



Therapies for major infectious diseases and related cancers

Company Update 2013 : Shaw Stockbroking 23 July 2013

www.biodiem.com
(ASX:BDM)

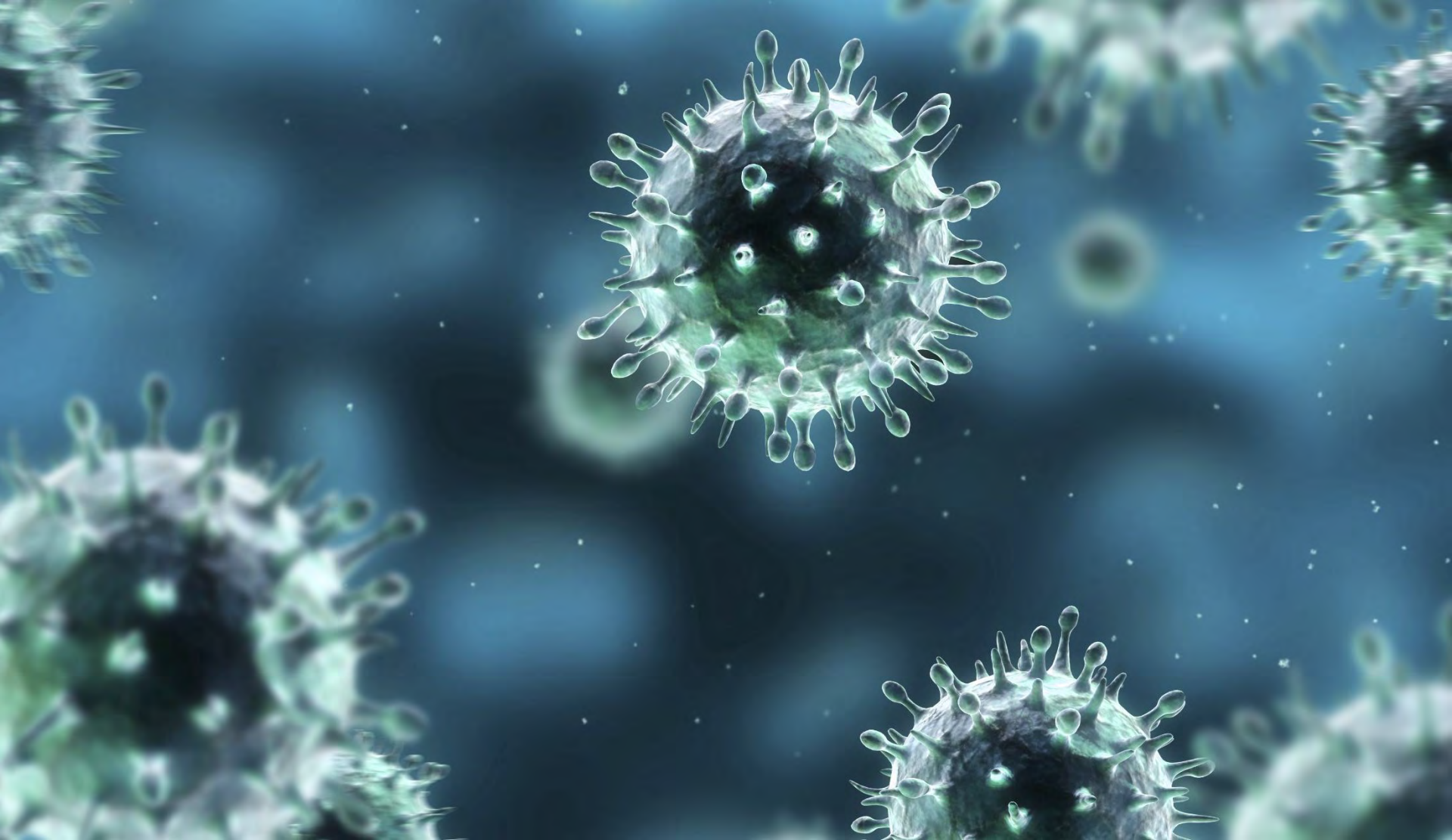
Ms Julie Phillips

Chief Executive Officer

BioDiem Ltd

(ASX:BDM)

BioDiem Challenges



BioDiem Challenges



Increasing resistance

To antibiotics – major concern healthcare systems worldwide



Hard to treat

Fungal infections, affecting vulnerable patients



No vaccines available

For worldwide diseases eg. hep B, C and D



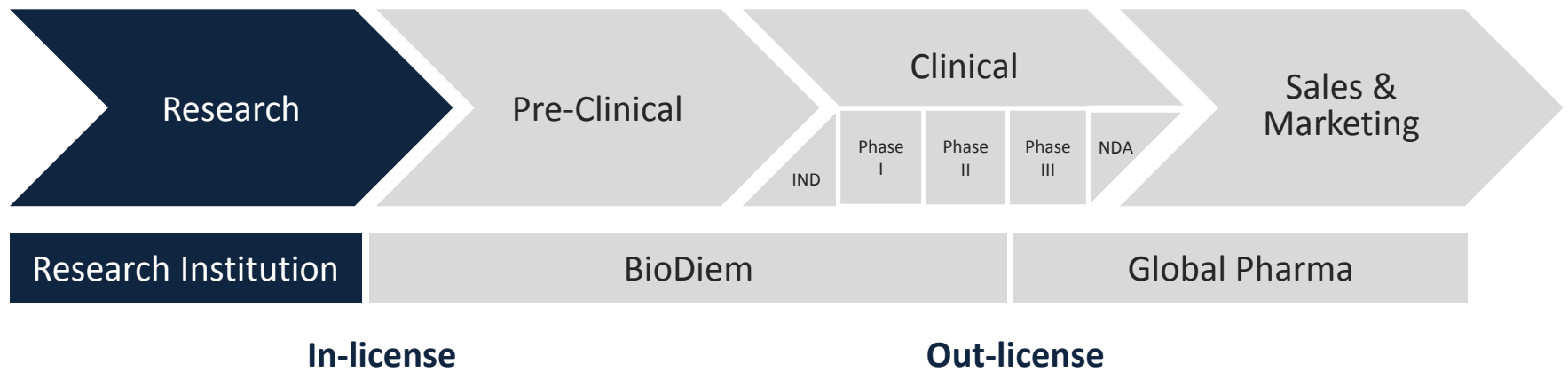
Product pipelines diminish

Large Pharma focus on innovation, as product pipelines diminish > acquisition opportunities

