

Benitec Biopharma Ltd

ABN 64 068 943 662

F6A / 1-15 Barr Street Balmain NSW 2041 Australia

> Tel: +61 (0) 2 9555 6986 Email: info@benitec.com

> > www.benitec.com

#### **ASX ANNOUNCEMENT**

#### BENITEC INVESTOR PRESENTATION

**Sydney, 5 August 2014:** Benitec Biopharma Limited (ASX: BLT) (OTC: BTEBY) is pleased to release a copy of the presentation that Dr David Suhy, Senior VP Research & Development, will be delivering to investors during a non-deal roadshow in Melbourne and Sydney.

The presentation highlights Benitec's progress on the company's ddRNAi programs and provides an update on Phase I/IIa Hepatitis C trials.

For further information regarding Benitec and its activities, please contact the persons below, or visit the Benitec website at <a href="https://www.benitec.com">www.benitec.com</a>.

Company	Investor relations	
Carl Stubbings	Jane Lowe	
Chief Business Officer	Buchan Consulting	
Tel: +61 (2) 9555 6986	Tel: +61 (2) 9237 2807	
Email: <a href="mailto:cstubbings@benitec.com">cstubbings@benitec.com</a>	Email: <u>jlowe@buchanwe.com.au</u>	

#### **About Benitec Biopharma Limited:**

Benitec Biopharma Limited is an ASX-listed biotechnology company (ASX: BLT, OTC: BTEBY) based in Sydney, Australia. The company has a pipeline of in-house and partnered therapeutic programs based on its patented gene-silencing technology, ddRNAi. Benitec is developing treatments for chronic and life-threatening human conditions such as Hepatitis C, Hepatitis B, wet age-related macular degeneration, cancer-associated pain, drug resistant lung cancer and oculopharyngeal muscular dystrophy based on this technology. In addition, Benitec has licensed ddRNAi technology to other biopharmaceutical companies who are progressing their programs towards the clinic for applications including HIV/AIDS, retinitis pigmentosa and Huntington's disease. For more information on Benitec refer to the Company's website at www.benitec.com.

## Benitec Biopharma:

"In it for the long haul": Differentiating ddRNAi from its peers in the RNAi space

Dr David Suhy, PhD Senior VP Research & Development, Benitec Biopharma
August 2014



## Forward looking statement

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.

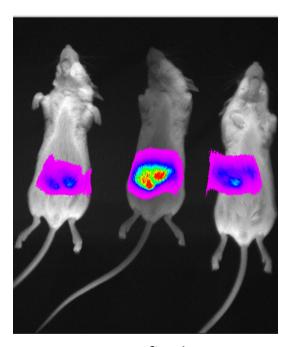
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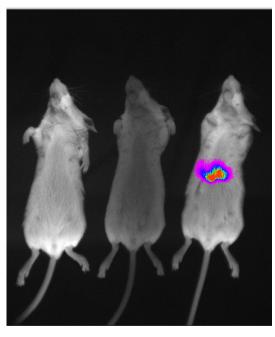
#### RNAi....It's simply about knocking down genes...



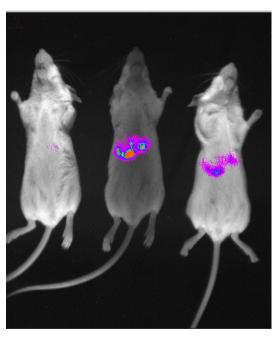
#### OR IS IT? What differentiates the Benitec ddRNAi Technology?



