

## ASX ANNOUNCEMENT

### Benitec Presents at Canary Biotech and Healthcare Investor Forum

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**Sydney, Australia, 17 March 2016:** Benitec Biopharma Limited (ASX: BLT; NASDAQ: BNTC; NASDAQ: BNTCW), a clinical-stage biotechnology company developing innovative therapeutics based on its gene silencing technology, DNA-directed RNA interference (ddRNAi), is pleased to announce that Chief Business Officer, Carl Stubbings will be presenting today at the Canary Biotech and Healthcare Investor Forum in Sydney.

A copy of the presentation is included in this announcement.

For further information regarding Benitec and its activities, please contact the persons below, or visit the Benitec website at [www.benitec.com](http://www.benitec.com)

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**About Benitec Biopharma Limited:**

Benitec Biopharma Limited (ASX: BLT; NASDAQ: BNTC; NASDAQ: BNTCW) is a clinical-stage biotechnology company developing innovative therapeutics based on its patented gene-silencing technology called ddRNAi or 'expressed RNAi'. Based in Sydney, Australia with labs in Hayward, CA (USA) and collaborators and licensees around the world, the company is developing ddRNAi-based therapeutics for chronic and life-threatening human conditions including hepatitis B, wet age-related macular degeneration and OPMD. Benitec has also licensed ddRNAi to other biopharmaceutical companies for applications including HIV/AIDS, Huntington's Disease, chronic neuropathic pain and retinitis pigmentosa.

**Safe Harbor Statement:**

This press release contains "forward-looking statements" within the meaning of section 27A of the US Securities Act of 1933 and section 21E of the US Securities Exchange Act of 1934. Benitec has tried to identify such forward-looking statements by use of such words as "expects," "intends," "hopes," "anticipates," "believes," "could," "may," "evidences" and "estimates," and other similar expressions, but these words are not the exclusive means of identifying such statements. Such statements include, but are not limited to, any statements relating to Benitec's pipeline of ddRNAi-based therapeutics, including the initiation, progress and outcomes of clinical trials and any other statements that are not historical facts. Such forward-looking statements involve risks and uncertainties, including, but not limited to, risks and uncertainties relating to the difficulties or delays in our plans to develop and potentially commercialize our product candidates, the timing of the initiation and completion of preclinical and clinical trials, the timing of patient enrolment and dosing in clinical trials, the timing of expected regulatory filings, the clinical utility and potential attributes and benefits of ddRNAi and our product candidates, potential future out-licenses and collaborations, our intellectual property position and duration of our patent portfolio, the ability to procure additional sources of financing and other risks detailed from time to time in filings that Benitec makes with US Securities and Exchange Commission, including our most recent annual report on Form 20-F and our reports on Form 6-K. Such statements are based on management's current expectations, but actual results may differ materially due to various factors, including those risks and uncertainties mentioned or referred to in this press release. Accordingly, you should not rely on those forward-looking statements as a prediction of actual future results.



**Benitec Biopharma**  
**NASDAQ: BNTC**  
**ASX: BLT**

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# Company Overview



## NOVEL GENE SILENCING PLATFORM

ddRNAi combines RNAi with gene therapy delivery to potentially provide “one shot” treatments and cures for a variety of diseases

## FOCUSED PIPELINE

Programs in indications with high unmet clinical need or large patient populations such as hepatitis B, OPMD and AMD

## COMMERCIAL STRATEGY

Three-pronged approach – commercialize in-house, out-license, partner

## IP PORTFOLIO

Portfolio of patents, patent applications, and rights to intellectual property directed to our ddRNAi platform and each product candidate



- Our ddRNAi technology combines RNAi with gene therapy to potentially provide “one shot” treatments and cures for a variety of diseases
- Strategic framework for development – focus on diseases with high unmet needs with greatest commercial upside
- Technology developed in Australia by CSIRO (Commonwealth Scientific and Industrial Research Organisation)
- Global team – positioning ourselves amongst other RNAi companies in the US
- Benitec listed on the ASX in 1997 and NADSAQ in 2015; Australia corporate office in US lab