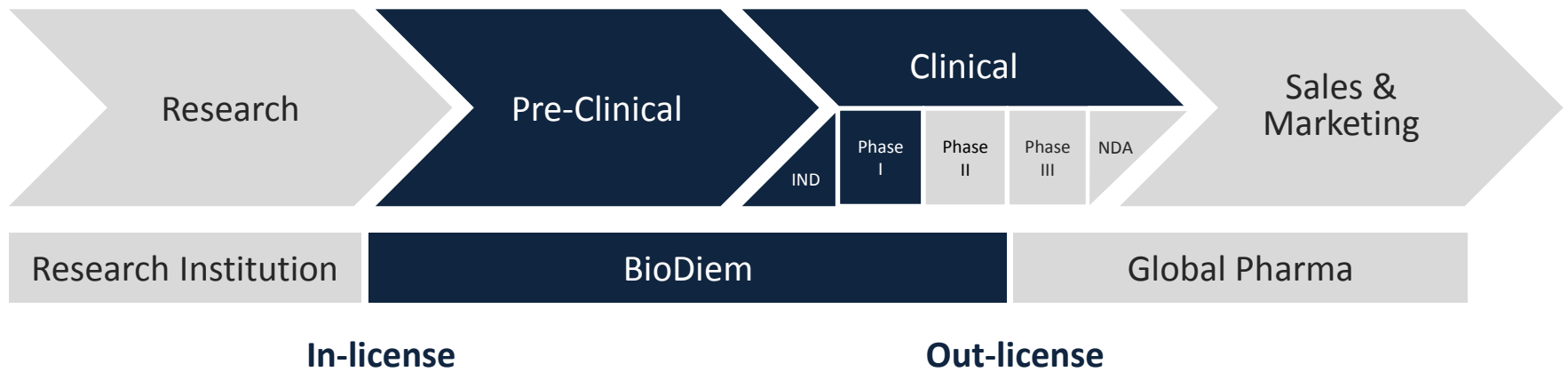
BioDiem Company Focus



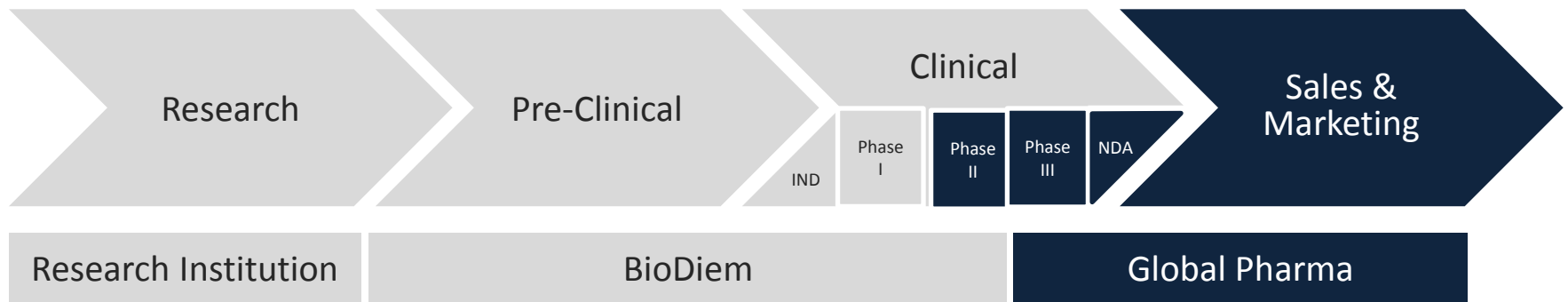
BioDiem Business Model



BioDiem Business Model



BioDiem Business Model



In-license

Out-license



Phase I trials

Testing the drug on healthy volunteers



Phase II trials

Testing the drug on a small number of patients with the disease



Phase III trials

Testing the drug on hundreds/thousands of patients with the disease

BioDiem Three core development programs



Target



Core Technology

Influenza vaccines (seasonal and pandemic)



LAIV vaccine – licensed in multiple countries

Vaccine development platforms
Hepatitis B/D, nasopharyngeal carcinoma, TB



SAVINE technology, LAIV viral vector, flavi and hepatitis virus technologies for novel therapeutic vaccines

Infectious disease therapies
Fungal disease: difficult to treat
Bacterial disease: MRSA
Parasites: Schistosomiasis



BDM-I antimicrobial compound

BioDiem Influenza Vaccines



Live Attenuated Influenza Virus: LAIV

Advantages



Needle-free nasal delivery

No trained personnel and blood/sharps precautions unnecessary



Extensive clinical and market experience > 100m doses

In Russia efficacy and safety in >500,000 adults/140,000 children



Broader immune response

Than seen with inactivated influenza vaccines



High yields

In egg-based or cell-based production (with no reliance on eggs)



No adjuvant required

Live Attenuated Influenza Virus: LAIV

Product	Disease Targets	Current Partners	Development Status
LAIV (Influenza)	Influenza – Seasonal & Pandemic	WHO SII (India) BCHT (China) IEM (Russia)	Marketed with license revenues \$A1.3m FY2012 Phase II (cell-based technology) Seeking growth & out-licensing in more markets
	Avian (Bird) Flu	IEM/WHO	Clinical trials completed in Thailand and Russia

BioDiem Vaccine development platforms



BioDiem LAIV Vector & SAVINE

Opportunity to target multiple infectious diseases and related cancers



LAIV Vector
(Vaccine delivery)



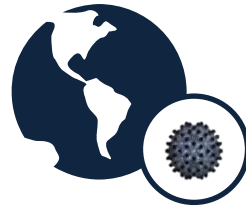
SAVINE
(Custom vaccines)

Disease Targets	Vaccine development	Nasopharyngeal carcinoma (NPC), tuberculosis (TB)
Current Partners	VIVALIS	In-house
Development Status	First stage of development project completed	Seeking partner for more advanced data in animals

BioDiem Hepatitis Vaccine (therapeutic)



Hepatitis D



Hepatitis B



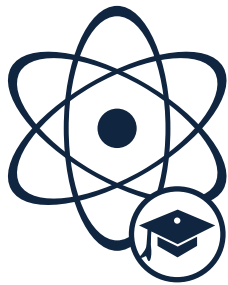
Hepatitis C

Rights licensed from the University of Canberra

R&D program underway

BioDiem Dengue Fever vaccine (therapeutic)

Rights licensed from the Australian National University



Technology
licensed



Vaccine effect
demonstration



Publication
pending



Extension into other
mosquito-borne
disease targets

BioDiem Infectious disease therapies



BioDiem BDM-I antimicrobial disease targets

BDM-I currently in development as treatment against

- 'superbugs' such as antibiotic-resistant bacteria incl. TB, and others
- **hard-to-treat fungal** infections

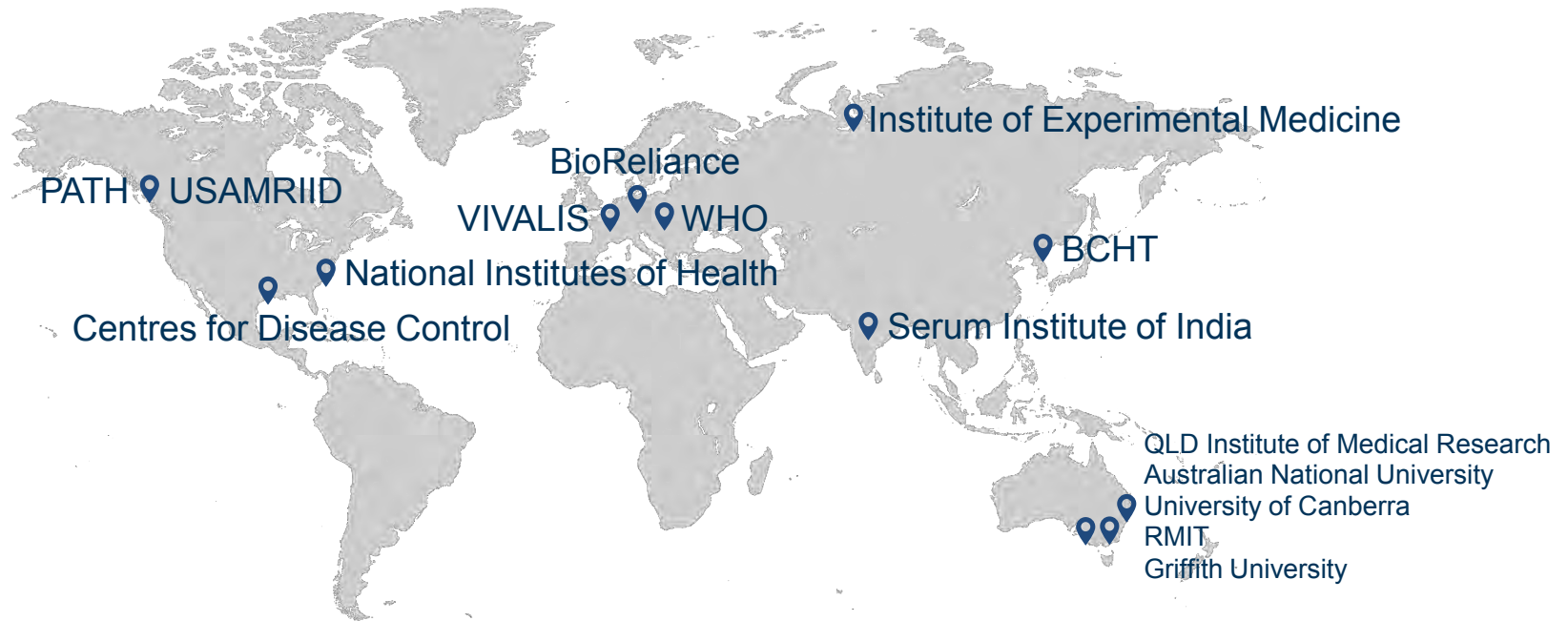
Product	Disease Targets	Current Partners	Development Status
BDM-I (Antimicrobial)	Bacterial infections (tuberculosis, others)	US government backed research institutions	Entered <i>in vivo</i> testing in 2013
	Fungal infections	US government backed research institutions	Entered <i>in vivo</i> testing in 2013
	Parasitic diseases (schistosomiasis, others)	QIMR program	Entered <i>in vivo</i> testing in 2013