Non-specific shRNA

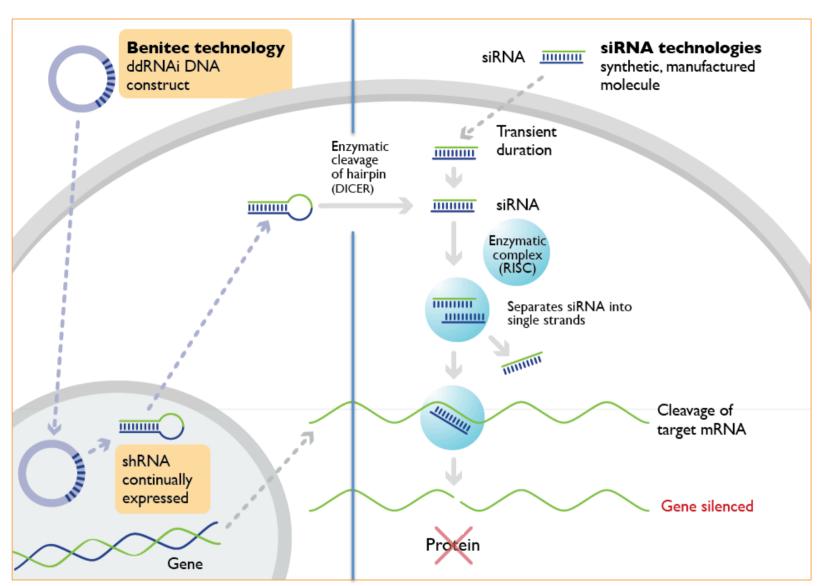


**HCV shRNA-8** 



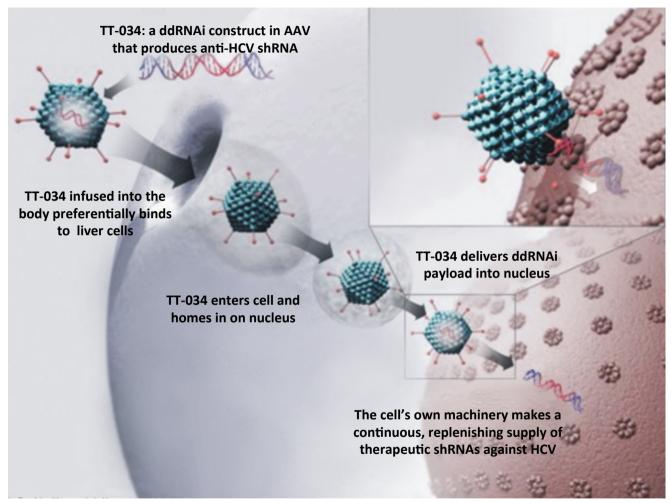
Firefly Luc shRNA







#### TT-034: Delivery to liver via AAV vector





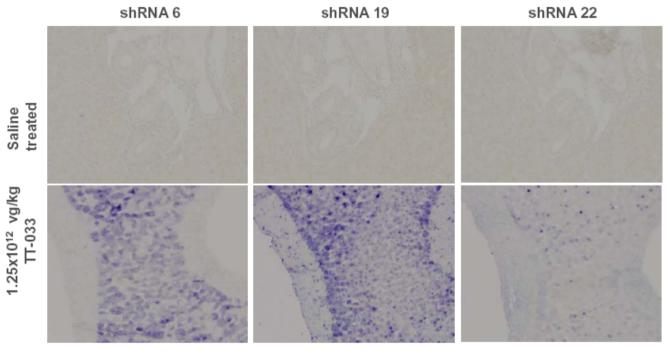
## Utilization of viral vectors can permit exquisite tissue specific delivery



animal	CCANO	Famala	
	SSAN3 Female		
dose	1.25 E12 vg/kg		
TICOLIE	copies per cell		
TISSUE	mean	sd	
Liver-LT-Caudal	199.6	43.9	
Liver-RT-Caudal	165.2	29.9	
Liver-Medial	142.8	14.5	
Spleen	23.7	0.7	
LN-Inguinal	15.9	0.6	
LN-Mandibular	13.2	0.8	
Injection Site	7.3	1.4	
Bone Marrow	3.4	0.1	
LN-Mesenteric	2.5	0.0	
Kidney	1.0	0.1	
Heart-LT Ventricle	1.0	0.0	
Heart-RT Ventricle	0.4	0.0	
Thyroid	0.3	0.1	
Lung	0.3	0.0	
Cecum	0.3	0.0	
Jejunum	0.2	0.0	
Heart-Septum	0.2	0.0	
lleum	0.1	0.0	
Duodenum	0.1	0.0	
Colon	0.1	0.0	
Ovary	0.1	0.0	
Brain-Diencephelon	0.1	0.0	
Pancreas	0.0	0.0	
Brain-cerebellum	0.0	0.0	
Skeletal muscle	0.0	0.0	
Urinary Bladder	0.0	0.0	
Thymus	0.0	0.0	
Rectum	0.0	0.0	
Brain-Parietal			
Gallbladder			
Adrenals	Tissue NA		
LN-axillary	Tissue NA		