# Technology:

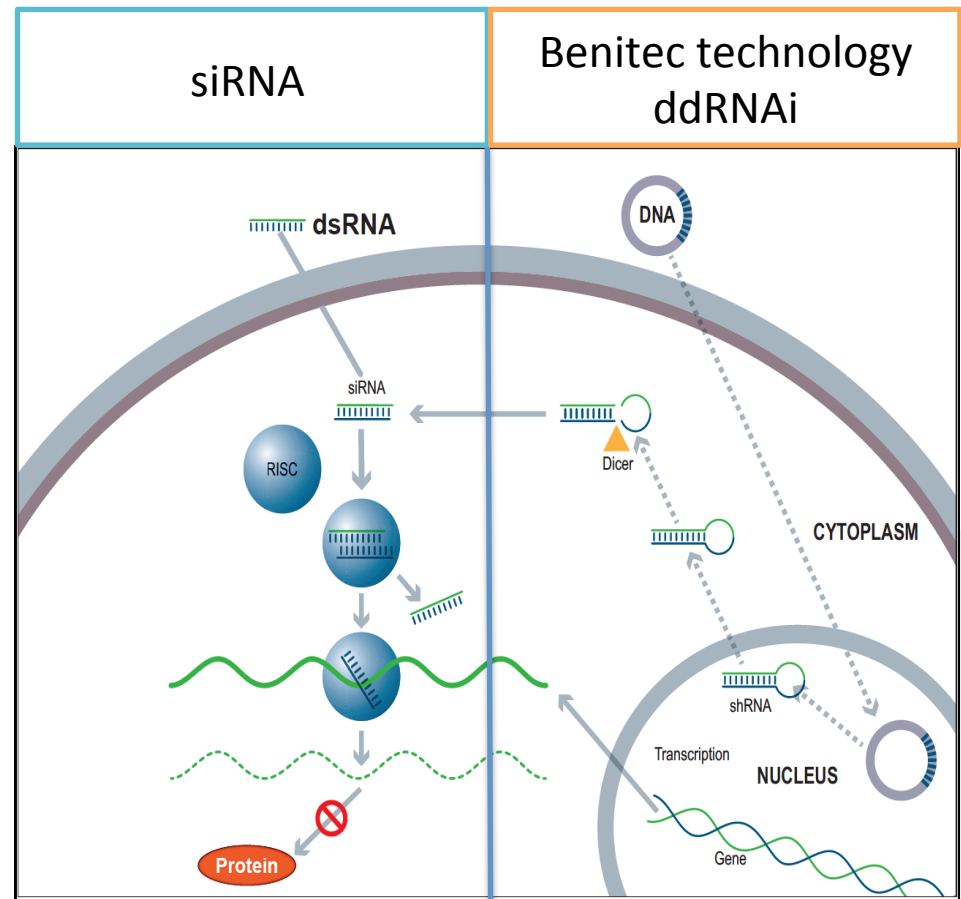
A long-lasting method for  
turning off disease-associated  
genes





# Our Technology: DNA-directed RNAi Therapeutics


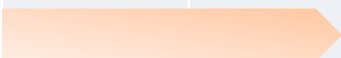
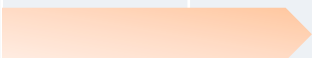
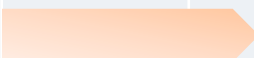
- Uses gene therapy vectors for different tissue distribution
- Steady state levels of drug
- Long term expression from a single injection
- Multi target from a single drug
- Possibility of silence/replace strategies





# Pipeline Programs

# Pipeline Programs

Program	Discovery	Preclinical	IND-Enabling	Phase I/II	Phase III	Status
Infectious Disease						
Hepatitis C <i>TT-034</i>						<ul style="list-style-type: none"><li>• Nine patients dosed</li><li>• Program terminated February 2016</li><li>• Safe and well tolerated</li><li>• All patients dosed will be followed to study completion</li><li>• Data package due Q4 2016</li></ul>
Hepatitis B <i>BB-HB-331</i>						<ul style="list-style-type: none"><li>• In vitro POC completed</li><li>• In vivo POC underway</li></ul>
Ocular Disease						
AMD <i>BB-AMD-211</i>						<ul style="list-style-type: none"><li>• Vector screening in process</li></ul>
Genetic Disease						
OPMD <i>BB-OP-1-31</i>						<ul style="list-style-type: none"><li>• Finalization of clinical candidate in process</li></ul>