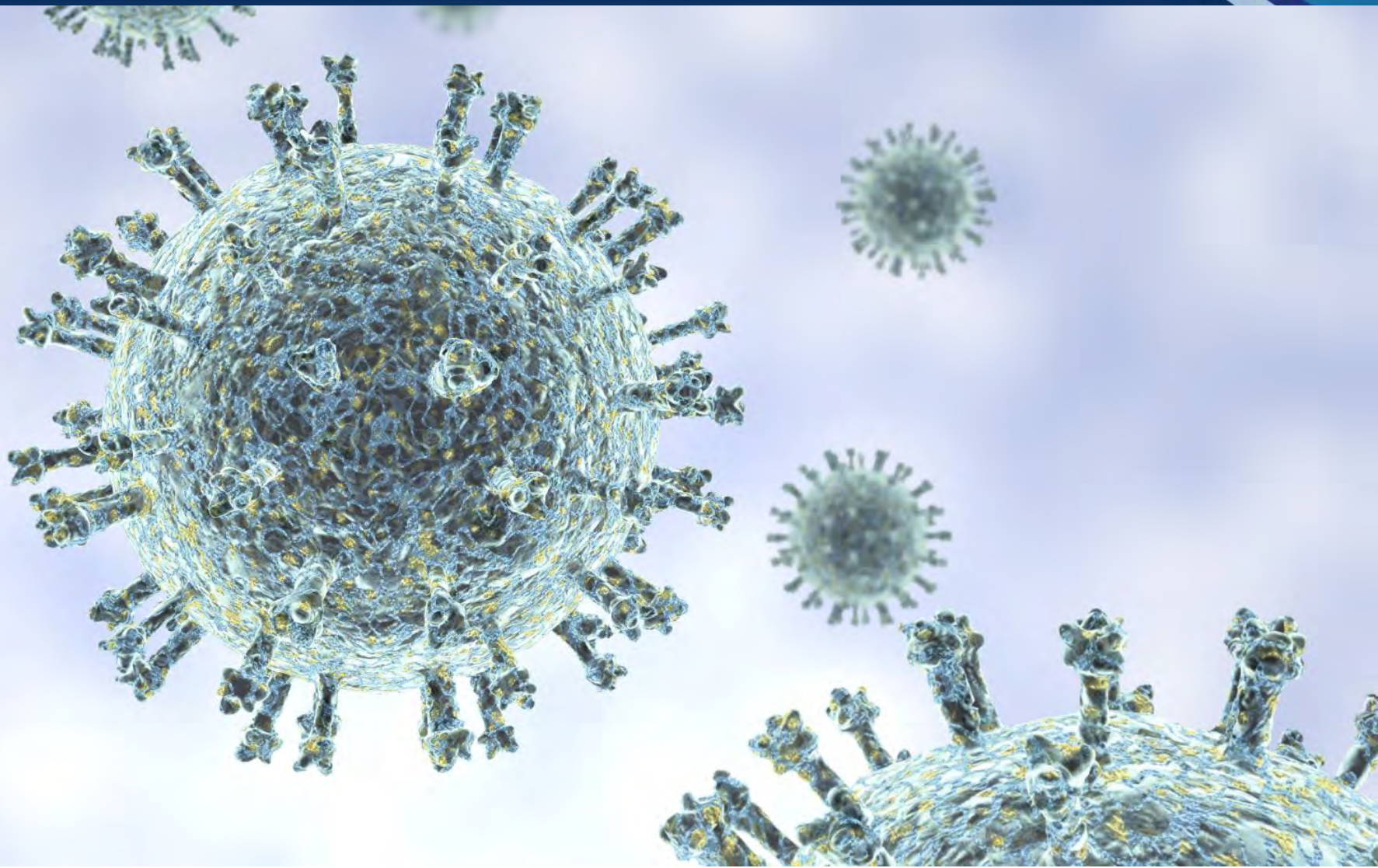
Expanding Global Partnerships and Alliances



Global partnering & commercialisation network



BioDiem Current Achievements



BioDiem License & Pipeline Portfolio

Vaccine Development Pipeline

	Research	Preclinical	Phase I	Phase II	Phase III	Marketed
Influenza vaccines (Seasonal & Pandemic)	Cell based production					
	Egg based production					
	Licensed to World Health Organisation for public market in Developing Countries Licensed to Serum Institute of India and Changchun BCHO Biotech Co. for certain Developing Country private markets					
LAIV Viral Vector platform						
Hepatitis D PLATFORM (Hepatitis D/Hepatitis B therapeutic vaccine)						
Flavivirus PLATFORM (Dengue fever, West Nile, Murray River encephalitis)						
SAVINE antigen technology (Tuberculosis, NPC)						

BioDiem Pipeline Portfolio

BDM-I Development Pipeline

	Research	Preclinical	Phase I	Phase II	Phase III	On market
Bacterial targets (Biological warfare agents, MSRA, tuberculosis, other)	➔					
Fungal targets (Difficult to treat fungi, incl. Scedosporium, Pneumocystis & Candida spp.)	➔					
Parasitic targets (schistosomiasis, other)	➔					

BioDiem Partnership Portfolio

Expanding Global Partnership Network



WHO



National Institutes
of Health

National Institutes
of Health (USA)



PATH (Program for
Appropriate Technology
in Health)



Centres for Disease Control
and Prevention (US)



Changchun BCHT
Biotech Co, China
(BCHT)

Vivalis

VIVALIS
(now Valneva)



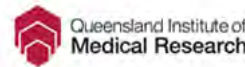
Serum Institute of
India (SII)



IEM
(St Petersburg,
Russia)



US Army Research Institute of
Infectious Diseases (USAMRIID)



Queensland Institute of
Medical research (QIMR)

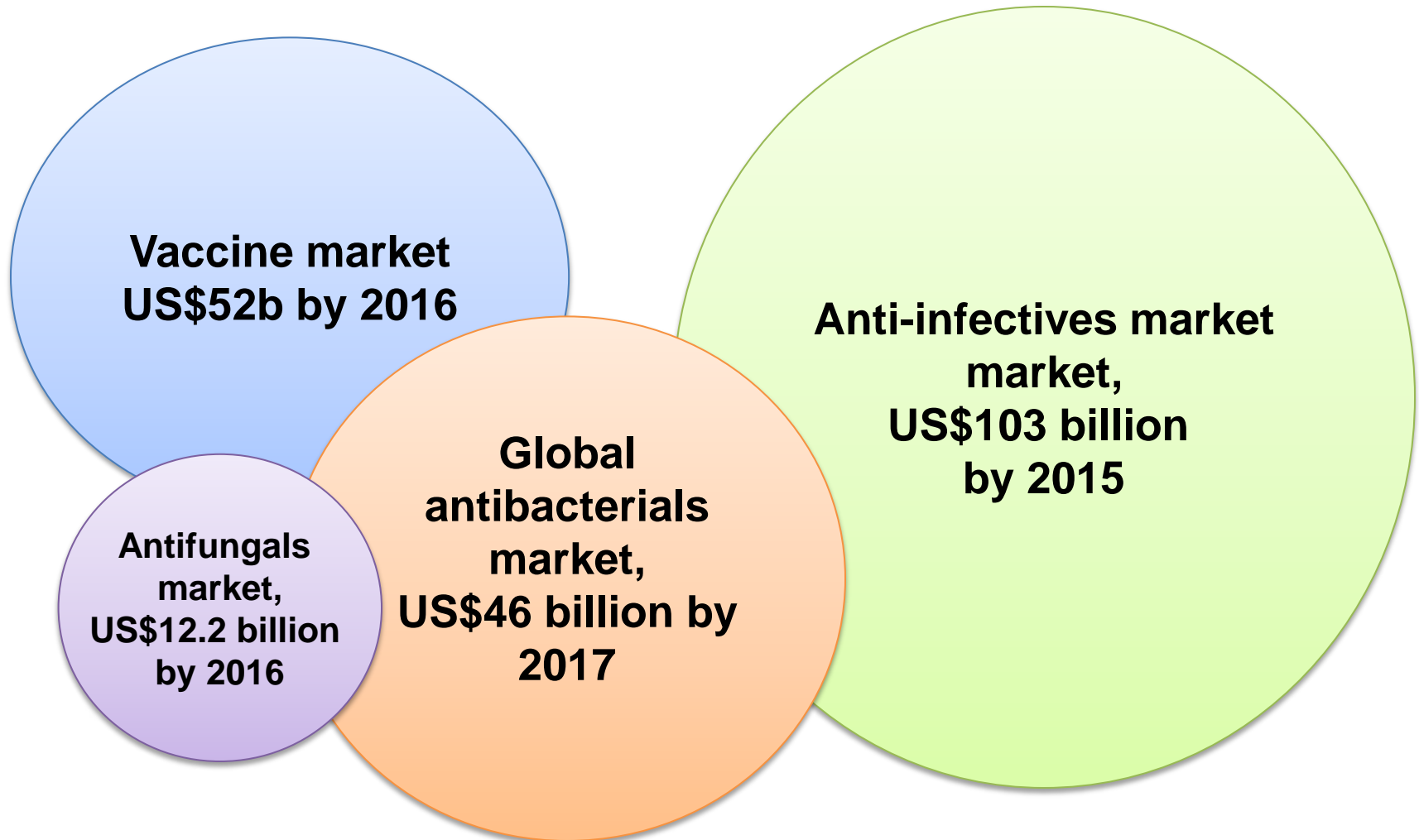


University of
Canberra, Australia

BioDiem Future Investment Opportunity



BioDiem Market Size Potential

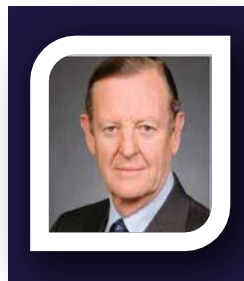


BioDiem BioDiem Limited

As at 30 May 2013 (\$AUD)