Biodistribution Analysis: >90% into hepatic tissues

In Situ Hybridization analysis demonstrates near complete transduction and uniform expression of therapeutic sequences



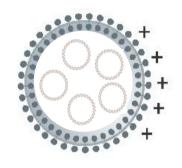
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# Flexibility in delivery platform to fit disease indication and tissue location

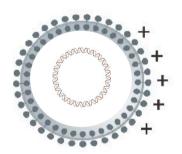


#### **Viral Vectors**

(HCV, HBV, Ocular, Pain, OPMD)

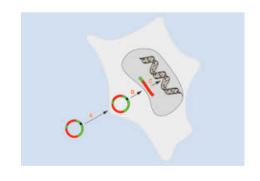


Nanoparticle delivery of minicircle DNA or minitranscription cassettes



Nanoparticle delivery of DNA plasmids

(lung cancer)



Delivery of transduced cells expressing shRNA



# Tissues and/or cell types targeted in Benitec pipeline programs

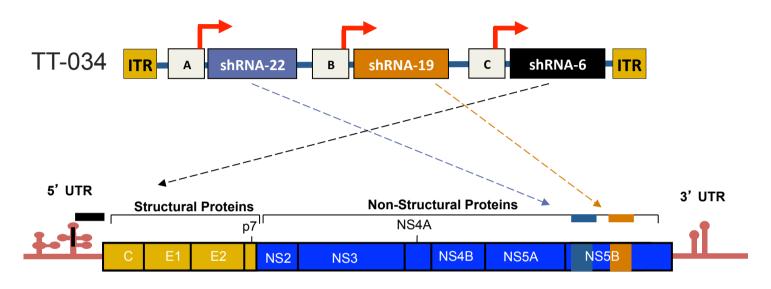
Focus	Indication	Partners / Collaborators	Discovery	Pre-clinical	Clinical
Infectious Disease	Hepatitis C		LIVER		
	Hepatitis B	Biomics Biotechnology (JV)	LIVER		
Cancer	Non Small Cell* Lung Cancer	University of New South Wales (RC)	LUNG		
	Cancer Associated Pain	Stanford University (RC)	CNS/NE	URONAL	
Ocular Disease	AMD**		EYE/RET	<b>TN</b> A	
Genetic Disease	OPMD***	Royal Holloway London University (RC)	MUSCLE		



RC = research collaboration JV = joint venture

\*and other chemotherapy-resistant cancers \*\*Age-Related Macular Degeneration \*\*\*Oculopharyngeal Muscular Dystrophy, an orphan disease

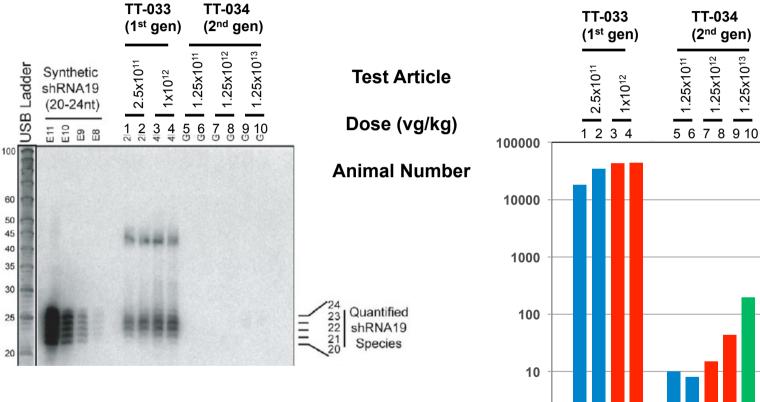
## **Expression of multiple therapeutic agents from a single vector**



- 3 independently transcribed RNAi elements target 3 separate, well-conserved regions of the HCV genome; helps prevent the generation of viral escape mutants
- Combination drug in one therapeutic entity provides broad patient applicability, while maintaining specificity