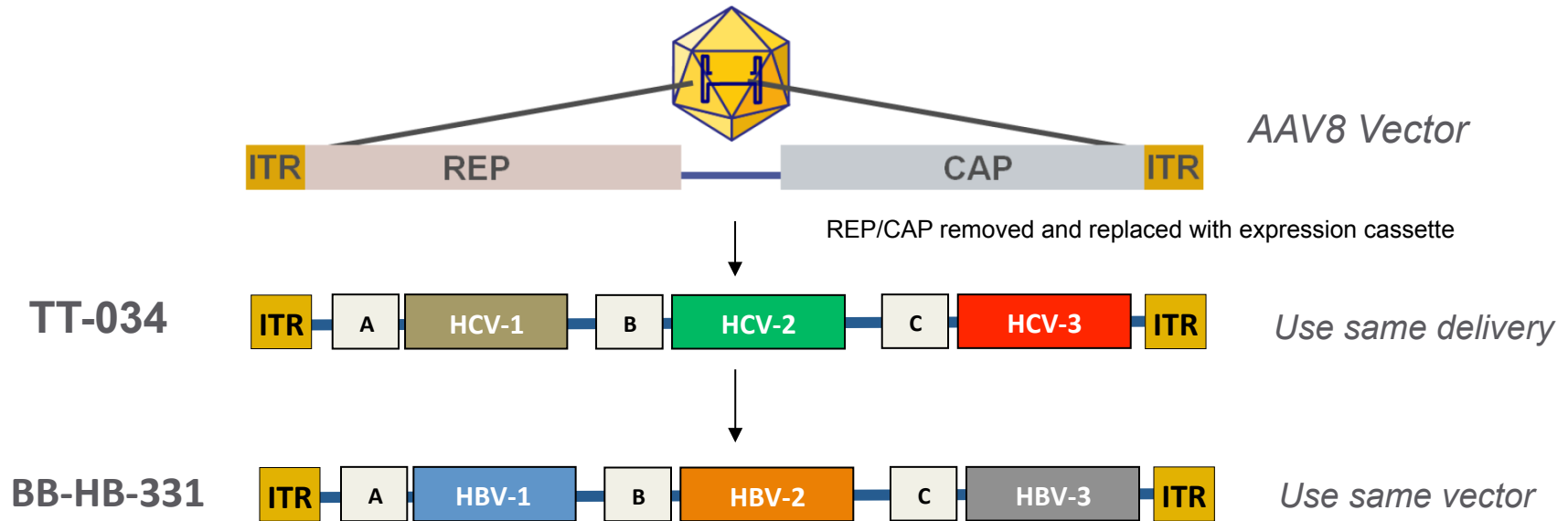
# Out-licensed Programs

Focus	Indication	Product Candidate	Company	Discovery	Preclinical	Phase I/IIa
Infectious Disease	HIV/AIDs	Cal-1	Calimmune			
Cancer	Cancer Immunotherapy	dCellVax	Regen Biopharma			
Ocular Disease	Retinitis Pigmentosa	RhoNova	Genable			
Genetic Disease	Huntington's Disease		uniQure			
Central Nervous System	Intractable Neuropathic Pain		Circuit Therapeutics			



How the  
Technology is  
Applied

- Hepatitis B is a DNA virus with an unmet medical need
- 240 million infected worldwide, resulting in up to 780,000 deaths per year
- Hepatitis B virus causes 60-80% of the world's primary liver cancers
- Existing therapies have single digit percentage cure rates and require life long treatment
- Ending hepatitis B with a single infusion is a huge advantage over other treatments



- Similar HCV construct for HBV
- May be able to fast track REG/TOX studies using TT-034 data as part of IND package
- TT-034 clinical data guides HBV protocol development and simplifies regulatory path
- Goal is to achieve complete and sustained elimination of virus with a single infusion

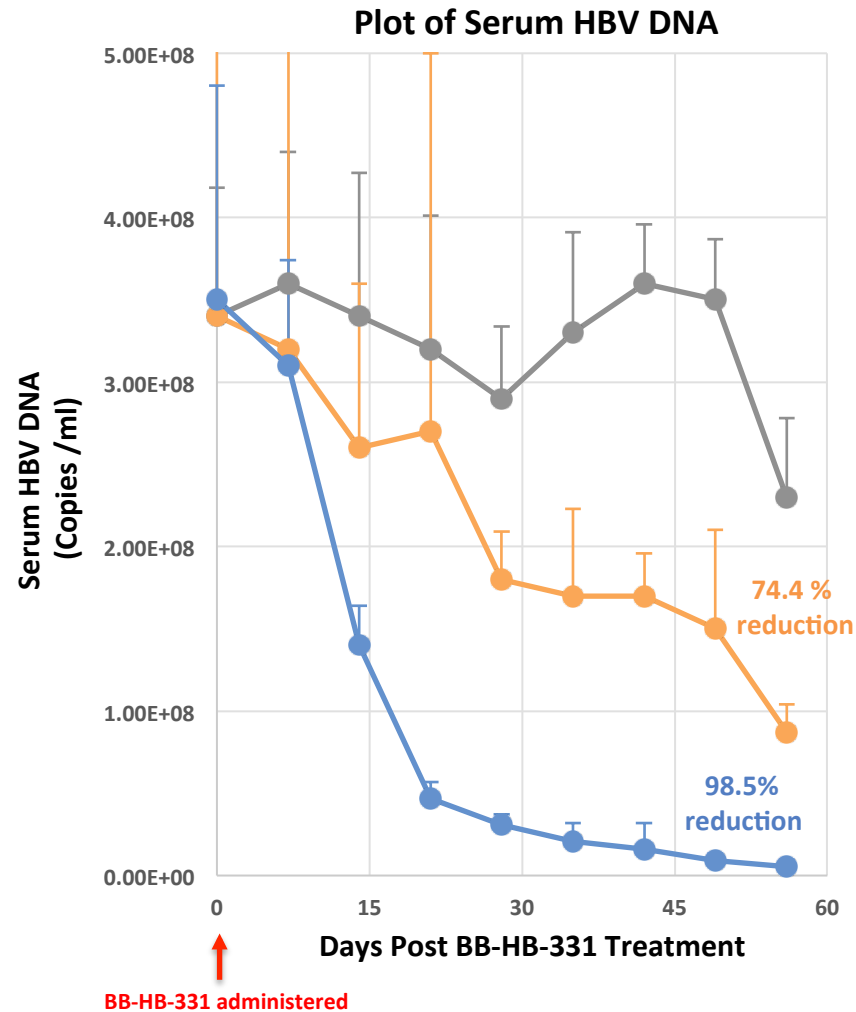
# AAV Delivery Systems – Getting the Product into the Target Area