Market Cap	\$4.26 M
52 week range	\$0.025 – \$0.079
Cash as of 31-03-13	\$1.819M
Shares	142,105,934
Shareholders	919
Listed Options	24,638, 574

Hugh Morgan AC



Chairman

Julie Phillips



CEO

Prof Larisa Rudenko



Non-executive
Director

Prof Arthur Li



Non-executive
Director

Don Brooks



Non-executive
Director

BioDiem Next 12 months



Additional
license revenues



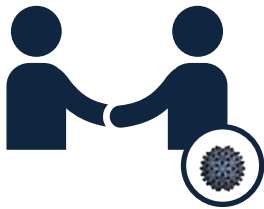
Clinical
trial results



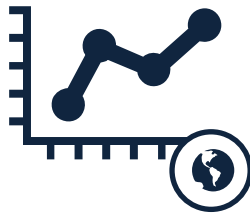
Vector program



Results from
expanded studies



Hepatitis
vaccine progress



Expand sales and
use of LAIV in new
territories



BDM-I testing in
animal models



Completion of BDM-E
out-licensing or sale

Prof Ian Ramshaw

Director Centre for Research into Therapeutic
Solutions

Faculty Of Education Science Technology and
Mathematics

University of Canberra

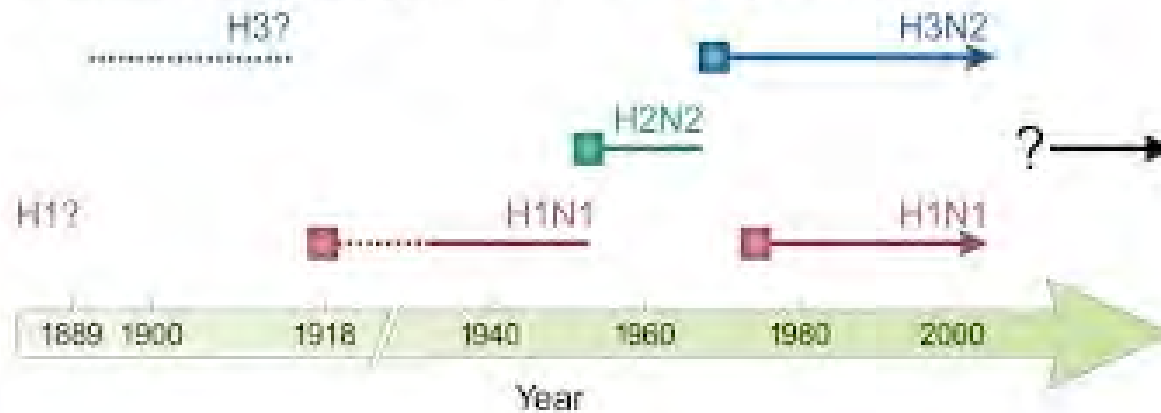
Program Overview



- ☐ Influenza vaccine (LAIV)
- ☐ Hepatitis vaccine (therapeutic)
- ☐ Antimicrobial (BDM-I)

Influenza vaccine- LAIV

Influenza A virus subtypes in the human population



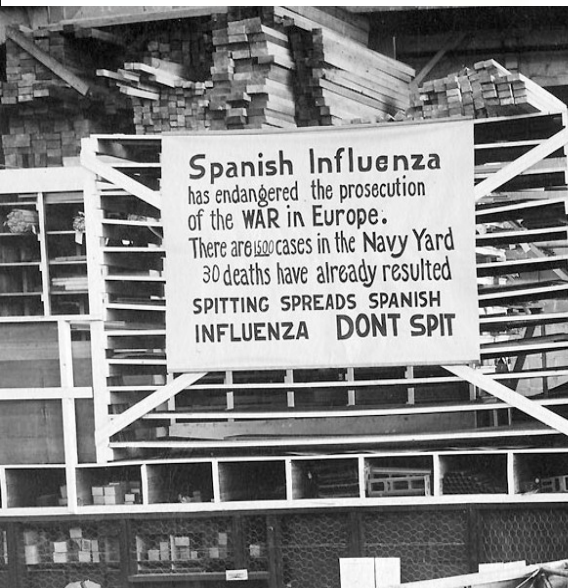
Pandemics Death Toll Since 1900

1918-1919	
U.S....	675,000+
Worldwide...	50,000,000+

This as per the CDC.

1957-1958	
U.S....	70,000+
Worldwide...	1-2,000,000

1968-1969	
U.S....	34,000+
Worldwide...	700,000+





BioDiem's flu vaccine

Live Attenuated Influenza Virus: LAIV

Advantages



Needle-free nasal delivery

No trained personnel and blood/sharps precautions unnecessary



Extensive clinical and market experience > 100m doses

In Russia efficacy and safety in >500,000 adults/140,000 children



Broader immune response

Than seen with inactivated influenza vaccines



High yields

In egg-based or cell-based production (with no reliance on eggs)



No adjuvant required

“A live attenuated influenza virus has been available since 1967. This is administered by nasal spray and is therefore easier to use in children, whereas the inactivated vaccine is administered mainly by intramuscular or subcutaneous injection. The live attenuated vaccine has also been found to stimulate a broader immune response against new viral strains resulting from antigenic drift, than the inactivated vaccine.”

WHO, UNICEF, World Bank. “State of the world’s vaccines and immunization” (3rd edition), Geneva, World Health Organisation, 2009 (p. 119)

(see also Plotkin S, Orenstein W, Offit P. Vaccines. 5th ed. Saunders, 2008)

Production methods



Traditional egg method



Mammalian cell method

BioDiem's LAIV provides broad protection against “drifted” variants of influenza.

MAJOR ARTICLE

Comparative Immunogenicity and Cross-Clade Protective Efficacy of Mammalian Cell-Grown Inactivated and Live Attenuated H5N1 Reassortant Vaccines in Ferrets

Kortney M. Gustin,¹ Taronna R. Maines,¹ Jessica A. Belser,¹ Neal van Hoeven,¹ Xuihua Lu,¹ Libo Dong,¹ Irina Isakova-Sivak,^{1,2} Li-Mei Chen,¹ J. Theo M. Voeten,³ Jacco G. M. Heldens,³ Han van den Bosch,³ Nancy J. Cox,¹ Terrence M. Tumpey,¹ Alexander I. Klimov,¹ Larisa Rudenko,² Ruben O. Donis,¹ and Jacqueline M. Katz¹

¹Influenza Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia;

²Department of Virology, Institute for Experimental Medicine, Russian Academy of Medical Science, St. Petersburg, Russia; and ³Department of Virological R&D Nobilon International BV, Boxmeer, The Netherlands



Hepatitis program

Approximately
1 in 12
persons worldwide,
or some
500 million
people, are living
with chronic viral
hepatitis

World
Hepatitis
Day
—
July 28th

Hepatitis program

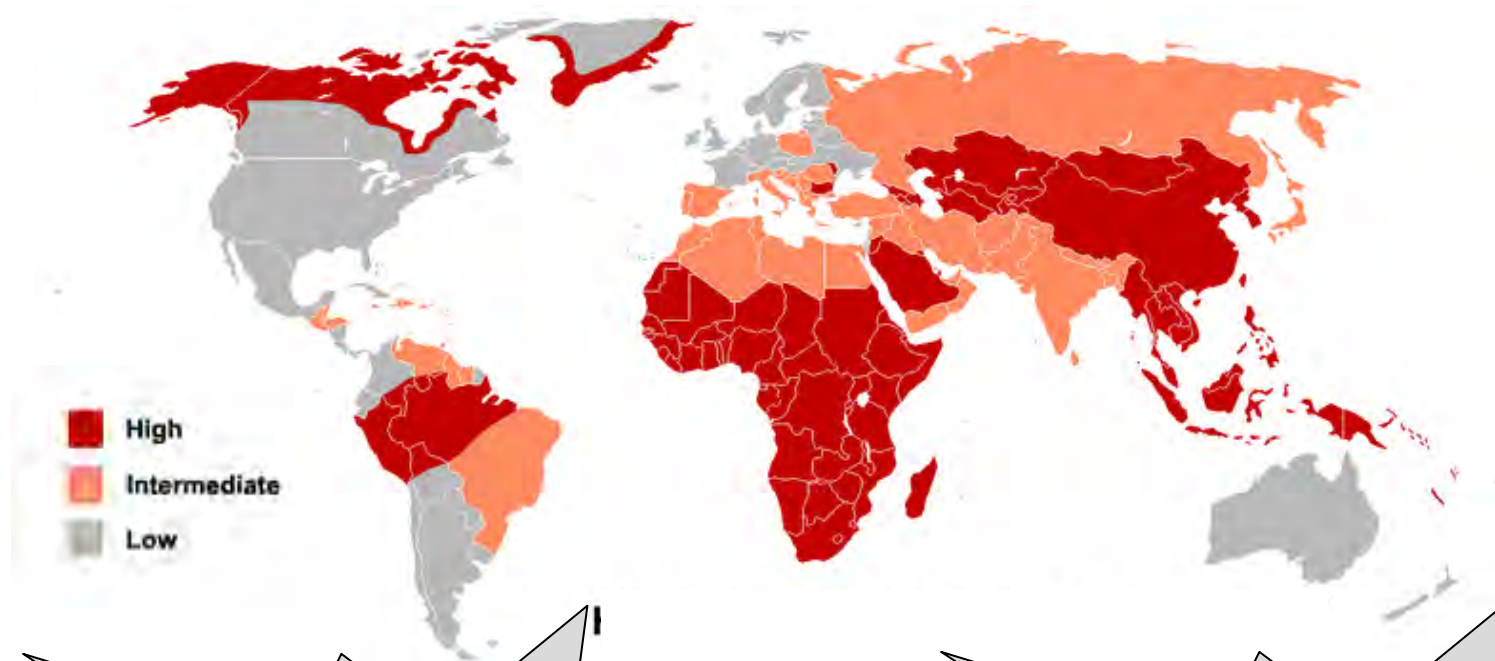
Aim:

- ☐ Generation of a new liver-specific gene delivery vehicle

Applications:

- ☐ Therapeutic vaccine against chronic **hepatitis B**
(targeted delivery of therapeutic interferon)
- ☐ Therapeutic vaccine against chronic **hepatitis C**
(targeted delivery of a therapeutic interferon)
- ☐ Delivery of therapeutics against liver cancer

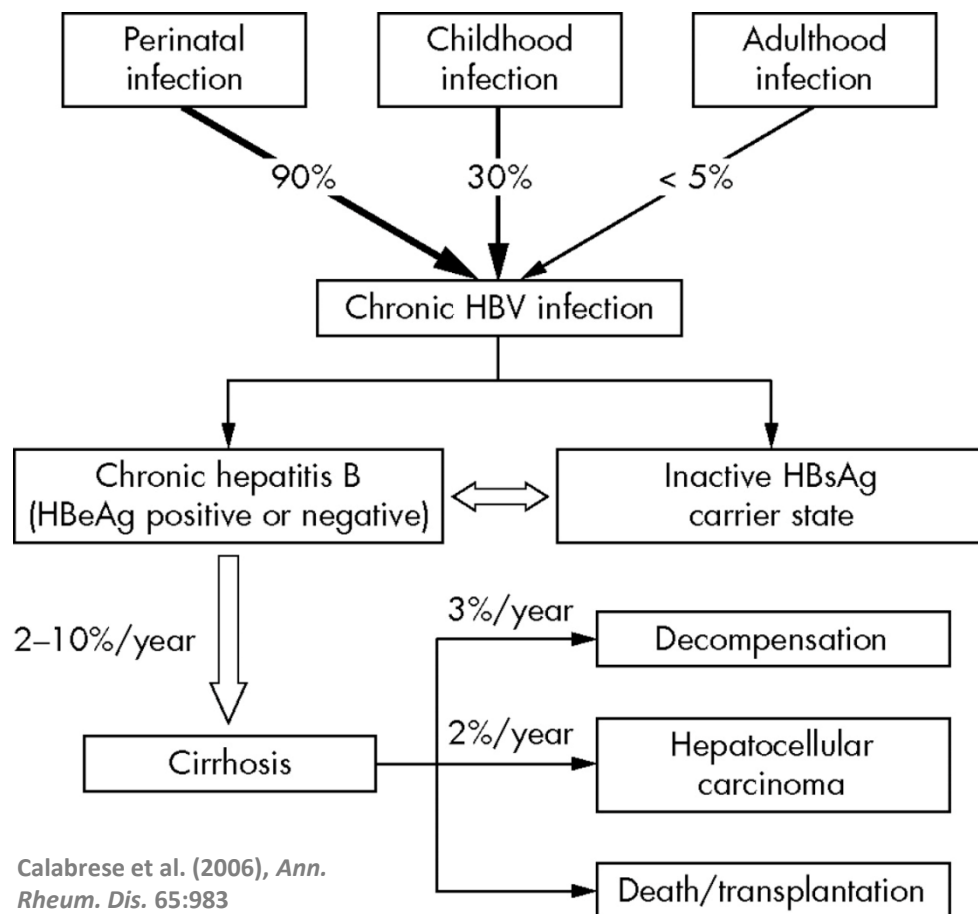
Distribution of HBV



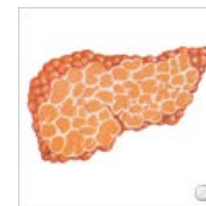
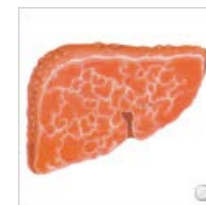
Worldwide **150 million** individuals are persistently infected with HCV