### Ability to regulate shRNA expression and quantify their expression in target tissues



Northern Blot Analysis



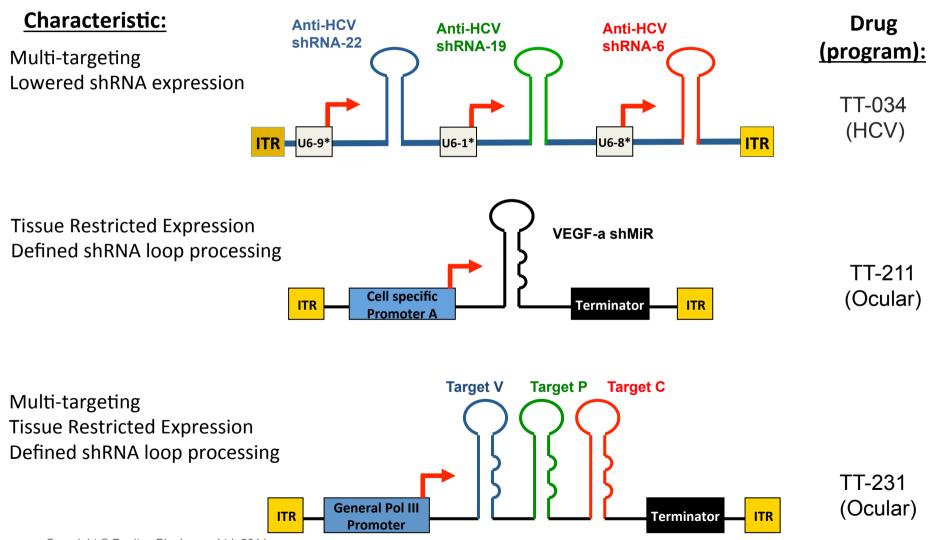
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**Custom QPCR Analysis** 

1.25×10<sup>13</sup>

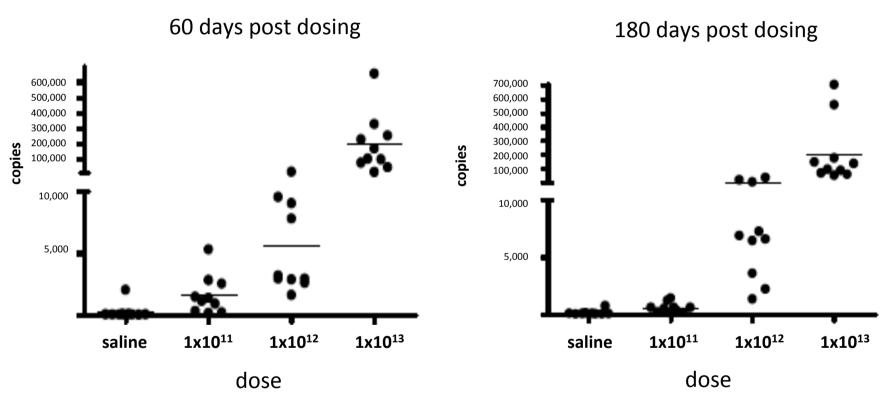
## Ability to use next generation ddRNAi technologies to develop more efficient, safe drugs





## Durability: Expression in hepatic tissues from a single IV administration

Levels of shRNA22 in murine hepatic tissues



ddrnai has the POTENTIAL to Deliver "ONE-SHOT CURES"



#### From bench to bedside: TT-034 regulatory path

- First shRNA-based RNAi therapeutic to be applied systemically using nonwithdrawable viral vector in humans
- Program oversight by FDA (CBER), NIH OBA, EMA, MHRA, AFSSAPS, & Swiss Medic
- Being a first in class therapeutic, all agencies interested in learning how to regulate as well as providing regulatory guidance
- Favorable review at meeting at National Institutes of Health Recombinant DNA Advisory Committee (RAC) June 2013
- No clinical hold after 30 day review of IND filing by FDA 'OK to proceed' with trial was given January 15, 2014















#### **Benitec Biopharma Exclusive and Robust IP**

Exclusive license for the global development and commercialisation of human therapeutics using the unique and durable gene-silencing technology, ddRNAi