- Benitec uses a very specific and effective viral delivery system – AAV
- To date, AAV has been used in 137 clinical trials with an excellent safety record
- Sustained expression (months/years) following single injection
- Complete transduction of liver hepatocytes with serotype 8 (AAV8)

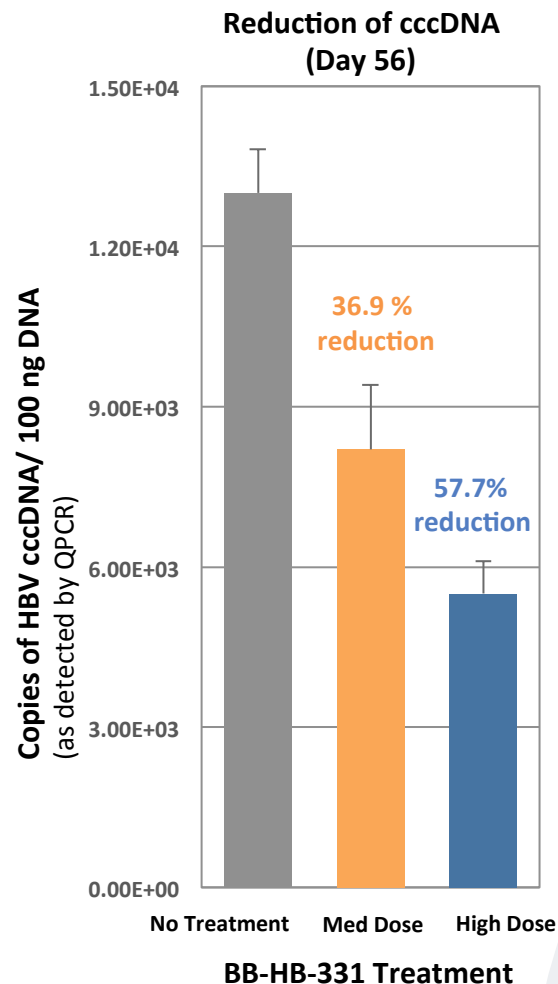
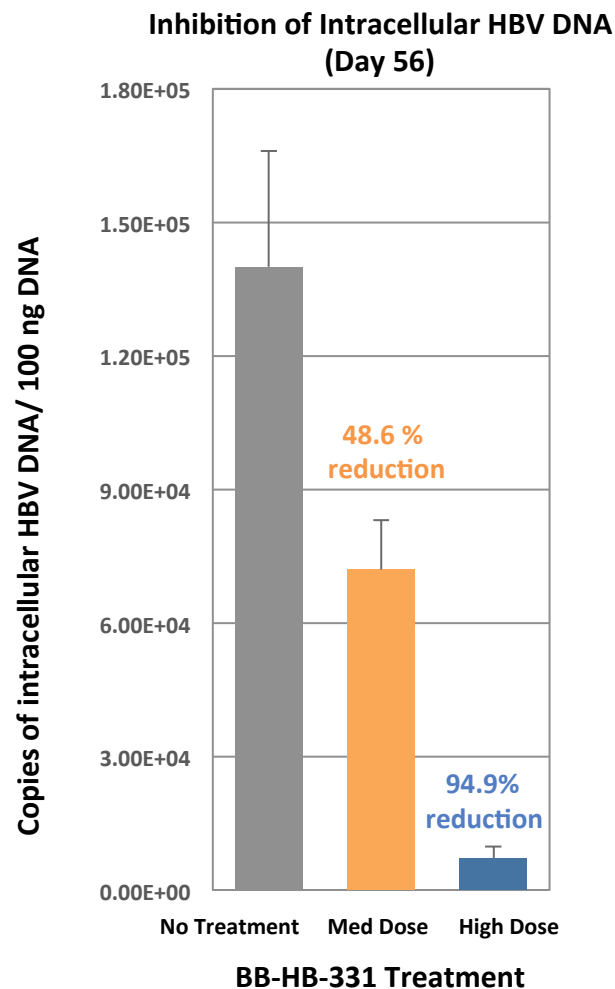


