

# Benitec Biopharma's ddRNAi technology

The next therapeutic revolution?

July 2012

*This presentation contains forward looking statements that involve risks and uncertainties.*

*Although we believe that the expectations reflected in the forward looking statements are reasonable at this time, Benitec Biopharma can give no assurance that these expectations will prove to be correct.*

*Actual results could differ materially from those anticipated. Reasons may include risks associated with drug development and manufacture, risks inherent in the regulatory processes, delays in clinical trials, risks associated with patent protection, future capital needs or other general risks or factors.*

# Benitec Biopharma Ltd (ASX:BLT)



## Aim:

To create appropriate return on investment by commercializing CSIRO gene silencing technology.

## Strategy:

- To execute commercial partnerships with global pharmaceutical companies.
- To demonstrate the broad applicability of our technology.

# Company Overview



- Potent long-lasting gene silencing platform technology
- Proven clinical efficacy and safety
- Robust global patent protection
- Broad pipeline in multiple therapeutic areas
- Experienced Board and Management

# Benitec has developed the equivalent of a gene silencing *penknife*

- ddRNAi can silence any gene
- Potential application for human disease is enormous
- Programs strategically selected to showcase the breadth of therapeutic applications of ddRNAi



# How ddRNAi Technology works?

- Genes within a patient's cells produce proteins that cause disease
- Specific RNA can block the activity of that gene – “silencing” the gene
- ddRNAi utilizes the patient's own cells to continually produce that RNA
- Thus long term cure from a single treatment

# How to make a ddRNAi product in eight steps

1. **Identify the key gene**
2. **Identify** the gene's 'Achilles' heel'
3. **Design and manufacture a construct** that will produce the silencing molecule
4. **Test the construct *in vitro***
5. **Identify a delivery vehicle** that will carry that construct to the target organ
6. **Test the construct *in vivo***
7. **Determine toxicity**
8. **Test in clinical trials** – major inflection point for value creation

# Two Pathways to Revenue

- Advancement of in-house pipeline programs to the clinic
- Out-licensed projects utilising Benitec Biopharma's ddRNAi technology



# Program 1: Cancer-Associated Pain

- **Approximately 65% of all cancer patients experience pain**
- **11.7 million people in the US with cancer**

**The global market for cancer-associated pain products is valued at \$2 billion and is expected to increase to \$2.9 billion by 2016**

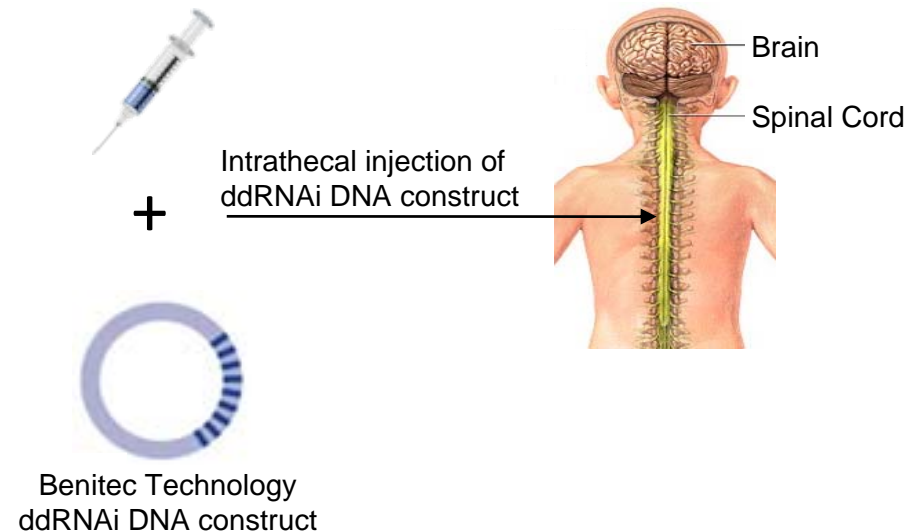
# ddRNAi Technology For Cancer Pain Treatment

Utilizing the ddRNAi platform, Benitec has developed their gene silencing technology for the treatment of pain in terminal cancer patients.