> 59 granted or allowed patents with more than 60 additional patents pending, including:

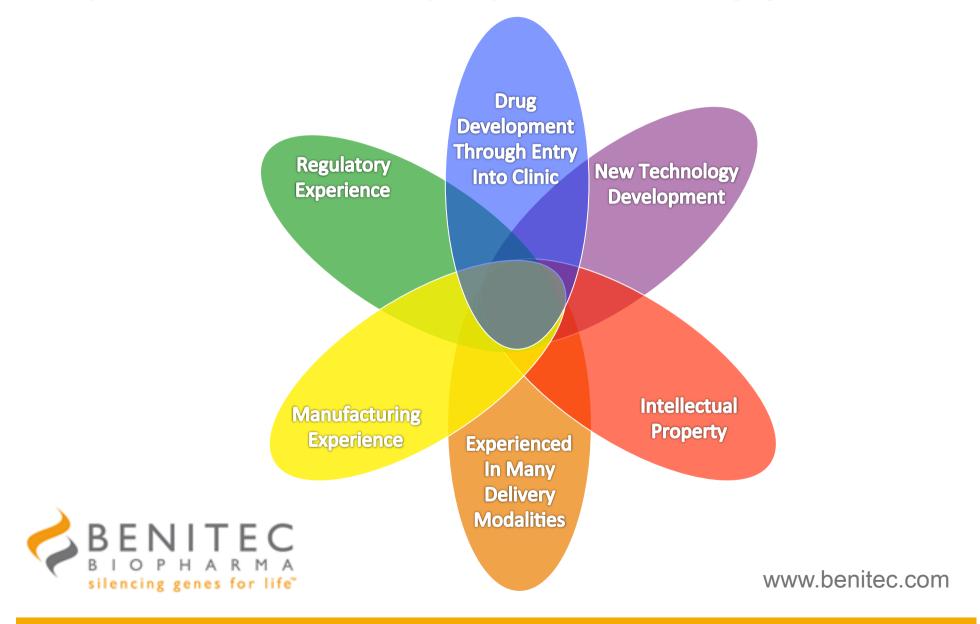
Intellectual Property Summary	Details
Graham family patents:	US 8067383, Granted November 2011 US 8048670, Granted November 2011 US 8053419, Granted November 2011 US 8168774, Granted May 2012 Europe 1555317, Issued January 2012; currently under opposition at the EPO* Europe 1624060, Issued January 2012; currently under opposition at the EPO*
Waterhouse family patents:	Europe 1068311, Accepted April 2011, currently under opposition at the EPO*
Benitec Biopharma- owned patents:	Multi-promoter multi cassette: Europe 1725660, Granted May 2011 Single-promoter, multi-cassette: US 8076471, Granted December 2011 Minigene Expression cassette: US 8129510, Granted March 2012

<sup>\*</sup> part of the standard process for patent granting in Europe)

- ➤ Benitec Biopharma's has been challenged in a number of territories
  - All disputes have been overcome and patents reissued, with the exception of European patents undergoing a standard review



Although shRNA-directed RNAi is routinely practiced on the lab bench, only Benitec Biopharma has all of the necessary components from for bringing it into the clinic



### Commercially focused management and board

#### Management

- MD and CEO: Peter French, MBA, PhD
  - CSIRO, St Vincent's,
  - Cryosite founder.
- CSO: Michael Graham, PhD
  - Inventor of ddRNAi technology
  - CSIRO, Benitec founder
- CBO: Carl Stubbings, BSc
  - Panbio, Quest Diagnostics, Focus Diagnostics
- SVP R&D: David Suhy, PhD
  - Tacere Therapeutics, Avocel, Antara Biosciences, PPD Discovery
- CFO: Greg West, CA
  - Price Waterhouse, Bankers Trust, Deutsche Bank, NZI



#### Board

#### Chairman:

- Peter Francis, LLB, Grad Dip. (Intellectual Property)
  - Partner at Francis Abourizk Lightowlers