- Following a single administration, the study showed that BB-HB-331 reduced serum HBV DNA by 98.5% in a hybrid mouse model in which their liver cells have been replaced with with human hepatocytes (liver cells)
- Treatment with BB-HB-331 resulted in a 97.6 and 93.6% reduction in the levels of hepatitis B surface antigen (HBsAg) and e-antigen (HBeAg) respectively, as compared to untreated controls
- BB-HB-331 treatment also resulted in a 94.9% reduction in the levels of intracellular HBV DNA and a 57.7% reduction in cccDNA, the latter is a key obstacle for a cure of chronic hepatitis B
- We anticipate that BB-HB-331 may be used as either as a monotherapy or in combination with other hepatitis B drugs to treat the disease

# Preclinical Results: BB-HB-331 in PXB Mice



# Preclinical Results: BB-HB-331 in PXB Mice



## Next Steps

- Benitec is working on pharma partnering opportunities ahead of clinical development
- The Company will commence an IND filing in Q3 2017
- **Hepatitis B preclinical data presents a compelling story to Big Pharma and Investors**

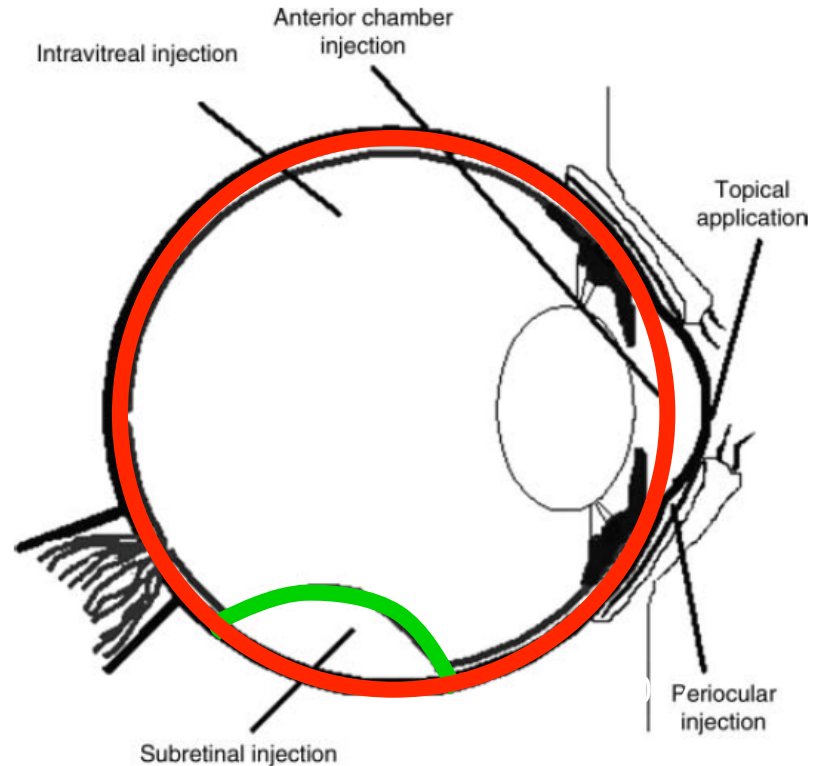
# Age Related Macular Degeneration: BB-AMD-211 and BB-AMD-231

- Designed to provide sustained inhibition of VEGF-A from a single intravitreal injection
- Two shots on goal:
  - BB-AMD-211 is being developed for wet AMD
  - BB-AMD-231 is being developed for wet and dry AMD
- BB-AMD-231 is a second generation product candidate designed to target three different genes, VEGF receptor 2, PDGF- $\beta$  and human complement factor B, all of which play a role in progression of AMD
- Developing intravitreal delivery vector (AAV) in collaboration with 4D Molecular Therapeutics – unique and commercially viable means of delivery
- AAV Vector screening in process