## The ddRNAi Platform Technology

- Benitec's novel ddRNAi technology allows for **long-term gene silencing**.
- The technology can be targeted to silence a **specific gene or multiple selected genes**.
- Unlike current treatments for pain, this product is long-lasting and has the potential to cause **only minimal side effects**.
- The ddRNAi product is **injected intrathecally** into the spinal canal where it transfects the PKC  $\gamma$ -containing interneurons.

## A ddRNAi Construct for Treating Cancer Pain



Source: <http://www.nlm.nih.gov/medlineplus/ency/imagepages/19621.htm>

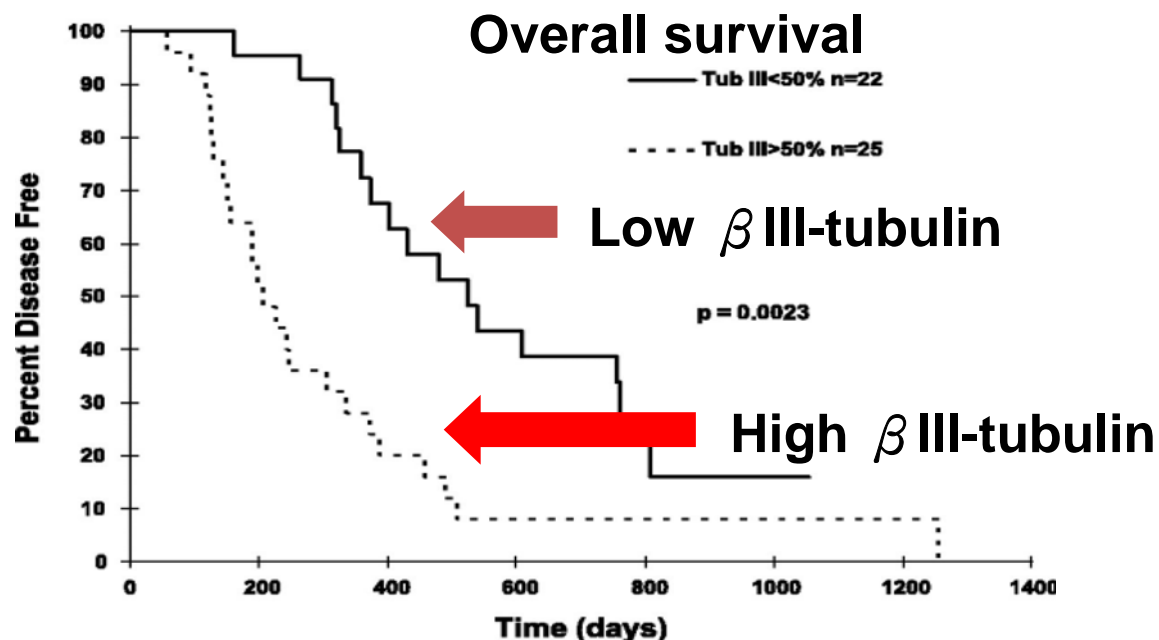
# Program 1: Introducing Nervarna™



## Program 2: Drug-resistant cancer

- Non Small Cell Lung Cancer (NSCLC) is the one of the most common cancers: 1.6 M new cases per year globally
- Dismal prognosis, with a high proportion becoming resistant to conventional drug therapy within a short period of time

$\beta$ III-tubulin  
associated with  
drug resistance



## Program 2: Introducing Tribetarna™

In collaboration with  
Children's Cancer Institute  
Australia, UNSW



## Program 3: Viral disease – Hepatitis B

- More than 2,000 million people alive today have been infected with HBV at some time in their lives
- ~350 million remain chronically infected and become carriers of the virus



**Global Business  
Intelligence  
Hepatitis Market to  
2017**

For example, USA:

- Over 1.25 million people living with the consequences of chronic active HBV
- Over 60,000 new cases per year