#### Directors:

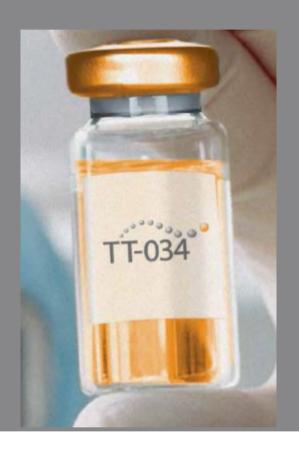
- John Chiplin, PhD
  - Polynoma, Arana, ITI Life Science Fund
- lain Ross, BSc, CH.D.
  - Silence Therapeutics, Tissue Therapies, Ark Therapeutics
- Kevin Buchi
  - Cephalon, Teva, Mesoblast, Tetralogic

#### Key Recent Additions to the team:

- Terrie-Anne Cock, R&D Program Manager
- Sakura Holloway, Internal Patent Counsel
- Tin Mao, Senior Scientist
- Shih-chu Kao, Senior Scientist

## TT-034 trial specifics

- An open label, single dose, dose escalation study in 14 patients infected with genotype 1 HCV
- Goal is to achieve complete and sustained elimination of virus with a single infusion
- Trial sites:
  - Duke Clinical Research Unit, North Carolina - currently dosing & continuing to screen additional patients
  - University of California, San Diego





## Clinical trial endpoints

#### Primary endpoints: safety

- Incidence of treatment-emergent adverse effects
- Changes in clinical and laboratory parameters

#### **Secondary endpoints: efficacy**

- Sustained reduction in HCV viral load
- Assessment of shRNA expression in liver biopsy and serum exosomes



### **Trial cohorts**

Cohort	Dose (vg/kg)	Dose escalation step (log 10)	Total No subjects	Dosing scheme for subjects	Observation period per subject and between cohorts before dose escalation
1	$4.00 \times 10^{10}$	Starting dose	2	Sequential (1+1)	6 week
2	1.25 × 10 <sup>11</sup>	0.5	3	Sequential and parallel (1+2)	6 week
3	4.00 × 10 <sup>11</sup>	0.5	3	Sequential and parallel (1+2)	6 week
4	1.25 × 10 <sup>12</sup>	0.5	3	Sequential and parallel (1+2)	10 weeks
5	4.00 × 10 <sup>12</sup>	0.5	3	Sequential and parallel (1+2)	10 weeks

- DSMB review after first patient in each cohort and between cohorts
- Extensive safety monitoring during 24 weeks observation



## **Update on Phase I/IIa HCV trial:**

First subject was dosed at Duke in Late May

No adverse safety events have been detected as a result of TT-034 dosing

A liver biopsy taken from the subject at Day 21 confirms: TT-034 has transduced liver cells of the subject TT-034 produced low levels of shRNA in the liver cells

DSMB (Data Safety Monitoring Board) recommends that the trial continue as planned

UCSD now active as a recruiting site



## **Key Inclusion Criteria:**

- 1. Signed Informed Consent Form
- 2.  $\geq$  18 years old and  $\leq$  65 years of age
- 3. Females of non-childbearing potential
- 4. Males and their partners must be willing to comply with double barrier contraception
- 5. A history of chronic HCV genotype 1 infection with baseline HCV RNA level of > 100,000 IU/mL, and one or more of the following:
  - Treatment failures or relapse to current SoC
  - Ineligible or unwilling to receive current SoC
- 6. No evidence of cirrhosis at screening
- 7. Alanine aminotransferase levels  $\leq 4 \times$  the ULN
- 8. At least 3 months since prior therapy for HCV



## Key Exclusion Criteria:

- 1. Body mass index < 18.5 or > 30.
- 2. Serum Neutralizing Antibodies to AAV8 (may abrogate transduction)
- 3. Signs of severe liver disease
- 4. Hepatocellular carcinoma or suspicion of HCC
- 5. Positive for human immunodeficiency virus 1 (HIV1) or HIV2 antibody
- 6. Co-infection with hepatitis B virus
- 7. Treatment with an investigational drug within 6 months
- 8. Received an AAV vector at any time, or any other gene transfer agent in the previous 6 months
- 9. Use of immunosuppressive medications within 6 months before, except for inhaled or topical corticosteroids.



# Thank you