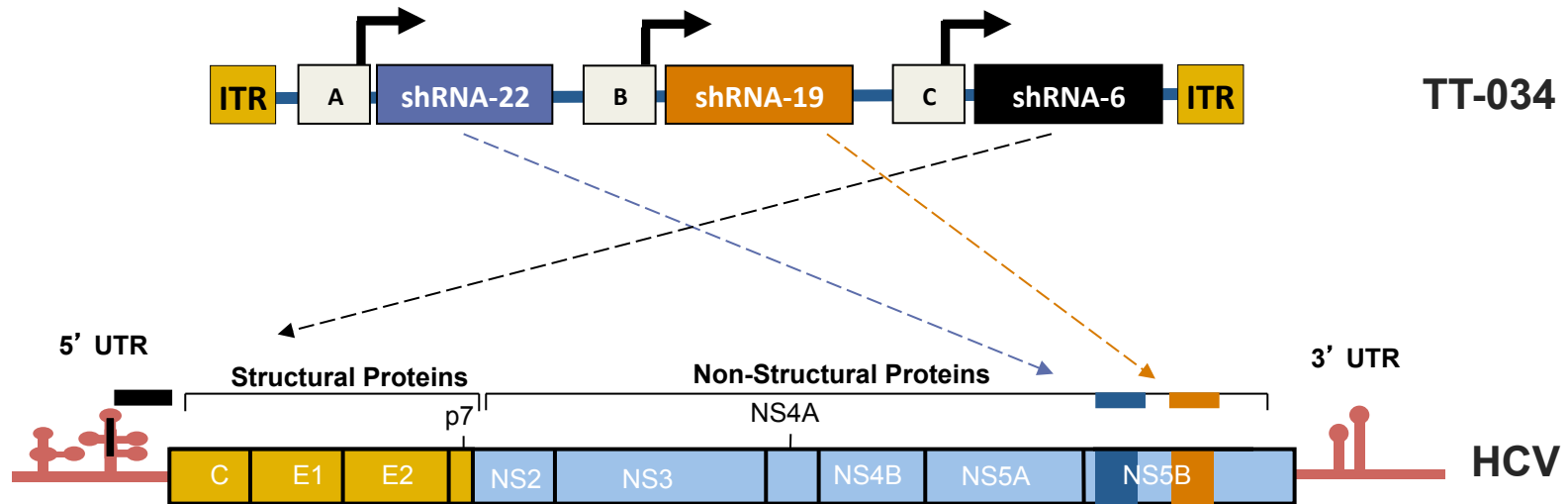
# New AAV Vectors for Superior Delivery

- Benitec has an exclusive license for RNAi applications from 4D Molecular Therapeutics
- Vectors developed using a intravitreal specific route of delivery
- Intravitreal is more commercially viable than a subretinal injection (typically used by most gene therapy vectors for ocular diseases)
- Vectors developed through 'directed evolution' process



- Benitec is developing a ddRNAi-based therapeutic for the treatment of OPMD, a rare genetic disease
- OPMD is an autosomal-dominant inherited, slow-progressing, late-onset degenerative muscle disorder
- Benitec utilizes a “silence and replace” approach designed to silence the expression of mutant PABPN1 gene and replace the mutant gene with the normal PABPN1
- Monotherapy delivered via intramuscular injection using an AAV vector
- Collaborating with Royal Holloway University of London
- Finalisation of clinical candidate in process

# Hepatitis C – Scientific Construct



- Three independently transcribed RNAi elements target three separate, well-conserved regions of the HCV genome (diagram above)
- Delivered with AAV8 vectors (delivery system) through an intravenous infusion
- Goal is to achieve complete and sustained elimination of virus with a single infusion
- **Further development of this program was halted in February 2016 due to commercial reasons**



## Primary Endpoints (Safety):

- Incidence of adverse events
- Changes in clinical parameters

## Secondary Endpoints (Efficacy):

- Sustained reduction in HCV viral load in the blood
- Assessment of TT-034 levels in day 21 liver biopsy
- Assessment of shRNA expression in liver biopsy