## Program 3: Introducing Hepbarna™

Collaboration with Biomics  
Biotechnologies Co Ltd, China

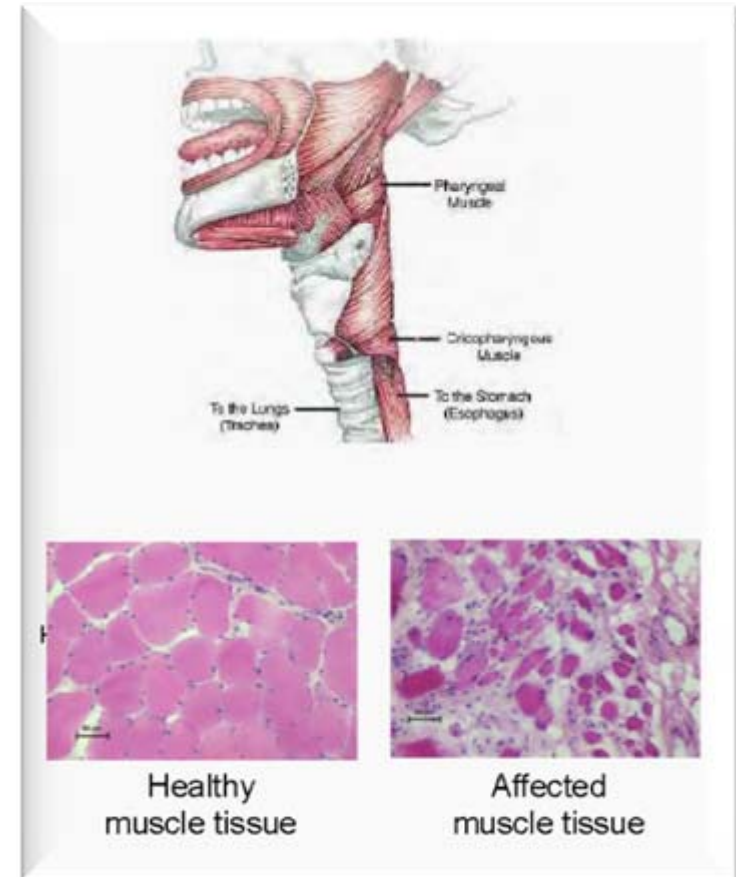


# Program 4: Genetic Disease - OPMD (oculopharyngeal muscular dystrophy)

- No effective treatment exists
- Symptoms: swallowing difficulties leading to choking and death

OPMD is classified as an **orphan disease**

It is a rare condition  
(1 in 100 000 in Europe)  
with a worldwide distribution





