Benitec Biopharma's ddRNAi technology

The next therapeutic revolution?

October 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.

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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.

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Company Overview

- Benitec Biopharma (ASX:BLT) is an ASX-listed biotechnology company based in Sydney, Australia
- The company holds a dominant global intellectual property position in gene silencing technology that utilizes DNA Directed RNAi (ddRNAi) ;
- The ddRNAi Technology:
    - "Turns off" (silences) disease-causing genes by delivering short hairpin RNA (shRNA) that binds to a specific target gene sequence in a target cell;
    - Uses a gene therapy vector that causes the patients' cells to continuously manufacture the silencing shRNA
    - Provides long term silencing with a single administration; conventional "delivered" siRNA approaches requires repetitive administration of therapeutic entity.
- Developing a pipeline of in-house and partnered therapeutic programs selected for fit with technology and to fulfill critical unmet medical needs.

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How ddRNAi Technology works

- Genes within a patient's cells or in a disease-causing virus produce proteins that are responsible for the progression of disease
- Specific sequences of double stranded RNA that correspond to those genes can block the activity of the gene – "silencing" the gene and altering the course of disease – "RNA interference" or RNAi
- ddRNAi utilizes the patient's own cells to continually produce the silencing dsRNA from a DNA construct
- Thus long term cure from a single treatment is potentially possible

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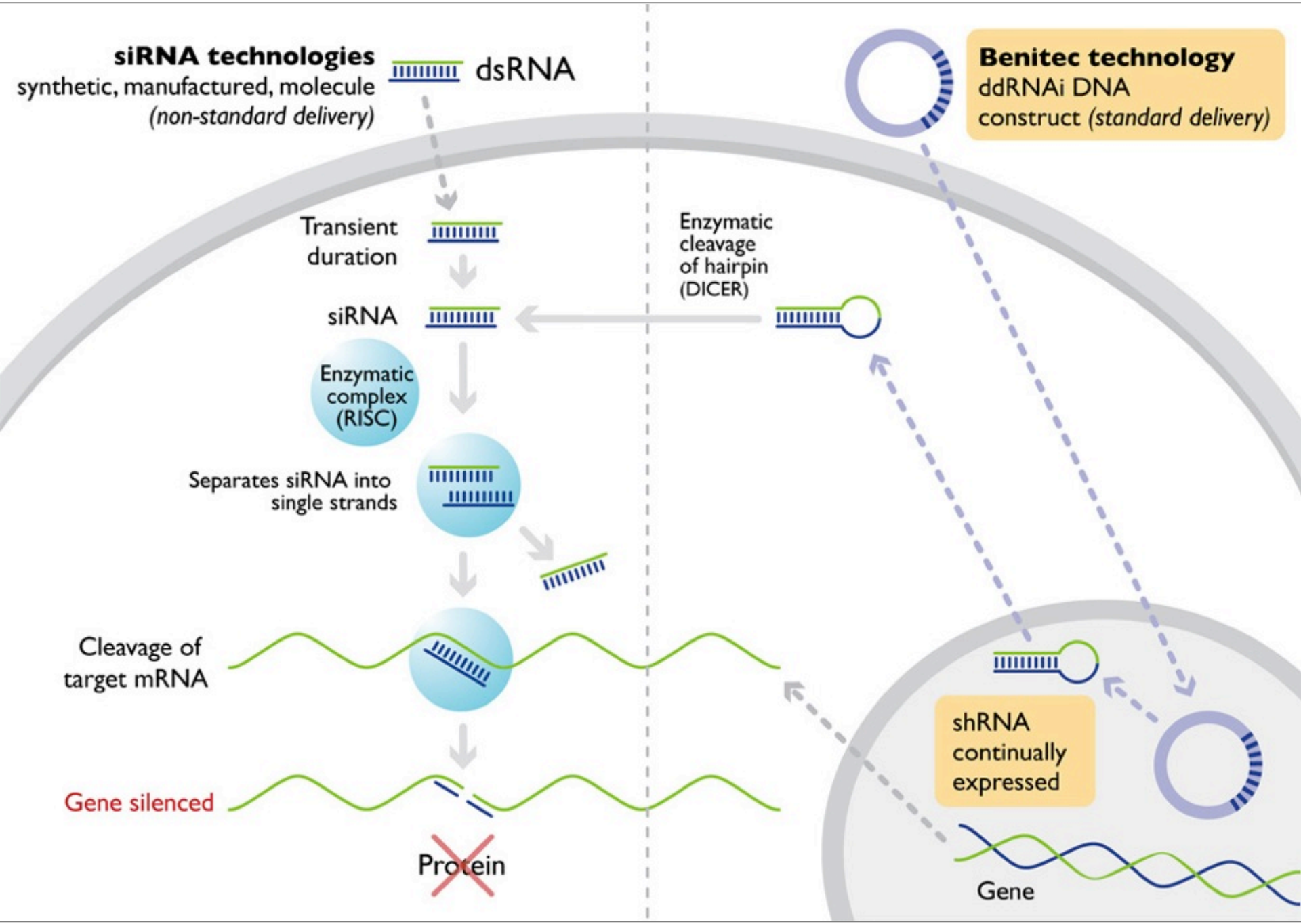
siRNA technologies
synthetic, manufactured, molecule
(non-standard delivery)
dsRNA
Benitec technology
ddRNAi DNA
construct (standard delivery)
Transient
duration
siRNA
Enzymatic
complex
(RISC)
Separates siRNA into
single strands
Cleavage of
target mRNA
Gene silenced
Protein
Enzymatic
cleavage
of hairpin
(DICER)
shRNA
continually
expressed
Gene