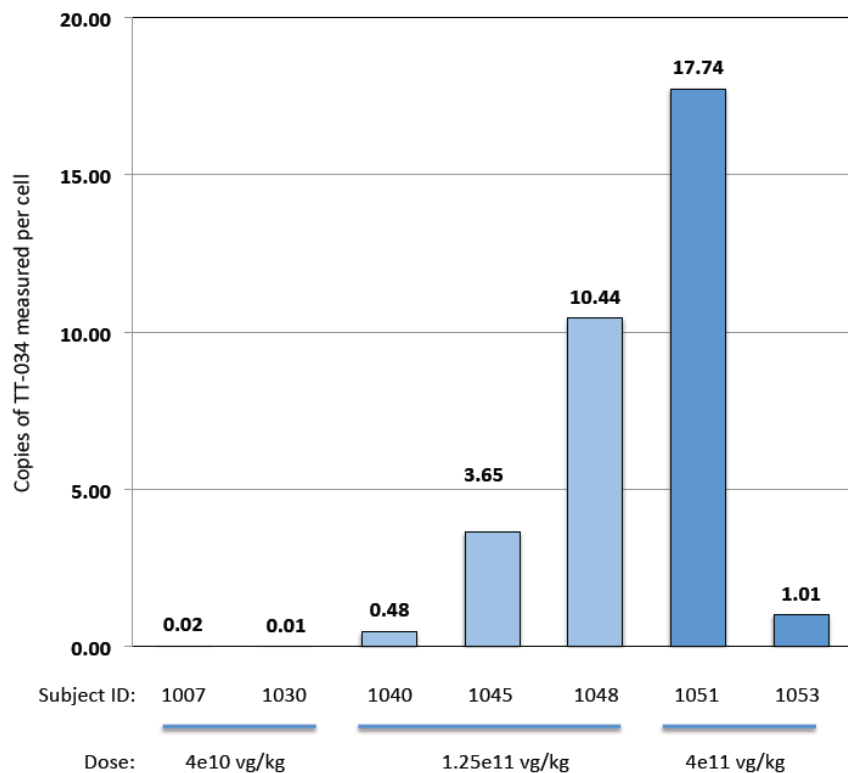
## Trial sites

- Duke Clinical Research Unit, Durham, North Carolina
- University of California, San Diego, California
- Texas Liver Institute, San Antonio, Texas
- Methodist Health System Clinical Research Institute, Dallas, Texas

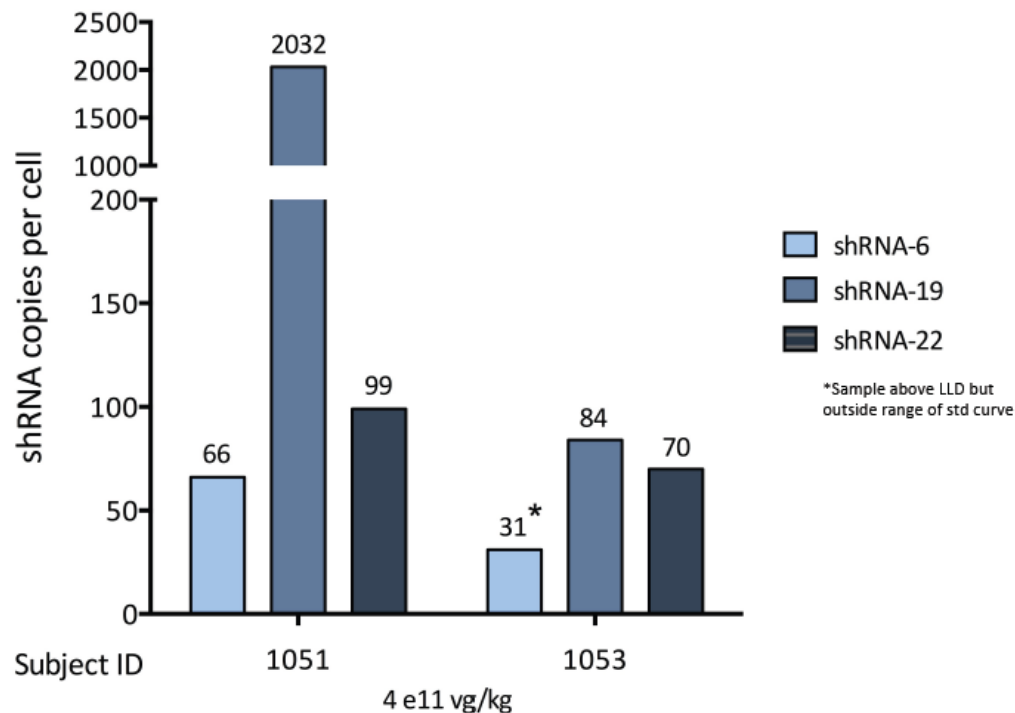


- No reported serious adverse events relating to TT-034
- Cohort two biopsies detected levels of TT-034 in the liver cells yielding 0.48, 3.65 and 10.44 copies of TT-034 DNA per cell
- The first subject administered with the third dose (4.00E11 vg/kg) had 17.74 copies of TT-034 per cell, indicating that a significant portion of their liver cells have been transduced
- At higher doses, substantial portions of hepatocytes are transduced and result in concurrent dose-dependent expression of anti-HCV shRNAs
- Interim data is encouraging