Worldwide **350 million** individuals are persistently infected with HBV

HBV Pathology



Calabrese et al. (2006), *Ann. Rheum. Dis.* 65:983

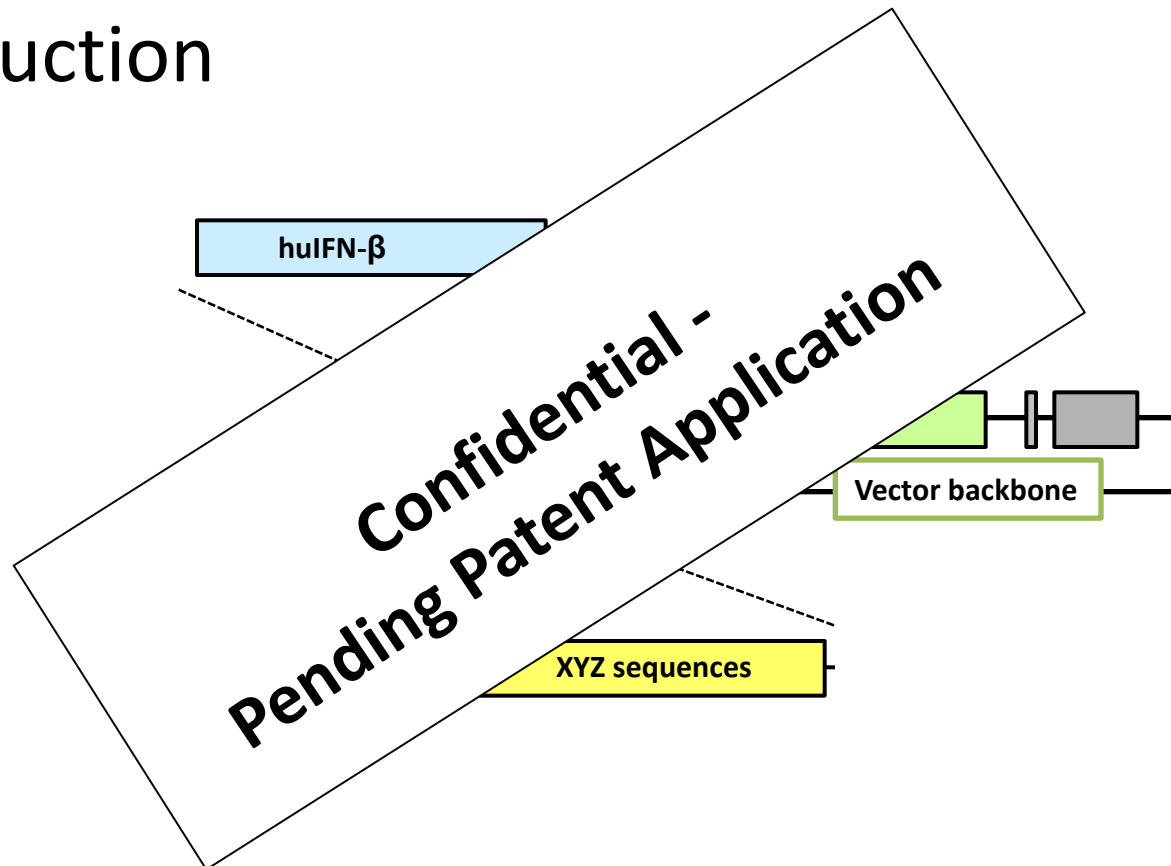


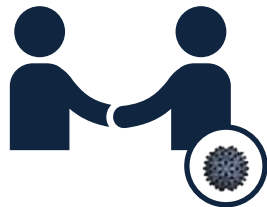
Current HBV Therapies

Table 1 Response rates (%) to approved therapies for HBeAg-positive and HBeAg-negative chronic hepatitis B							
Treatment response parameters	Approved therapies						
	Lamivudine	Adefovir dipivoxil	Entecavir	Telbivudine	Tenofovir disoproxil	PEG-IFN*	PEG-IFN plus lamivudine*
<i>HBeAg-positive patients at week 48 or 52</i>							
Histologic improvement [‡]	49–62	53–68	72	65	74	38	41
Undetectable HBV DNA	40–44	21	67	60	76	25	69
HBeAg seroconversion	16–21	12	21	22	21	27	24
HBsAg loss	<1	0	2	0	3	3	3
<i>HBeAg-positive patients during extended treatment[§]</i>							
Undetectable HBV DNA	NA	39(5.0)	94(5.0)	79(4.0)	77(4.0)	13 (4.5)	26 (4.5)
HBeAg seroconversion	47 (3.0)	48 (5.0)	41 (5.0)	42 (4.0)	31 (3.0)	37 (4.5)	36 (4.5)
HBsAg loss	0–3 (2.0–3.0)	2(5.0)	5 (2.0)	1 (2.0)	10 (4.0)	8 (4.5)	15 (4.5)
<i>HBeAg-negative patients at week 48 or 52</i>							
Histologic improvement [‡]	60–66	64–69	70	67	72	48	38
Undetectable HBV DNA	60–73	51	90	88	93	63	87
HBsAg loss	<1	NA	<1	<1	0	4	3
<i>HBeAg-negative patients during extended treatment[§]</i>							
Undetectable HBV DNA	6 (4.0)	67 (5.0)	NA	84(4.0)	86(3.0)	18 (4.0)	13 (4.0)
HBsAg loss	<1 (4.0)	5 (5.0)	NA	<1 (2.0)	0 (4.0)	8 (4.0)	8 (4.0)
Data obtained from several sources. ^{16–21,29–40,42,44–46,47,59} *Liver biopsy performed 24 weeks after stopping treatment. [‡] Histologic improvement defined as a >2-point decrease in the necroinflammatory score and no worsening of the fibrosis score. [§] The time point at which response was assessed in years is shown in brackets. Assessment performed off treatment. Abbreviations: HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; NA, not available.							

BioDiem New Liver-Specific Gene Delivery Vehicle

Construction

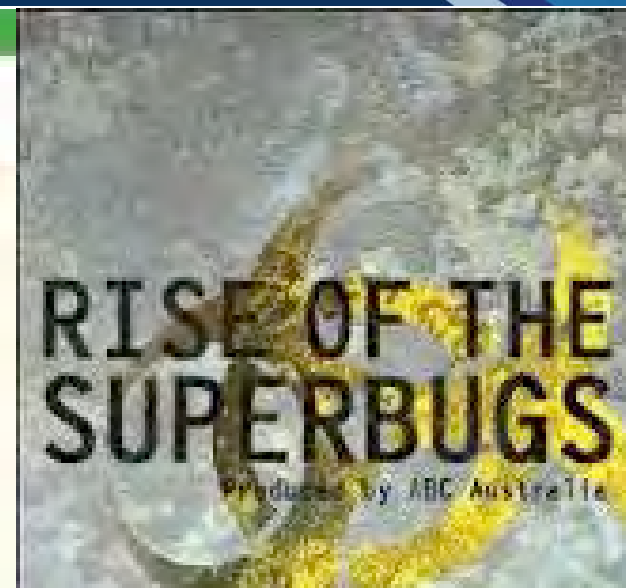




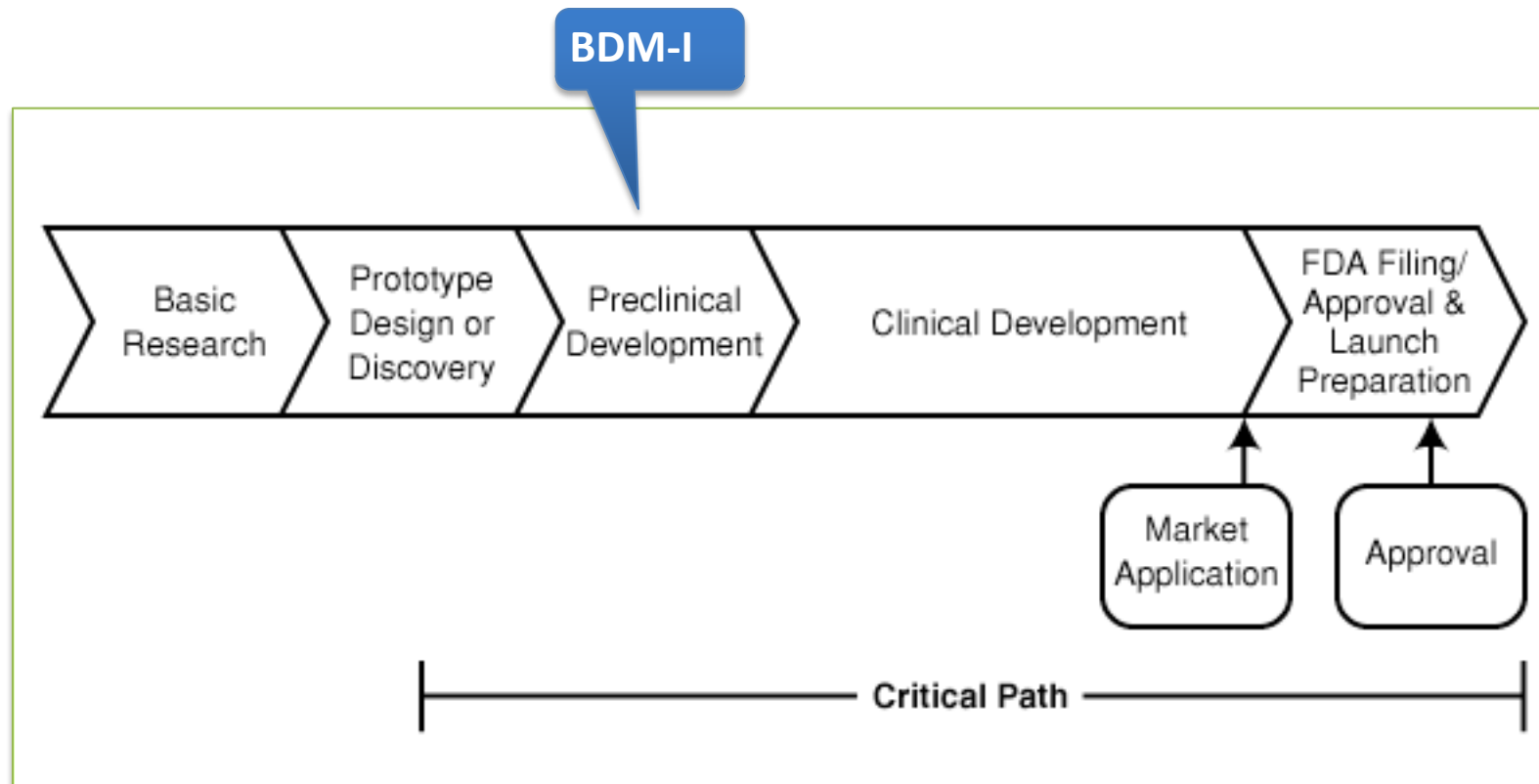
Hepatitis
vaccine progress

System designed

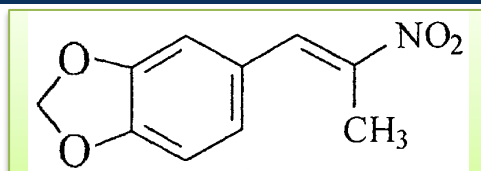
- to target the liver specifically to deliver therapies directly there.
- relevant for hepatitis and liver cancer, for example.
- smaller dosages of currently used therapies could result in higher cure rates and/or fewer dose-related side effects.



Drug development



BDM-I Status



✓ TB – ✓ Bacteria –
✓ Fungi - ✓ Protozoa



Preclinical
- Disease Model testing

Preparation for clinical trial



Jenny Herz

BioIntelect Pty Ltd

INFLUENZA VACCINE

- LAIV

Influenza - opportunity

- ❑ Seasonal Influenza vaccine policy and uptake is fragmented but evolving rapidly
- ❑ Vaccination of children is increasingly a priority and is already quite well established in some Asian markets and the Americas
- ❑ LAIV has advantages compared to TIV in children
 - Ease of administration: intranasal
 - Superior efficacy (breadth of immune response)
- ❑ LAIV nasal delivery will have high acceptance in some private market segments
- ❑ A significant opportunity exists for BioDiem to capitalise on the rapid development by SSI and to commercialize LAIV in new markets

Influenza – vaccine policy

- ❑ Until recently, influenza was perceived to be a disease of the elderly. Adult immunization is not as well developed as paediatric immunization, especially in lower and middle income countries
- ❑ Developed markets like Australia, New Zealand, USA, Canada and EU all have influenza vaccines included in the publicly funded program – hence market access issues are similar to paediatric vaccines
- ❑ Developing countries are much more heterogenous – influenza vaccine policy may be absent (Africa), evolving (India, China) or well established (PAHO countries, Korea, Taiwan)
- ❑ Often, influenza vaccine is still privately funded. In some it is publicly funded for some recommended groups and privately funded for others.
- ❑ Influenza vaccine policy is evolving rapidly, especially since the 2009 pandemic. World Health Organisation (WHO) plays a leading role.
- ❑ In 2009 BioDiem entered into a licence agreement with the WHO for all developing countries.