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

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

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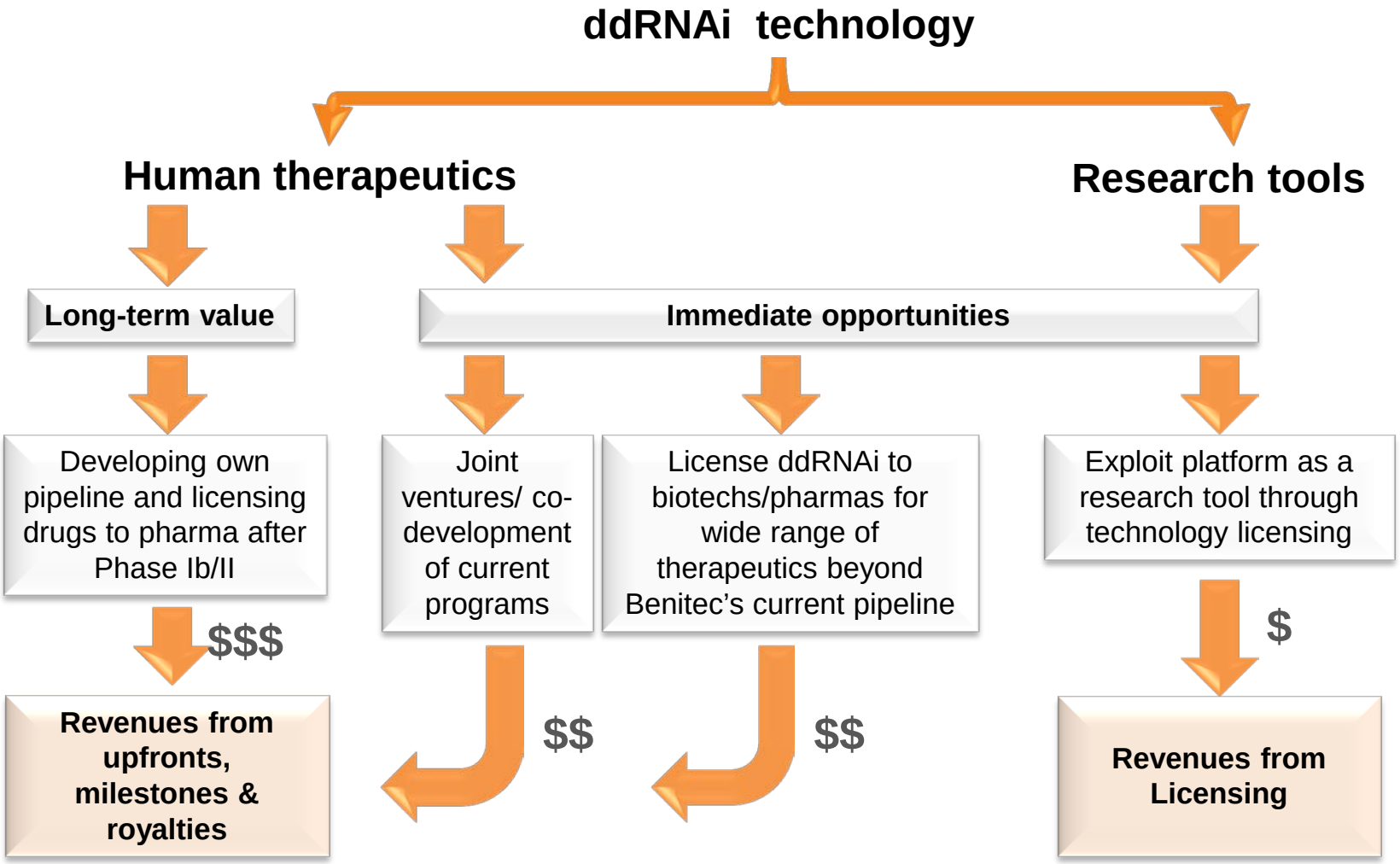
Pathways to Revenue

- Advance in-house pipeline programs to the clinic then seek to partner
- Out-license other targets for ddRNAi technology to biotech and pharma companies

Strategy to build value



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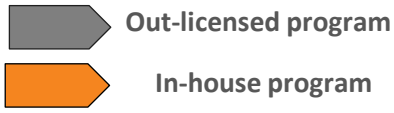
Pipeline and Licensed Programs

Indication	Partners/ Collaborators	Discovery	Pre-clinical	Clinical
HIV/AIDS	Calimmune			
Hepatitis C	**Addition from Tacere**			
Drug resistant lung cancer	University of New South Wales			
Cancer-associated neuropathic pain	Stanford University			
Hepatitis B	Biomics Biotechnologies			
Oculopharyngeal muscular dystrophy	Royal Holloway, University of London			
Age-Related Macular Degeneration	**Addition from Tacere**			
Retinitis Pigmentosa	Genable			



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Hepatitis C Market Opportunity

- There are over 170 million HCV infected people worldwide and HCV is a leading cause of cirrhosis, hepatocellular carcinoma, and liver transplantation
- There are three genotypes (GT) - 1, 2 & 3
  - 75% of all cases are genotype 1 (GT1)
  - GT 2 & 3 are comparatively well-served by the current standard of care
  - GT1 is the most prevalent genotype in China and dwarfs western markets in numbers of patients
- Current therapies only address approximately 40% of GT1 patients
- Current therapies use a combination of interferon, ribavirin and protease inhibitors – interferon side effects severely limit long time use.
- Emerging drugs are predicted to improve cure rates to 70% in previously treated GT1 patients, BUT this leaves over 3,000,000 patients in USA, Europe and Japan with unmet medical need

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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**."

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Hepatitis C Asset Acquisition

- Benitec Biopharma announced on October 11th 2012 that it will acquire Tacere Therapeutics, including all non-cash assets, in an all share transaction.
- Tacere history:
  - Established in 2006 with a license to Benitec's ddRNAi technology for a Hepatitis C virus therapeutic, TT-034
  - Partnered with Pfizer in 2008 to further develop the program
  - Pfizer invested significant resources in developing the program over 3 year period to near to Phase I/II ready
  - TT-034 remained a high priority pre-clinical program for Pfizer prior to global reorganization in 2011
  - Pfizer closed its UK facility in 2011 and the program was subsequently put on hold
  - In 2012 all rights reverted to Tacere with no further financial obligations
- Opportunity to acquire Tacere complements and expands Benitec Biopharma's pipeline

