### Immur@n

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www.immuron.com

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The Manager The Company Announcement Office Australian Stock Exchange Sydney NSW

Dear Sir

Influenza Commercialisation Program.

Following an announcement made to the ASX on 3 August 2009 in respect of the positive results from Immuron's influenza research, the Company announces that it is commencing a drug development program for its prospective influenza treatment product.

For the information of shareholders, I attach a copy of the scientific presentation that will be made to interested parties over the coming weeks.

This presentation summarises the positive research results obtained from the various animal trials conducted for the treatment and prevention of influenza infections, and outlines strategies for further development of this possible new approach to preventing and treating influenza in humans.

Yours faithfully

Ambapman

Professor Colin Chapman Executive Chairman



# Treatment product

www.immuron.com August 2009

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### **Forward Looking Statements**

This presentation contains forward-looking statements which are subject to risks and uncertainties. These statements include those regarding the therapeutic and commercial potential of Immuron technologies and products in development and commercialization.

Any statement describing the company goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an "at-risk statement". Such statements involve known and unknown risks and important factors that may cause the actual results, performance or achievements to be different from the statements in this presentation.

Actual results could differ materially depending on a number of factors including, but are not limited to, results of studies and trials, the timing and effects of regulatory actions, ability to penetrate markets, the strength of competition and the effectiveness of patent protection.



### **Executive Summary**

- Immuron is a publicly listed company based in Melbourne, Australia.
- Immuron has developed a novel approach to influenza treatment and prevention.
- The product is based on dairy derived antibodies that neutralise virus and can be given orally or as a spray.
- Proof in principle in both treatment and prevention roles has been shown successfully in accepted animal (mouse) models of human influenza using a mouse adapted H1N1 influenza virus.
- Disease could be treated stopped in progress or infection prevented for up to 7 days
- The concept has been developed with the close involvement of Professor Lorena Brown and University of Melbourne, Microbiology and Immunology Department.
- Commonwealth funding has been approved for further development of the concept enabling use of current human influenza strains and the swine flu strain.
- Human clinical trials are expected to be conducted in 2010.
- A patent is lodged and pending on the technology.
- The product is expected to be an OTC product with the potential to commercialise / partner with a larger company with OTC interests.

### Key Results of the Influenza Program

- 1) Production of influenza virus neutralising preparations suitable for large scale production
- 2) Demonstraton of activity of antibodies *in vivo*
- 3) Successful **Treatment** of existing infections in non-lethal and lethal mouse models (slides 14-15 and slides 16-17)
- 4) Successful **Prevention** from infection in mouse models (slides 18-19)
- 5) Production of neutralising material to current 'conventional' strains





### **Board and Management**

- **Prof. Colin Chapman**, BPharm, BVSc (Hons) PhD FPS, Executive Chairman Professor of Pharmacy at Monash University
- **Prof. Roy Robins-Browne**, MB, BCh, PhD, FRCPA, FRCPath, FASM, Professor Microbiology and Immunology, University of Melbourne, Nonexecutive Director
- **Prof. Yaron Ilan**, M.D. Director, Dept of Medicine Hadassah University Hospital (to be appointed Medical Director of Immuron).
- **Dr Grant Rawlin**, BVSc, BSc(Vet)(Hons), GM and VP Research & Development,
- Mr Simon Salka, Non-executive Director
- Mr Arie Nudel, Non-executive Director.
- Mr Graeme Stevens, Chief Financial Officer / Company Secretary



### The Immuron Influenza Project

#### • Who is Immuron?

- ASX listed company since 1999 based in Melbourne.
- Core expertise around production of large scale polyclonal antibodies in hyperimmune colostrum for treatment of diseases.
- Why we work with University of Melbourne, Microbiology and Immunology on Influenza?
  - The Department has a long history in influenza research.
  - Professor Lorena Brown is a world recognised expert in influenza research.
  - The Influenza laboratory is well equipped and staffed with a team who over the past years have enthusiastically worked with us to develop the Immuron concept and now have proved that the principle works.



### Immuron's Therapeutic Antibody Platform

- Proprietary vaccines generate highly targeted antibody levels in dairy cattle.
- Antibodies are processed for oral administration under dairy GMP certification suitable for human use.
- Clinical studies and development programs are at leading universities and hospitals.
- High safety profile, Self-affirmed GRAS (Generally Regarded As Safe), low manufacturing cost.
- Rapid commercialization cycle.
- Commercialised one product (Travelan) for prevention of Travellers Diarrhoea being distributed throughout Australia, South Africa and USA.

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## Immuron works with Polyclonal antibodies. What are they?

- Polyclonal Antibodies are more general than monoclones.
  Polyclonals attach to many parts of their designated target eg bacteria, virus etc. Monoclonals only bind to one part of the designated target.
- Polyclonal antibodies are preferable in the Influenza project as they are likely to react with different sub types of influenza as the virus evolves.
- Monoclones are normally developed by Pharmaceutical companies for injection and are very expensive.
- Immuron polyclones are 1000 times cheaper to produce and can be used orally for nutraceuticals and pharmaceuticals in large doses.

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## Commercial pathway for Influenza products

- Immuron is already discussing the technology with several commercial parties with a view to licensing or partnering.
- The main parties appear to be attracted to the OTC compatibility of the product which differentiates it from other approaches on the market.
- Commonwealth funding will enable the technology to be developed closer to commercialisation thus increasing its value in current and future negotiations
- An offer of further investigations in humans has been received, this is being considered in the light of other commercialisation options and their needs for different endpoints.