BioDiem

WHO recommendations for influenza vaccination 2012

Pregnant women (TIV) at any stage of pregnancy. Children < 6 months should be protected through vaccination of their mothers

Children aged 6-23 months

**New in November 2012 = LAIV
opportunity**

Children aged 2-5 years. LAIV provides broader and higher levels of protection than TIV in this age group

Elderly persons >65 years

Persons with specific chronic diseases, including indigenous populations in some settings

Health care workers to protect the individual and reduce spread to vulnerable patient groups

International travellers belonging to any of the above risk groups



India Private Market evolving rapidly

BioDiem

- ❑ Demand low in India but growing quickly, but unreliable information..
- ❑ Estimated value US\$1.5 m 2006 to US\$250 m in 2012
- ❑ Estimated middle class of 200-300 million

- ❑ Population 1.27 billion
 - 0-14 years 32% = 406 million
 - 15-64 years 63% = 800 million
 - 65 years and over 5 % = 63 million

- ❑ Other private market opportunities in 15-64 age group



Private Vaccine Market in China

- ❑ Private market not well developed, fragmented, with many local producers and imported vaccines – highly competitive
- ❑ Growing wealthy middle class (estimated 250- 300 million)
- ❑ Some insurance companies support flu vaccination for employees
- ❑ Domestic manufacturing capacity estimated to be \approx 20-40 million doses in 2010 but rapidly evolving (market information disparate)
- ❑ Sanofi and GSK have partnerships with local producers, Novartis also present
- ❑ Prices estimated US\$13 for imported vaccines and \$7-10 for locally manufactured vaccines (TIV)

HEPATITIS VACCINE (THERAPEUTIC)

Hepatitis vaccine- opportunity

BioDiem

Worldwide

- 520-570 million with chronic hepatitis (B,C or D)

USA

- approx 4.6 million.

Most will carry the infection for life →

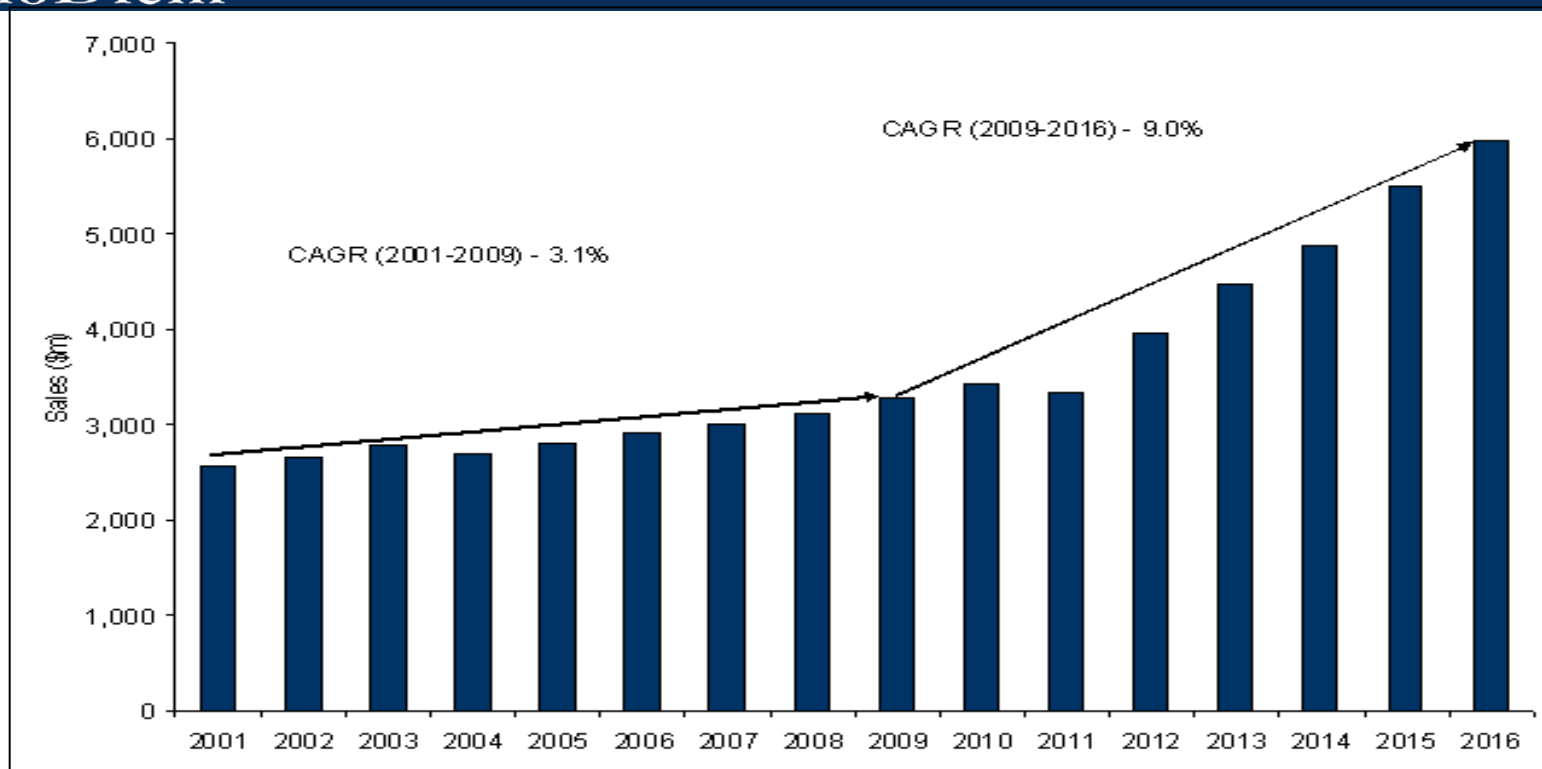
- cirrhosis
- Liver cancer
- Liver transplantation

Problems with current treatments:

- Develop resistance
- Serious side effects
- Expensive (annual cost US\$5K-35K) and can be ongoing



Hepatitis Therapeutics Market, Global, Sales Value (\$m), 2001–2016



Source: GBI Research's Internal Database, Annual Reports

This slide extracted on : 19 July 2013

There is a huge unmet need for cost-effective and tolerable therapies for viral hepatitis



Hepatitis B vaccine- deals

Arrowhead pharma deals for \$36 million private placement financing

Posted on 08 May 2013

Arrowhead Research pharma deals closing a previously announced private offering of common and convertible preferred stock with gross proceeds of \$36 million in financing.

The financing was led by RA Capital and included new pharma deals investors Camber Capital, Special Situations Fund, and Aquilo Capital, as well as existing pharma deals investors Sabby Capital, Sphera Global Healthcare Fund, and Jim Mellon.

Approximately 14.3 million shares of common stock were issued at \$1.83 per share.

9,900 shares of Series B convertible preferred stock were issued at \$1,000 per share, and each are convertible into 546 shares of common stock which is a conversion price of \$1.83 per share of common stock.

The Series B preferred was used in the pharma deals financing as an accommodation to those investors who desire to not own in excess of 9.99% of Arrowhead's outstanding voting securities following the financing.

Arrowhead Research is a clinical stage targeted therapeutics company with development programs in oncology, obesity, and chronic hepatitis B virus infection.

Hepatitis C vaccine - deals



- [Merck and Microbiotix in anti-infectives pharma partnering](#)
- Posted on 03 January 2013
- [Bio news: Achillion deal looming as hepatitis drugs fail: Real M&A](#)
- Posted on 30 August 2012
- [J&J Open to Expanding Hepatitis C Cooperation With Vertex](#)
- Posted on 24 April 2012
- [BMS snaps up Inhibitex for \\$2.5 billion for hep C portfolio](#)
- Posted on 10 January 2012
- [Novartis is open to deals of as much as \\$3 billion, CEO Jimenez says](#)
- Posted on 09 January 2012
- [Merck Hepatitis C Drug May 'Anchor' Future Worldwide Regimen](#)
- Posted on 12 January 2012
- [BMS and Tibotec to develop hepatitis C combination therapy](#)
- Posted on 02 December 2011
- [Who's next in the hepatitis C acquisition trail?](#)
- Posted on 23 November 2011



BDM-I

INFECTIOUS DISEASES

BDM-I - opportunity

- Increasing resistance
- Activity shown for organisms which cause serious diseases
- Non-dilutionary funding for development programs
- Currently in *in vivo* testing which is a prelude to clinical studies

Australia's chief scientist sounds antibiotic resistance warning

Report says there is 'a genuine threat of humanity returning to era where mortality due to common infections is rife'

Oliver Milman

guardian.co.uk, Friday 12 July 2013 17:35 AEST



A report from the Office of the Chief Scientist points to a 'collapse' in research and development of new antibiotics as an area of significant concern. Photograph: Murdo Macleod for the Guardian

The growth of antibiotic-resistant infections represents a "looming public health issue" for Australia that requires "urgent" new funding to prevent deaths from minor ailments such as sore throats and cut knees, the country's top scientist has warned.