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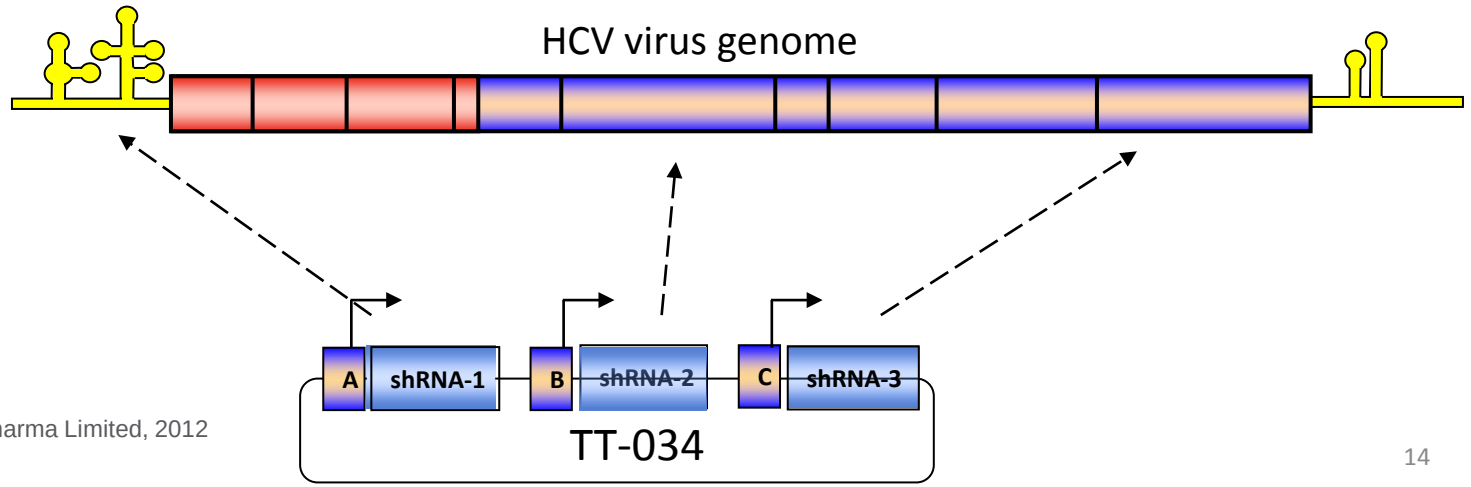
Description of Key Asset – TT034

- TT-034 is a next generation therapeutic designed to be superior to emerging HCV drugs
  - A “one shot monotherapy cure”; Intended to clear HCV with a single injection
  - May also be used in combination with existing and new small molecule drugs
- TT-034 is ready to enter a first in man phase I/IIa study subject to final regulatory approval
  - All safety and toxicology studies required have been conducted with an excellent safety profile
- TT-034 comprises **three shRNAs** targeting three separate, highly conserved regions on the HCV virus genome
- Inhibits HCV resistance development, while maintaining target specificity, high efficacy and low off-target effects.
- Mainly targeted to genotype 1, the most prevalent and underserved HCV genotype



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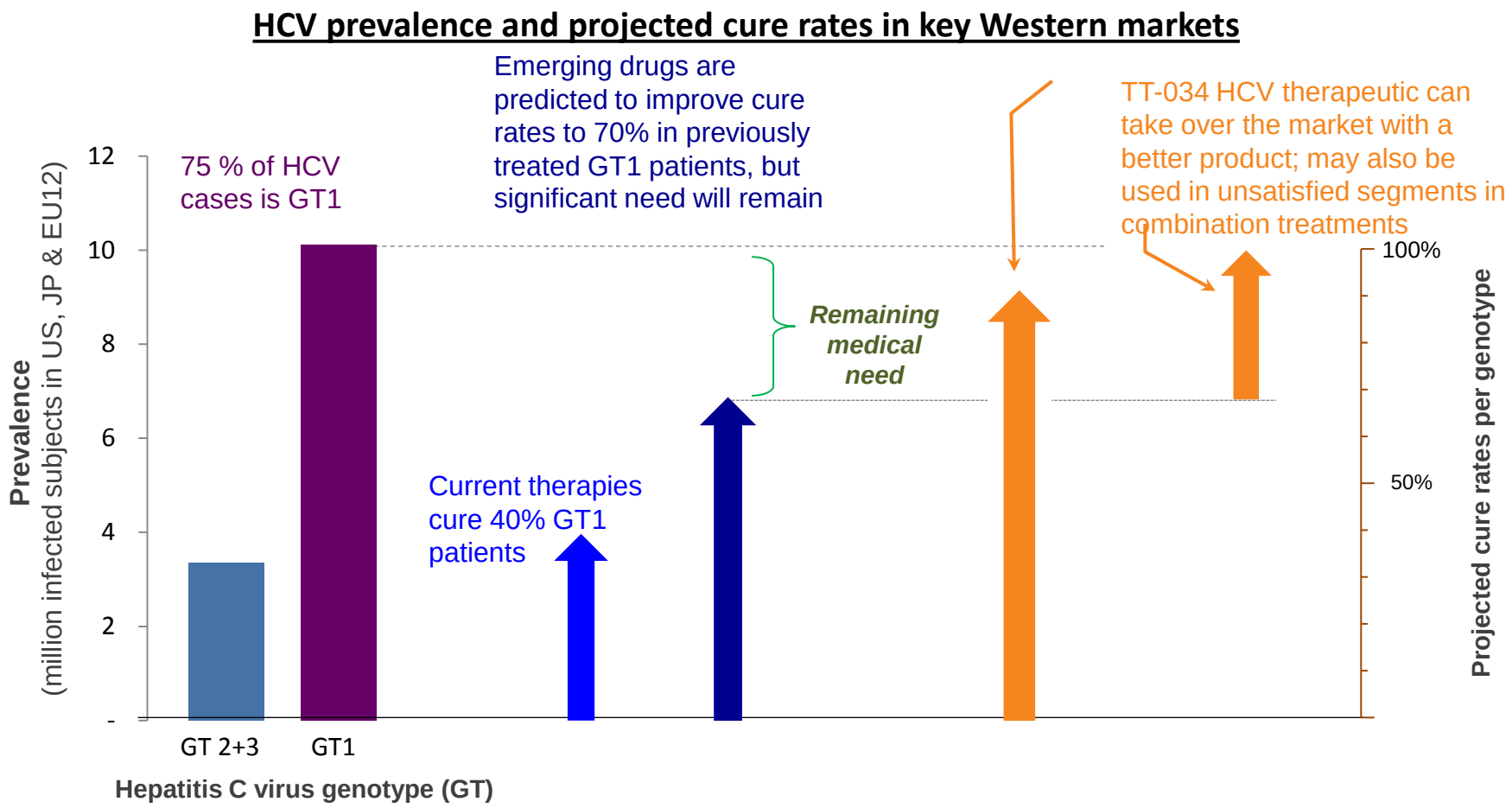
TT-034 positioning in the HCV market