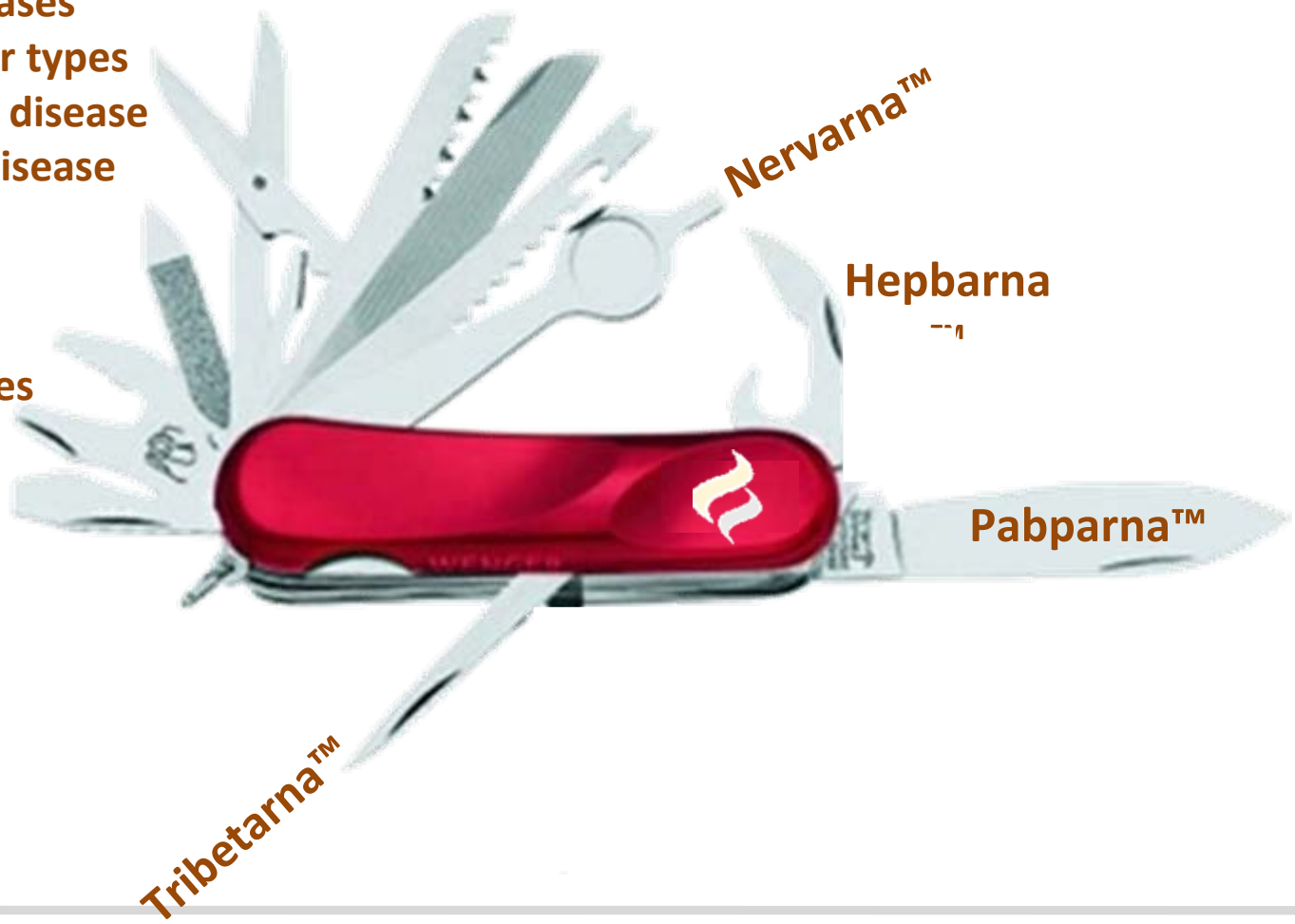
# Program 4: Pabparna™ development

In collaboration with Royal  
Holloway, University of London



# Other potential applications...

- Infectious diseases
- Multiple cancer types
- Cardiovascular disease
- Huntington's disease
- Alzheimer's
- Autoimmune
- Stem cells
- Genetic diseases