## Production of influenza virus neutralising preparations

- Best results have been developed using a killed, adjuvanted disrupted virus vaccine to induce antibodies in the cattle
- The results in the animal models have been with PR8 (H1N1) a commonly used laboratory mouse adapted human virus.
- Influenza vaccinology concepts are well developed but Immuron has a significant advantage as it can use more effective veterinary-derived adjuvants.
- The results showed that the Immuron vaccine created high yield and activity antibodies in the cattle that could be harvested and processed with its high volume compatible manufacturing technologies





### Do the preparations neutralise influenza virus?

- Polyclonal antibody preparations were successfully induced in the cattle and showed strong *in vitro* reaction against the target virus (PR-8)
- **Table 1** shows Hemagglutination inhibition (HI), ELISA antibodybinding titres and virus neutralizing (VN) activity of Immuron anti-PR8 IgG and F(ab')<sub>2</sub> antibody fragment preparations (Red lines of Table 1)
- The activity of the test preparations were much stronger in all laboratory measures of activity when compared to negative control preparation (from unvaccinated cattle). Results for negative control preparations are shown in black lines of Figure 1.



## Figure 1: *in vitro* measures of reaction against influenza (PR8) virus

Purified Ab sample	HI titre	ELISA titre (log <sub>10</sub> )	VN titre
Anti-PR8 IgG	1280	4.8	79,000
Anti-PR8 F(ab') <sub>2</sub>	2560	4.0	400,000
Non-immune IgG control	<10	1.2	<10
Non-immune F(ab') <sub>2</sub> control	<10	1.2	<10

Note:

Hemagglutination inhibition assay performed with chicken red blood cells. HI titres are expressed as the reciprocal of the mean antibody dilution inhibiting 3 out of 4 HA units of virus.

Dilutions of Ab we tested in ELISA for binding to split PR8 adsorbed to wells of polyvinyl plates. Antibody titres are expressed as the reciprocal of the dilution giving an optical density of 0.2.

Virus neutralization activity was measured by mixing dilutions of Ab with a standard amount of virus and, after incubation for 45 mins, the mixtures were inoculated onto MDCK cell monolayers and overlaid with agarose. Three days later, plaque formation was assessed. Virus neutralization activity is expressed as the reciprocal of the Ab dilution at which 50% of 50 plaque forming units were neutralized.

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### Successful **Treatment** of existing infections in a non-lethal mouse models

- Mice were infected with a sub-lethal dose of PR8 influenza virus to establish a total respiratory tract infection.
- Mice were then treated intranasally with various doses of immune (active) or non-immune (control) antibodies.
- 5 days after infection, the amount of virus present in the lungs was determined by plaque assay.

#### RESULT

- The assays (Figure 2) showed that there was significantly less virus in the lungs of treated mice compared to control mice and at higher doses, virus was below detectable limits.
- This demonstrates in many animals, the treatment halted the existing infection rather than to merely delay its clinical development .







Virus levels in the lungs of previously infected mice sampled 5 days after treatment with Immuron preparations and negative controls (PBS is Phosphate Buffered Saline negative control)



### Successful **Treatment** of existing infections in a lethal mouse model

- Groups of 5 mice were infected with a lethal dose of PR8 as a total respiratory tract infection and 24 hrs later the mice were treated intranasally with 1mg of immune or non-immune IgG or F (ab')<sub>2</sub>.
- The mice were monitored daily for clinical signs and their weights determined over a 16-day period (Figure 3a). Mice were culled at the humane endpoint and a survival curve plotted (Figure 3b).

#### RESULT

- The course of lethal disease was stopped in mice treated with the active preparations, while the disease proceeded in all groups treated with inactive preparations
- There were no significant clinical signs apparent in the treated mice (as indicated by no significant weight loss in these groups).

### Figure 3: Successful Treatment of existing infections in a lethal mouse model



Figure 3

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## Successful **Prevention** from infection in mouse models

- Groups of 5 mice were treated intranasally with 1mg of immune or non-immune IgG or immune F(ab)'2 fragments
- 48 or 72 hours or 7 days later mice were infected with a lethal dose of PR8 confined to the upper respiratory tract.
- On day 1 post infection, viral loads in the nasal turbinates were determined by plaque assay as a measure of infection.

#### RESULT

- Mice were 100% protected from infection with virulent influenza virus at 3 days (see Figure 4).
- 80% of mice were protected for 7 days

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## Figure 4: Successful **Prevention** from infection in mouse models



The two active treatment arms (A and B) showed full protection from infection after 3 days



## Production of neutralising preparation to current 'conventional' strains

- Antibody material has been produced against current (conventional) strains with similar high neutralisation rates (particularly to H1N1 epitopes) as was seen in against the laboratory adapted H1N1 PR8 strain.
- This material will be used in the funded University of Melbourne work in the ferret model.
- Immuron's current H1N1 reactive formulations are being tested for any cross reactivity to the recent Swine flu (H1N1).





## Immuron Influenza Program next 12 months

- Commonwealth ARC linkage grant awarded.
- Ferret trials with current human influenza isolates
- Dosage studies and delivery route studies to compare oral and nasal delivery (suckable tablets and sprays)
- Cross-neutralisation studies against new 'swine flu' virus.
- Human Phase 2 trial negotiations
- Commercial partnering negotiations





## Thank you and feel free to contact:• Prof. Colin Chapman,

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o Dr Grant Rawlin,

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