If successful, TT-034 could achieve a competitive share of the HCV market



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Sources: Datamonitor 2007 to 2011, Chak et al 2011, Sievert et al 2011, Esteban et al 2008.
EU 12 is Germany, France, Italy, UK, Spain, Netherlands, Belgium, Sweden, Denmark, Norway, Finland, Austria.
Cure rate = number of patients that achieve a cure as % of patients dosed. J.W. Pawlotsky (2011) J. Hepatology 53:1742-50.

Clinical trial opportunity in 2013

- First in man Phase I/IIa clinical trial intended to be conducted in 2013 in US HCV patients permitting the acquisition of safety and efficacy data in humans
- All safety and toxicology studies have been completed
- Pre-IND meetings with FDA have been held
- Sufficient GMP material has been produced to initiate clinical trials
- Key next steps:
  - Meeting with the FDA Recombinant Advisory Committee
  - Filing of the IND
  - Dosing of first patient

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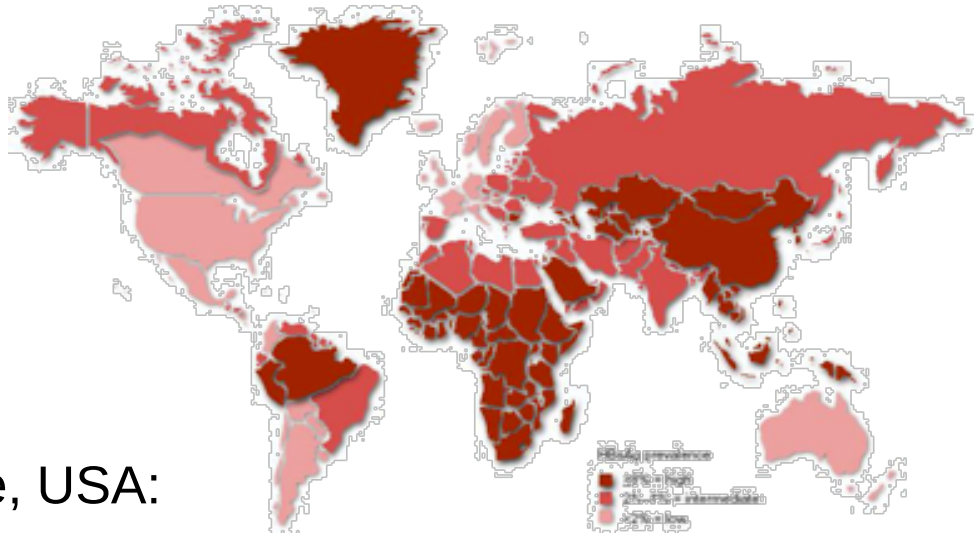
Hepatitis B

- 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

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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

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Identifying the key target pain gene

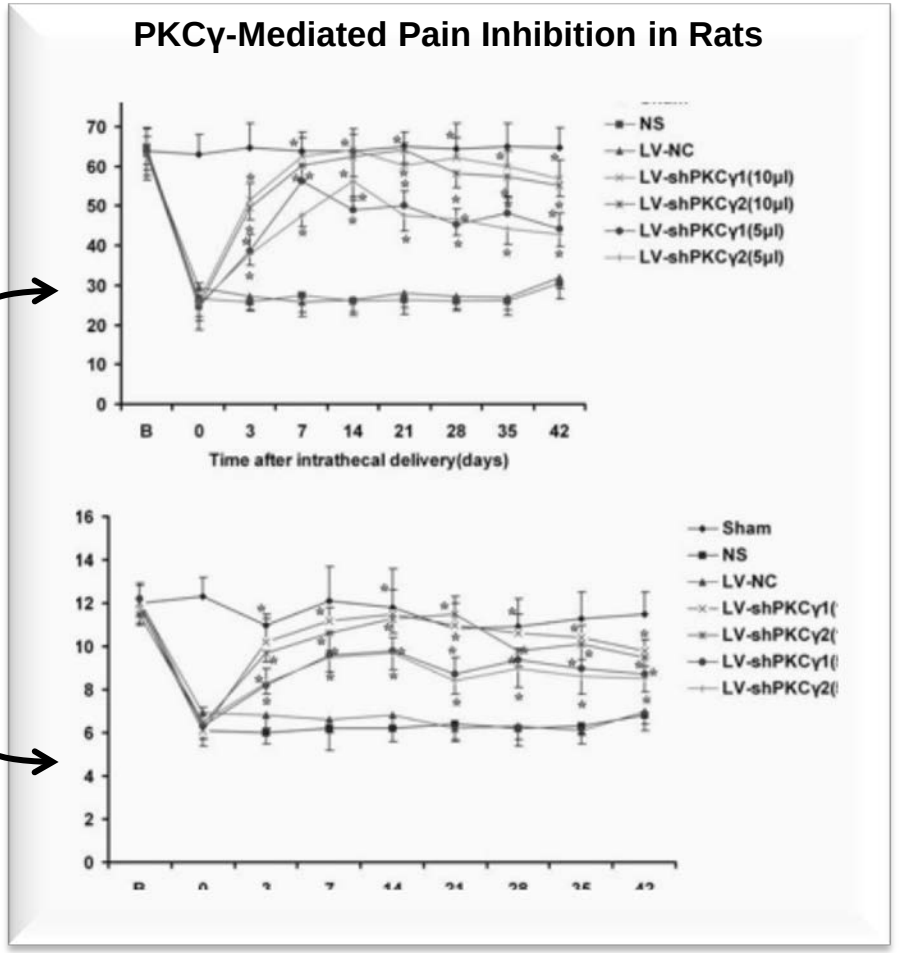
- Increased PKCγ found in the spinal cord in cancer pain

6 weeks

One dose of PKCγ-silencing ddRNAi construct

No toxicity

Dose-dependent increase in pain threshold



- Switching off PKCγ also overcomes morphine tolerance

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Source: Results of nine KOL interviews conducted by Campbell Alliance in July and August 2011.