# Outlicensed projects utilising Benitec Biopharma's ddRNAi technology

HIV/AIDS - Calimmune, USA

Hepatitis C - Tacere Therapeutics, USA

Retinitis Pigmentosa – Genable, Ireland

# Progress in ddRNAi-based programs

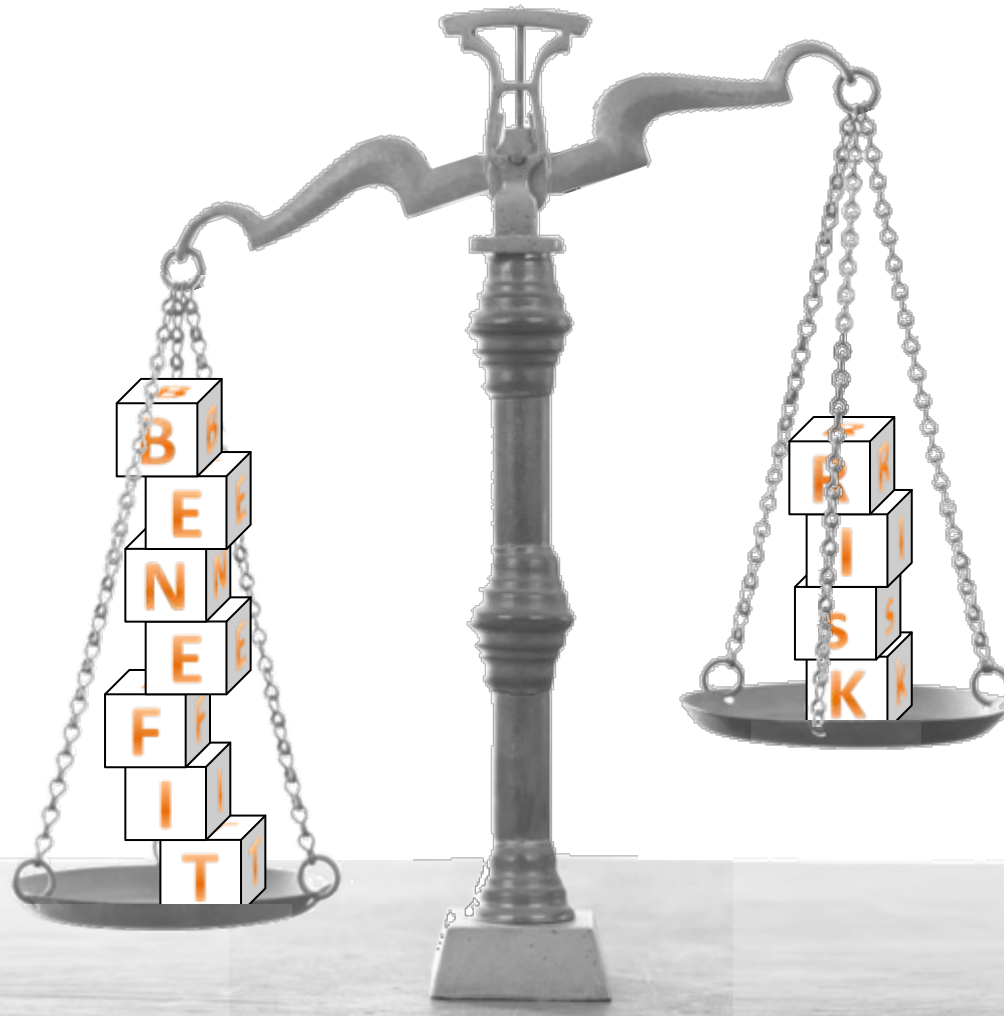
Indication	Discovery	Pre-clinical	Human clinical	Delivery Strategy	Market
Cancer-associated pain	Nervarna™			Localised via lentiviral injected intrathecally	\$2.6 billion by 2016
Drug resistant cancer	Tribetarna™			Systemic coupled with PEI nanoparticles	Leading form of cancer worldwide
Hepatitis B	Hepbarna™			Systemic via AAV	400 million globally
Oculopharyngeal muscular dystrophy	Pabparna™			Local injection (AAV) combined with gene therapy	Orphan disease affecting 1 in 100,000 in Europe
Hepatitis C (Tacere)				Systemic via AAV	>170 million people worldwide
HIV/AIDS (Calimmune)				Ex vivo lentiviral transfection of CD34 stem cells	1/200 infected with HIV worldwide
Advanced cancer (Gradalis)				shRNA cassette combined with therapeutic vaccine	11.7 million in the US
Retinitis pigmentosa (Genable)				Local injection (AAV) combined with gene therapy	Orphan disease

# Hepatitis C

## Hepatitis C is attracting huge interest in and deals for clinical assets

- Nov 2011:** Gilead paid **\$11 billion** to buy Pharmasset's oral compound in Phase II testing.
- Mar 2012:** Gilead announced the compound failed to suppress HCV in difficult-to-treat - or null - patients who had also failed prior therapy. Of eight with genotype 1, the most common form of the virus, all relapsed within four weeks after stopping the 12-week regimen.
- Jan 2012:** Achillion's CEO projected **HCV treatments would fetch \$20 billion by the end of this decade.**
- Jan 2012:** "Our goal is to be a leader in hepatitis C, and we will do what it takes to get there," **Merck** CEO Pomerantz said. "**We would consider small deals to large deals, whatever is necessary to lead in hepatitis.**"

