient's intestinal tract to treat disease and it has potential to impact clinical



practice by treating disease with a category of drugs. Rebiotix' products include: RBX2660, indicated for recurrent *Clostridium difficile* (*C. diff.*) infection; RBX7455, indicated for oral *C. diff.* Prevention; RBX8225, indicated for inflammatory bowel disease/ulcerative colitis; RBX2477, indicated for hepatic encephalopathy; and RBX6376, indicated for multi-drug resistant organisms. Last October, the company presented data from the Phase IIb PUNCH CD trial in the prevention of recurrent CDI. A total of 107 patients (median age 63, range: 18-92 years; 59.8% female) at 21 centers in the U.S. and Canada received at least 1 dose of RBX2660 with an overall success rate of 88.8% (95/107). Of these patients, 4.2% (4/95) developed a new episode of CDI confirmed by a positive test > 8 weeks after the last RBX2660 treatment. Beginning of 2017 a first patient has been treated in a Phase I study of RBX7455 for the prevention of recurrent CDI. RBX7455 is a lyophilized non-frozen oral capsule formulation of Rebiotix's Microbiota Restoration Therapy (MRT). product frozen or refrigerated. This prospective, single center, two-arm Phase 1 study is a proof of concept dosing study of RBX7455 for the prevention of recurrent CDI.

### *Seres Therapeutics (MCRB)*

Seres Therapeutics is a microbiome therapeutics platform company developing a novel class of biological drugs that are designed to treat disease by restoring the function of a dysbiotic microbiome, where the natural state of bacterial diversity and function is imbalanced. Seres' program SER-109 continues to be evaluated in a Phase II study in multiply recurrent *CDI*. Seres' second clinical candidate, SER-287, is being evaluated in a Phase Ib study in patients with mild-to-moderate ulcerative colitis (UC). Seres is also developing SER-262, the first ever synthetic microbiome therapeutic candidate, in a Phase 1b study in patients with primary CDI. The Phase II study enrolled 89 subjects in a randomized, double-blind, placebo-controlled 24-week study conducted to evaluate the safety and efficacy of SER-109 in patients with multiply recurrent CDI. Interim, eight-week, primary endpoint results demonstrated that the relative risk of CDI recurrence for the placebo population, compared to the SER-109 population, was not statistically significant. All patients from the SER-109 Phase 2II have now completed their 24-week end of study visit, and



full study clinical results are expected in early 2017. The Company also continues to obtain results from the SER-109 Phase 2 open label extension study. Seres intends to complete its full SER-109 study analyses and then discuss plans for further SER-109 clinical development with the US FDA.

### *Summit Therapeutics (SUMM.L, SMMT)*

Summit Therapeutics is an international biopharmaceutical company that is developing novel medicines for indications for which there are no existing or only inadequate therapies. Summit was founded in 2003 as a spin-out of the University of Oxford. Summit's lead CDI product candidate is ridinilazole (formerly SMT19969), an orally administered small molecule antibiotic. The company reported positive top-line results from a Phase II clinical trial of ridinilazole in November 2015 and reported additional data in April 2016. Ridinilazole is designed to selectively target *Clostridium difficile* bacteria without causing collateral damage to the gut flora and thereby reduce CDI recurrence rates, which is the key clinical issue in this disease. Data from the CoDiFy Phase II trial demonstrated statistical superiority of ridinilazole over vancomycin in sustained clinical response (SCR) in the treatment of CDI. SCR was defined as clinical cure at the end of treatment and no recurrence of CDI within 30 days of the end of treatment. The statistical superiority in SCR with ridinilazole was driven by a large numerical reduction in recurrent disease compared with vancomycin. Additionally, ridinilazole was generally well tolerated and the overall adverse event profiles of ridinilazole and vancomycin were comparable. The FDA has designated ridinilazole as a qualified infectious disease product, or QIDP, and the FDA granted ridinilazole fast track status in July 2015. The company is now preparing ridinilazole for Phase III clinical trials.

### *DaVolterra (private)*

DaVolterra is a privately-held biotechnology company, headquartered in Paris, France. The company was created in 2000 by Professor Antoine Andremont whose research is dedicated to understanding the impact of antibiotics on the intestinal flora. Its lead product DAV132 is a novel



medical device to be combined with antibiotic treatments, especially fluoroquinolones and cephalosporins, to prevent the occurrence and recurrence of *CDI*. DAV132 is a non specific adsorbent which can irreversibly capture antibiotics in the late ileum, caecum and colon before they could alter significantly the microbiota. It is encapsulated in a specific drug delivery system (specific coating) patented by Da Volterra that allows a precise delivery to the lower gastrointestinal tract in order to avoid all interactions with drug absorption that occurs in the small intestine. Three clinical trials of DAV132 were already performed successfully. The next trial in patients at risk of *C.difficile* is being prepared.





*Analyst: Marcel Wijma MSc*

*Marcel Wijma, Chief Research Officer and managing partner, has a longstanding history in financial biotech research. After selling Van Leeuwenhoek Research (VLR) to SNS Securities in 2006, he established an award winning analyst team in biotech/life sciences at SNS Securities. In 2009, Marcel was awarded by Financial Times/Starmine as being one of the Top-3 biotech analysts in Europe. Later that year, Marcel purchased VLR from SNS Securities after which the company was reconstituted. At VLR, he leads the professional VLR research organisation, which is augmented by selected external financial researchers with a specialisation in Life Sciences. Mr. Wijma has a Masters degree in Financial Economics from Erasmus University in Rotterdam.*

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