Target product profile – Nervarna™

- Terminally ill cancer patients
- Intractable neuropathic pain
- Morphine ineffective
- Single intrathecal injection of a single shRNA targeting PKCγ in a lentiviral vector
- Long term pain relief on its own or in conjunction with opioids.

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Nervarna™ Development Timeline

- Target PKCγ mRNA sequence identified - July 2012
- GMP LV constructs manufactured – August-Sept 2012
- In vivo proof of concept experiments in a spared nerve pain model underway at Stanford University - Sept-Nov 2012
- Tox and biodistribution studies - planned for 2013
- Clinical trial - aiming for 2013

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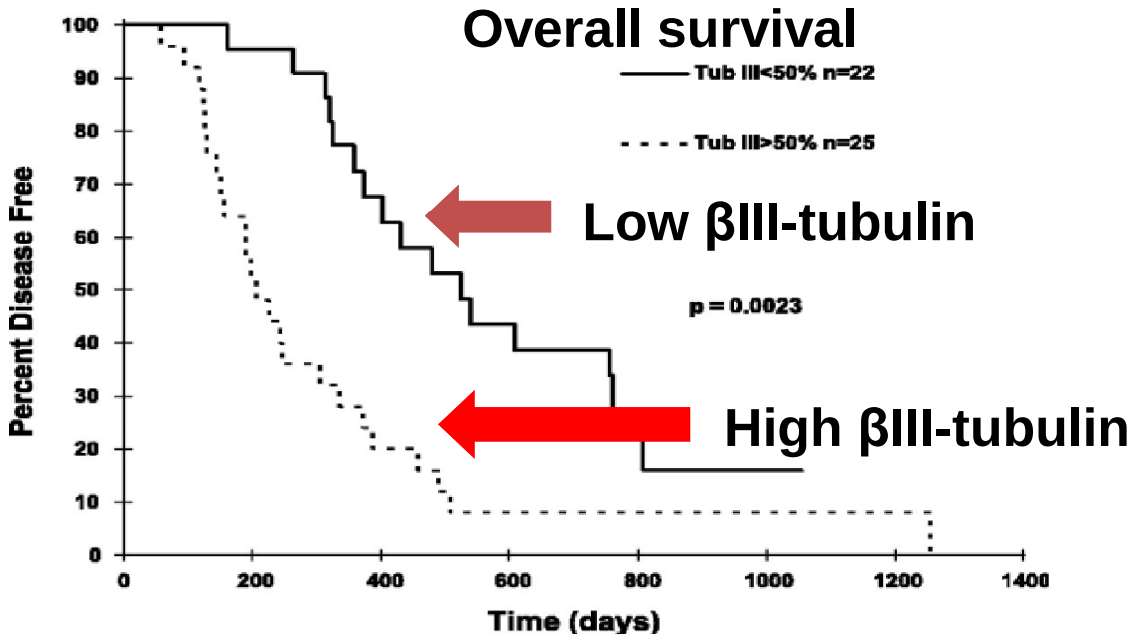
Drug-resistant lung cancer

- 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

βIII-tubulin associated with drug resistance



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Target product profile – Tribetarna™

- Non-small cell lung cancer patients
- Resistant to chemotherapy – DNA damaging agents and tubulin binding agents
- Single intravenous injection of a triple shRNA targeting βIII-tubulin in a non-viral vector
- Adjunct to chemotherapy – restoration of tumour sensitivity.

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Delivery and silencing of βIII-tubulin gene expression in NSCLC tumours in vivo

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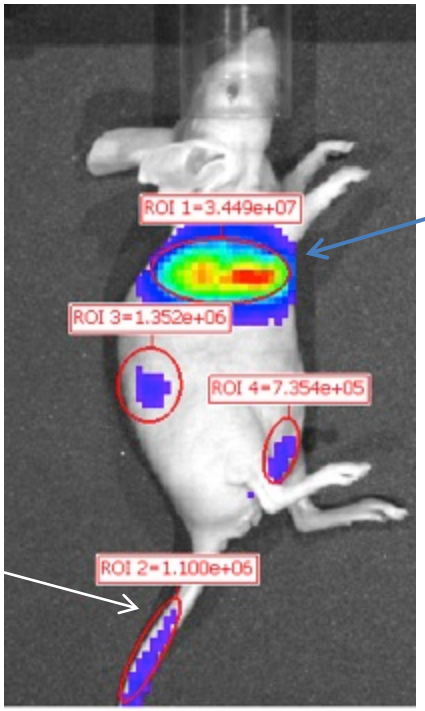
silencing genes for life™

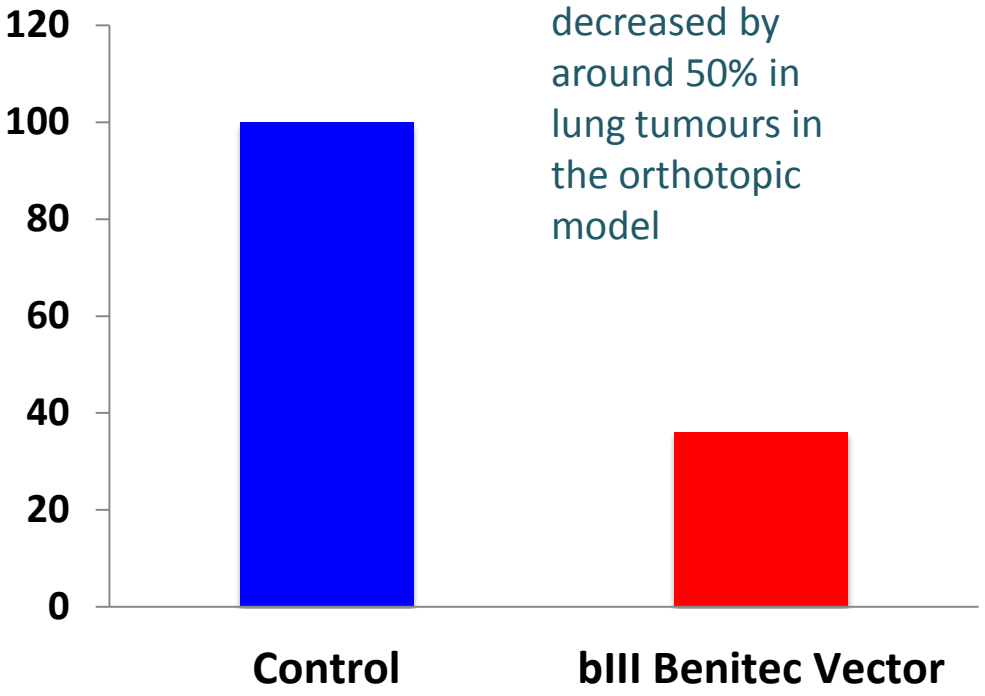
Treated mouse with orthotopic lung tumors