# Benitec Biopharma's strategy gives more weight to benefit



## The benefit-risk ratio will propel Benitec's programs over the regulatory hurdle



# Experienced Leadership Team



## Management

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### **Dr Peter French, PhD, MBA**

Chief Executive Officer

- ✓ 30 years experience in medical research and biotechnology
- ✓ Founder of Cryosite Ltd
- ✓ Published > 30 papers in cell & molecular biology

### **Greg West**

Chief Financial Officer/ Company Secretary

- ✓ Held senior finance executive roles in investment banking with Bankers Trust, Bain & Company
- ✓ a Director of ITC Limited

### **Dr Michael Graham, PhD**

Chief Scientist

- ✓ Molecular biologist
- ✓ Founder of Benitec
- ✓ Discoverer of Benitec Biopharma's technology

### **Carl Stubbings**

Chief Business Officer

- ✓ 30 years experience in Biotech/Diagnostics Sales & Marketing
- ✓ Broad international experience in commercialization of healthcare platforms

## Board

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### **Peter Francis, Chairman**

- ✓ Partner at Francis Abourizk Lightowlers (FAL), commercial and technology lawyers

### **Mel Bridges, non-executive director**

- ✓ 30 years experience in the global biotechnology and healthcare industry
- ✓ Chairman of Alchemia and Impedimed

### **Dr John Chiplin, non-executive director**

- ✓ CEO of Arana sold to Cephalon in July 2009
- ✓ head of the \$300M ITI Life Sciences investment fund in the UK

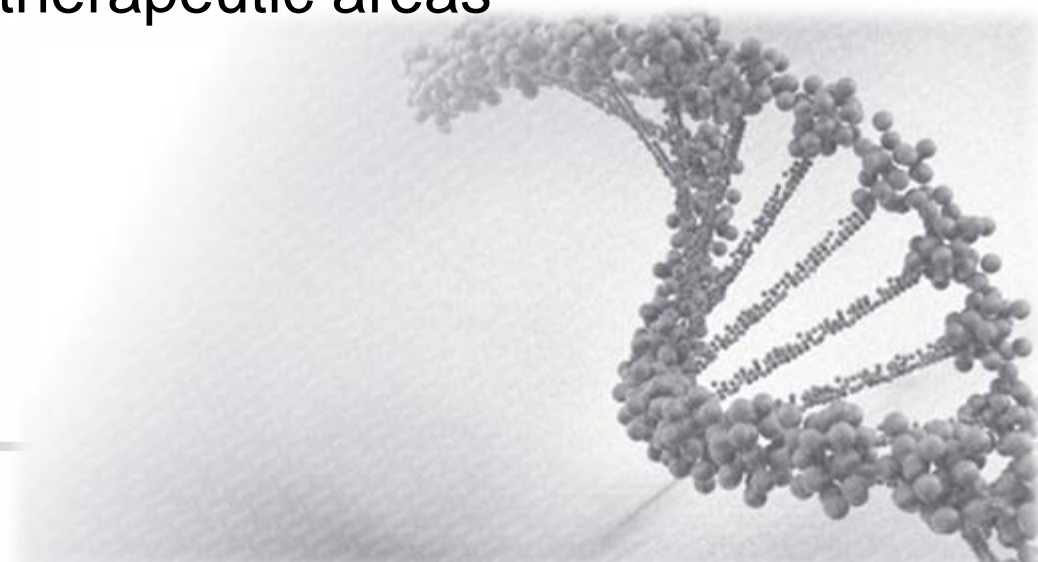
### **Ian Ross, non-executive director**

- ✓ Chairman of Ark Therapeutics, UK
- ✓ Former Chairman Silence Therapeutics



## In summary:

- Potent long-lasting gene silencing platform technology from CSIRO
- Multiple patent protection world wide
- Proven pre-clinical and clinical efficacy and safety
- Broad pipeline in multiple therapeutic areas



# Contact Information



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Benitec Biopharma video:

<http://www.youtube.com/watch?v=KYRRNgziRpQ>