A [report by the Office of the Chief Scientist \(pdf\)](#) states there is "a genuine threat of humanity returning to an era where mortality due to common infections is rife".

The paper blames the "misuse and overuse" of antibiotics, such as for animal husbandry, for driving up resistance levels in humans.

"Some bacteria are now so resistant that they are virtually untreatable with any of the currently available drugs," the report says.

UK raises alarm on deadly rise of superbugs

Britain to call for G8 action against spread of drug-resistant bacteria by clamping down on overuse of antibiotics

Ian Sample, Fiona Harvey and Denis Campbell

The Guardian, Wednesday 12 June 2013 04:33 AEST



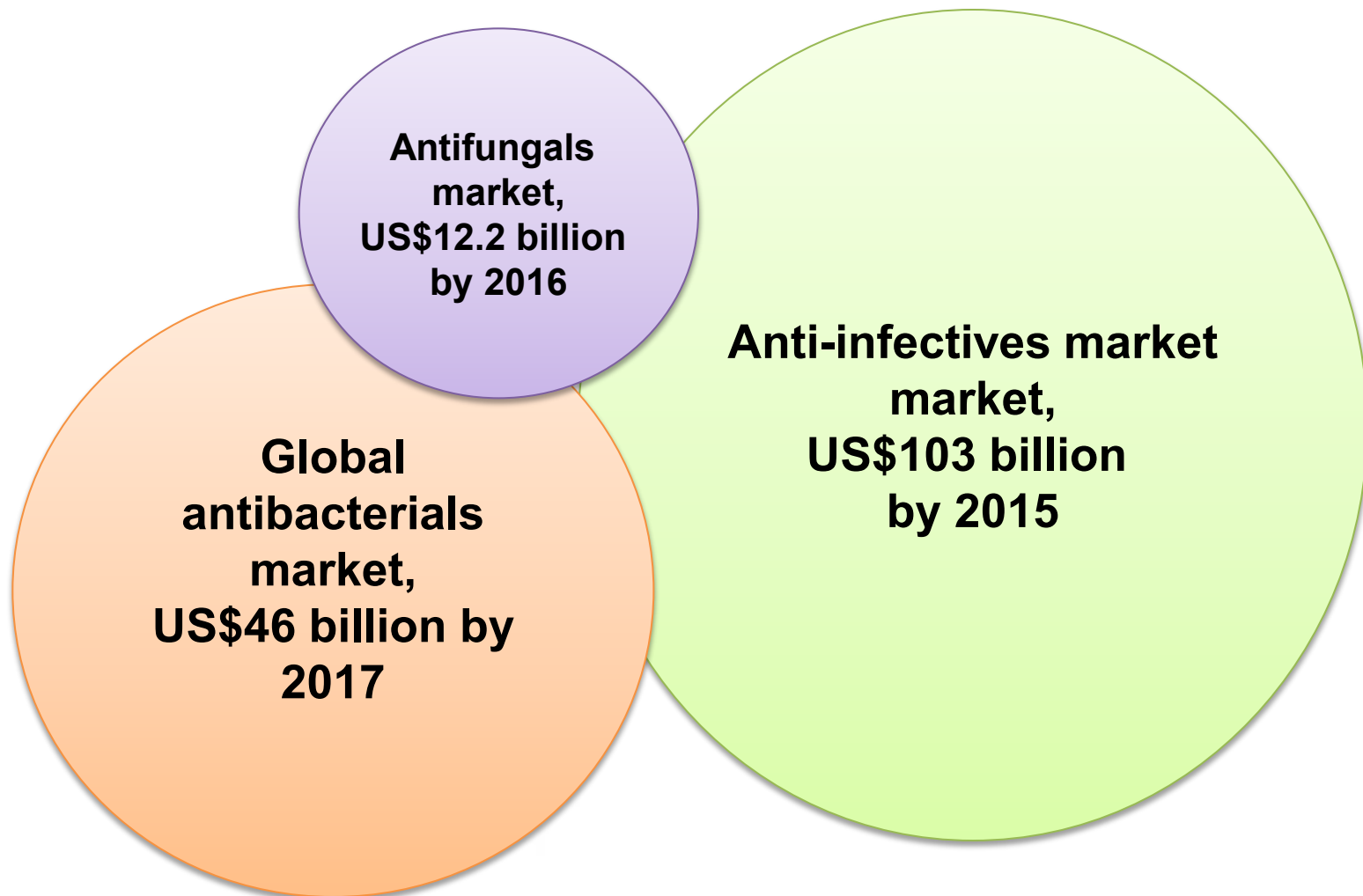
Resistant strains of bacteria are on the rise. Photograph: JR Bale/Alamy

Britain is to urge the G8 to take action against the spread of drug-resistant microbes as medical and veterinary experts warn that co-ordinated international action is needed to prevent soaring rates of potentially lethal infections turning into a public health catastrophe.

David Willetts, the science minister, will propose far-reaching measures that would clamp down on the overuse of antibiotics by GPs and hospital doctors. He will also try to restrict usage on farms and fisheries, where the drugs are blended with feed to boost yields.

Willetts will push for a consensus on ways to ramp up the discovery of new drugs to fight bacteria, speed their approval and delivery to patients, and strengthen cross-

Infectious disease - market size potential



The BioDiem logo features the word "BioDiem" in a white serif font, with a series of white dots of varying sizes arranged in a semi-circular arc above the letters "Bio".

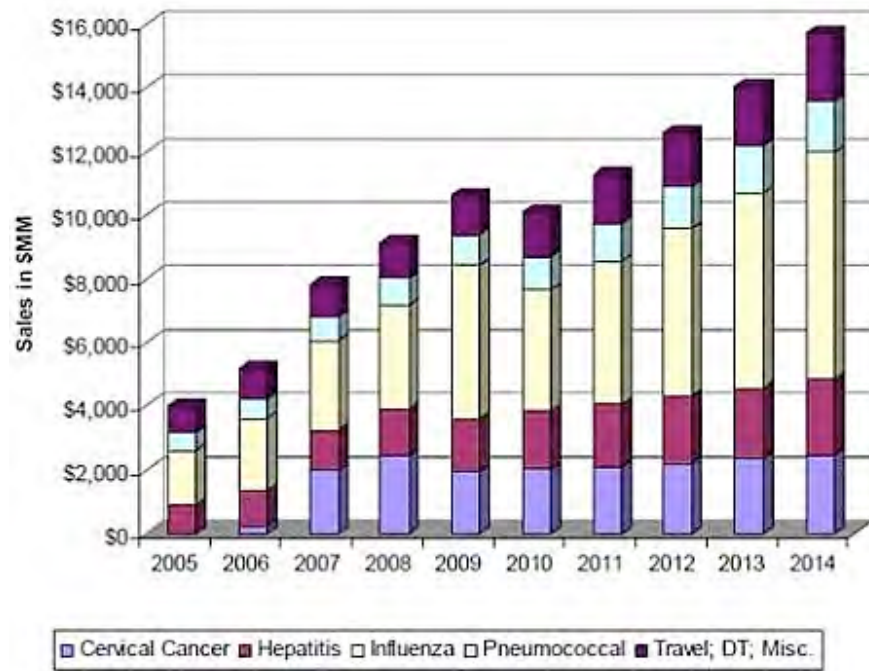
Infectious diseases - deal size

- ❑ **2013:** GSK pharma partners BARDA for drug resistance and bioterrorism developments (up to \$200m)
- ❑ **2013:** Novo Nordisk acquires Xellia for \$700m
- ❑ **2011:** Rib-X and Sanofi (up to \$100m per product and royalties on sales in low double digit)

Vaccines - market size potential

**Vaccine market
US\$52b by 2016**

World Market for Adult Vaccines 2005-2014
Revenues (in millions)



Vaccine company attractiveness - deal sizes



18 Jul 2013: Medicago announces agreement to be acquired by Mitsubishi Tanabe Pharma in a transaction valued at \$357m

29 May 2013: GSK strengthens vaccines business with acquisition of Okairos (US\$325m)

07 May 2013: Takeda beefs up new vaccines arm with \$250M bolt-on buyout of Inviragen

04 Feb 2013: Aduro BioTech Acquires GVAX Assets From BioSante Pharma

2012: Takeda acquired LigoCyte

2010: J&J acquires Crucell for \$2.2bn

Jul 2008: Sanofi Pasteur acquires UK-based Acambis

2007: Astra Zeneca acquires Medimmune



Therapies for major infectious diseases and related cancers

Company Update 2013 : Shaw Stockbroking 23 July 2013

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