Tail vein injection site

JetPEi specifically delivers the gene construct to lung cells

The uptake of the vector is almost 100x higher in lung tumor tissues than in comparator tissues



βIII tubulin is decreased by around 50% in lung tumours in the orthotopic model

Collaboration with the Children's Cancer Institute Australia at UNSW

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OPMD
(oculopharyngeal muscular dystrophy)

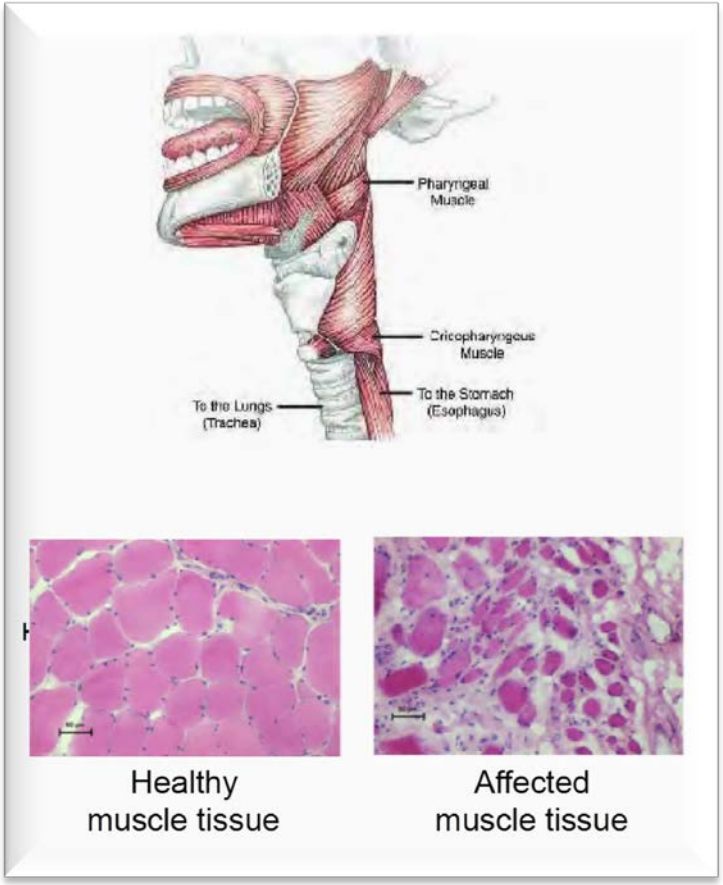
- No effective treatment exists
- Symptoms: swallowing difficulties leading to choking and death

OPMD is an orphan disease

- 1 in 100 000 in Europe, with a worldwide distribution
- Caused by mutation in PABPN1 gene

Benitec Biopharma Approach:
ddRNAi-based silencing of mutant gene and replacement with normal gene.

Collaboration with Royal Holloway, University of London



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Source: http://healthmedcare.com/Health/muscular-dystrophy/

Big Pharma are doing big deals in Benitec's program areas

Phase I/II clinical trials are Benitec Biopharma's next significant inflection point.

Companies	Condition	Stage	Deal	When
Xenon / Genentech	Pain	Phase II	A $646 million deal – undisclosed upfronts and milestones.	Jan 2012
Enanta / Novartis	Hep C	Phase I	$36 million up front, as much as $404 million more on clinical, regulatory, and commercial milestones	March 2012
Gilead / GlobeImmune	Hep B	Phase Ia	undisclosed upfront payment plus additional milestone payments and, potentially, royalties	Oct 2011
Avila / Clovis	Non small cell lung cancer	Pre clinic	unspecified upfront and regulatory and sales milestones that add up to $209 million	May 2010

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Other potential applications…

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

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Outlicensed projects utilising Benitec Biopharma's ddRNAi technology

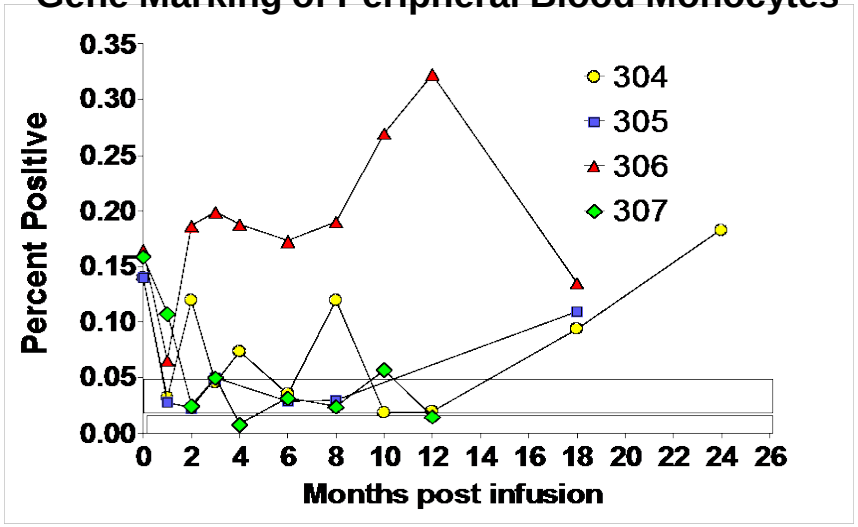
HIV/AIDS - Calimmune, USA

Retinitis Pigmentosa – Genable, Ireland

First human ddRNAi clinical trial: **HIV/AIDS** (City of Hope)