## TT-034 DNA levels



## Anti-HCV shRNA levels



- TT-034 has delivered important safety data and learnings that will inform the hepatitis B trial
- Hepatitis C trial will not progress beyond cohort 4; full data set to be reported in Q4 2016
- Benitec will focus on hepatitis B, AMD and OPMD programs where there is stronger partnering interest
- **The data collected from this clinical study has been exceptionally valuable in establishing the safety of the product as well as defining relationships between the amount of drug administered and the level of transduction and anti-HCV shRNA expression**

# Valuations of Our Peers

Company	Technology	Stage	Market Cap <sup>1</sup>
Alnylam	siRNA	Phase III	\$6 Billion
Ionis (previously Isis)	Antisense	Marketed	\$5.1 Billion
Arrowhead	siRNA	Phase II	\$277 Million
Dicerna	siRNA	Phase I	\$103 Million
Silence	siRNA	Phase II	\$94.5 Million
Benitec	ddRNAi	Phase I/IIa	\$13.5 Million

1. As of March, 2016
2. Converted into US\$

## ddRNAi Technology (CSIRO Licensed)

- International coverage for ddRNAi platform technology
- 30 Granted Patents (in-licensed)
- 9 Patent Applications (in-licensed)
- Expected expiration: 2019

## Additional IP Portfolio (Benitec Owned)

- Target indications, product candidates, technology improvements
- 32 Granted Patents (owned, co-owned or in-licensed)
- 29 Patent Applications (owned, co-owned or in-licensed)
- Expected expiration for target indications and product candidates at least 2025 and for technology improvements at least 2021

# Company Financial Snapshot

Key Financial Details	ASX: BLT NASDAQ: BNTC NASDAQ: BNTCW
BLT Share Price as of 15 March, 2016:	AU \$0.125
Market Capitalisation as of 15 March, 2016:	AUD \$18.3M
Issued Securities as of December, 2015:	
Ordinary shares	146,529,096
Options	38,566,203
Cash Balance as of 31 December, 2015:	AU \$24.5M
Offices:	Sydney, Australia San Francisco, CA

# Management Team

<b>Greg West</b> <b>Chief Financial Officer and Interim CEO</b>	<ul style="list-style-type: none"><li>• Former CFO, Immune Systems Therapeutics</li><li>• Prior roles at PriceWaterhouse, Bankers Trust, Deutsche Bank and NZI</li></ul>
<b>Dr. David Suhy</b> <b>Chief Scientific Officer</b>	<ul style="list-style-type: none"><li>• Former SVP of Research &amp; Development, Benitec Biopharma</li><li>• Prior roles at Antara Biosciences and PPD Discovery</li></ul>
<b>Carl Stubbings</b> <b>Chief Business Officer</b>	<ul style="list-style-type: none"><li>• Former VP of Sales &amp; Marketing, Focus Diagnostics</li><li>• Prior role at PanBio Pty Ltd</li></ul>
<b>Georgina Kilfoil</b> <b>Chief Clinical Officer</b>	<ul style="list-style-type: none"><li>• Former VP of Clinical Operations, Benitec Biopharma</li><li>• Prior roles at Anthera Pharmaceuticals, InClin and Peninsula Pharmaceuticals</li></ul>
<b>Dr. Michael Graham</b> <b>Head of Discovery and Founding Scientist</b>	<ul style="list-style-type: none"><li>• Discoverer of ddRNAi at CSIRO; Former Senior Research Fellow, University of Queensland</li><li>• Prior roles at Benitec, QDPI and CSIRO</li></ul>
<b>Sakura Holloway</b> <b>SVP, Corporate Development and IP Counsel</b>	<ul style="list-style-type: none"><li>• Former Head of RNAi Commercialization, CSIRO</li><li>• Prior roles at Cephalon Australia (Arana Therapeutics) and Garvan Institute, Sydney</li></ul>



<b>Peter Francis Chairman</b>	<ul style="list-style-type: none"><li>• Partner at Francis Abourizk Lightowlers Lawyers</li><li>• Former Director, Xceed Capital</li></ul>
<b>Kevin Buchi Director</b>	<ul style="list-style-type: none"><li>• President and CEO, TetraLogic Pharmaceuticals</li><li>• Director at Stemline Therapeutics, Inc., Forward Pharma A/S, Alexza Pharmaceuticals, Inc., and Epirus Biopharmaceuticals</li></ul>
<b>Dr. John Chiplin Director</b>	<ul style="list-style-type: none"><li>• Director at Cynata Pty</li><li>• Former CEO at Polynoma, Arana Therapeutics, and ITI Life Science Fund; Former Director at Medistem, Inc.</li></ul>
<b>Iain Ross Director</b>	<ul style="list-style-type: none"><li>• Chairman at Biomer Technology Ltd., and Premier Veterinary Group, plc</li><li>• Director at Amarantus Bioscience, Inc., Anatara Lifesciences, Novogen</li></ul>

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