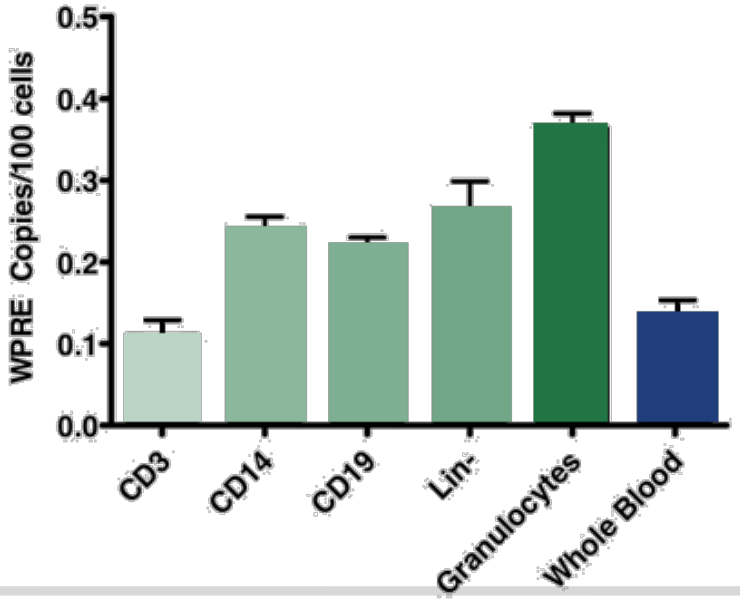
- Following only one stem cell-delivered treatment, constructs still present and active in stem cells and all immune cells after 3 years (data not shown)
- A completely new and resistant immune system potentially

Gene Marking of Peripheral Blood Monocytes



Expressed shRNA persists **for >3 years**

Gene Marking in Immune Cells



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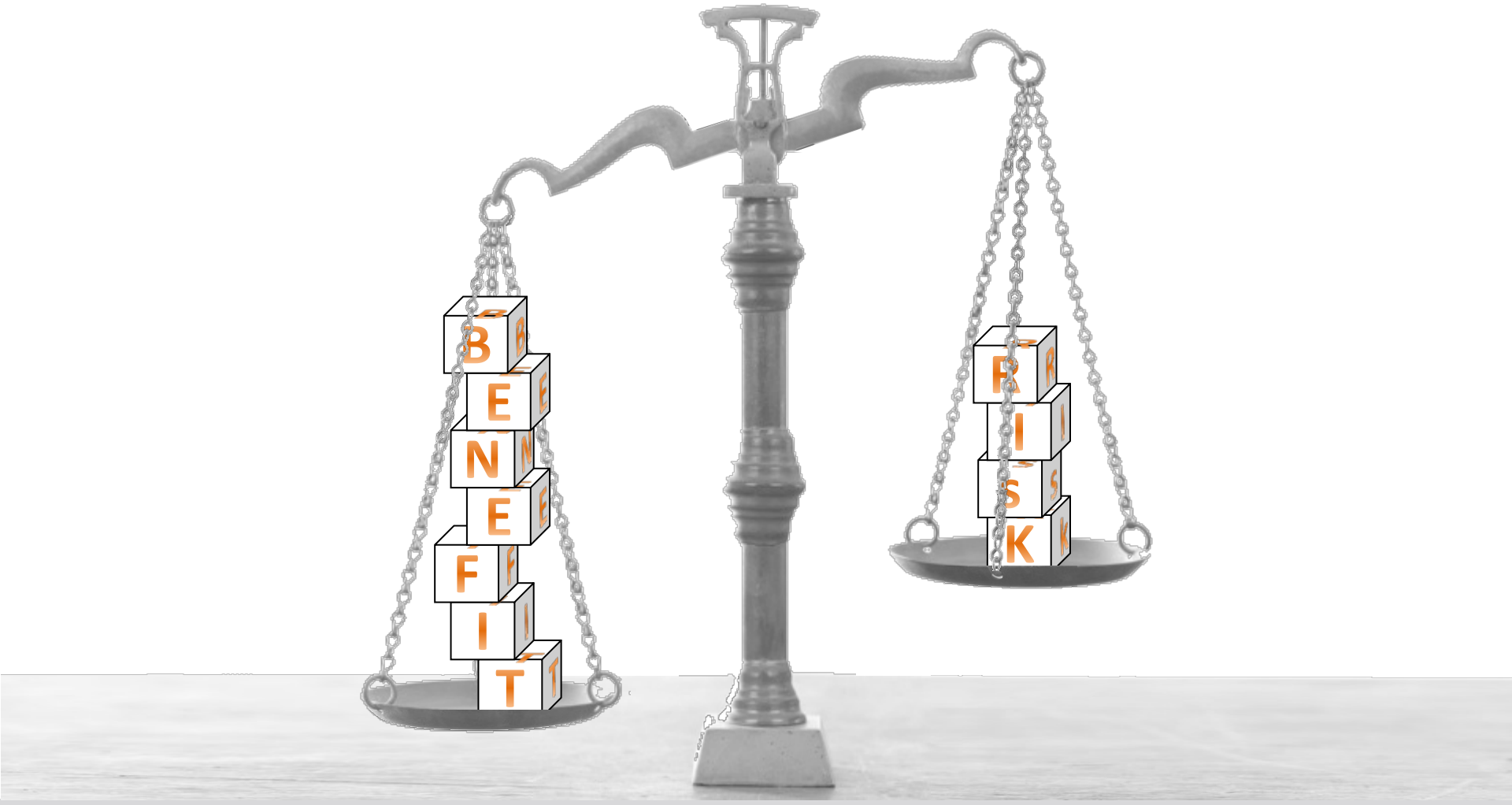
Benitec Biopharma's genetic therapy strategy gives more weight to benefit



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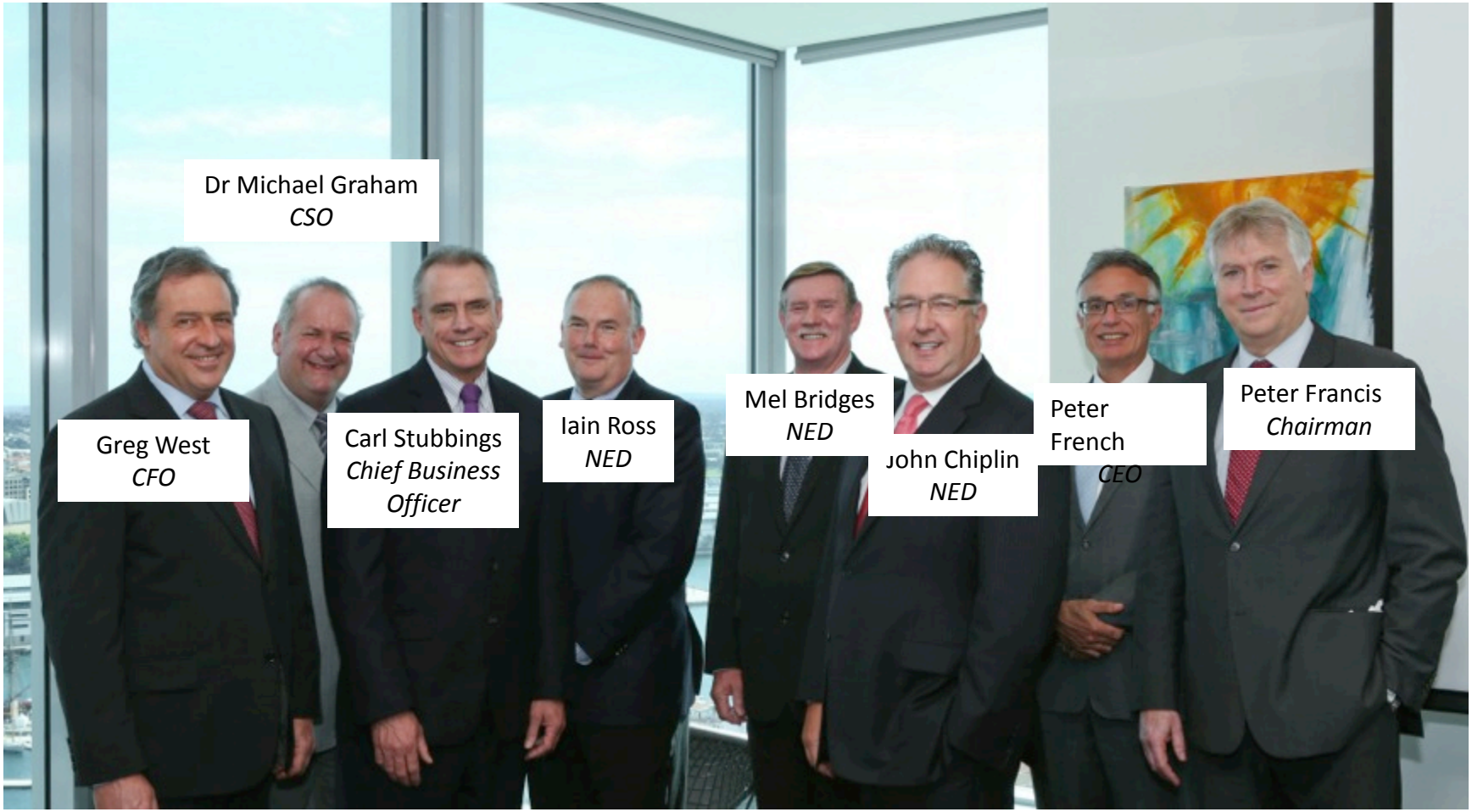
Experienced Leadership Team



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Experienced Leadership Team

Management

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

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

Dr 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

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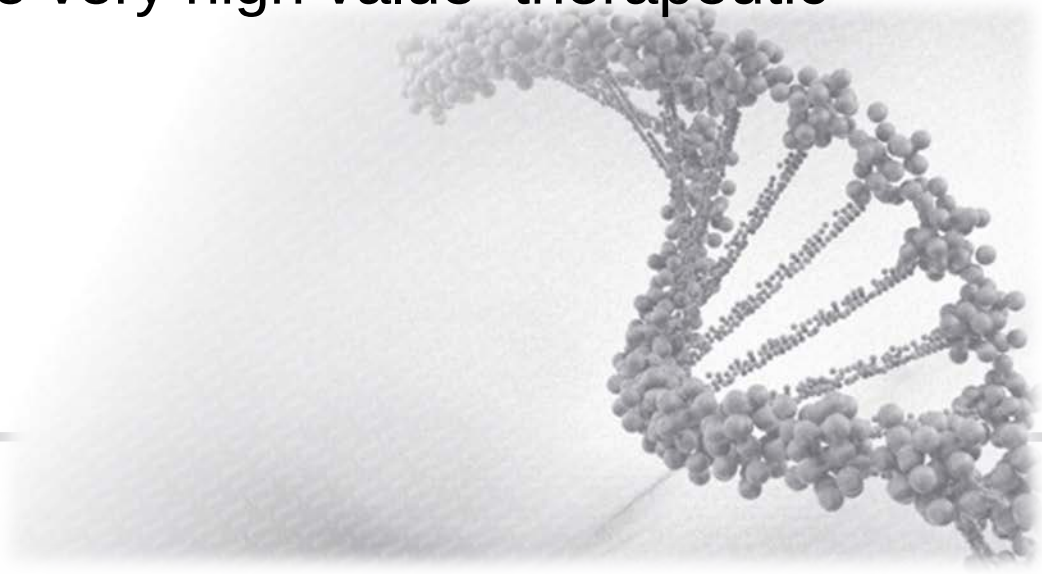
BENITEC BIOPHARMA
silencing genes for life™

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 very high value therapeutic areas



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Benitec Biopharma video:
http://www.youtube.com/watch?v=KYRRNgziRpQ

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