

ASX ANNOUNCEMENT

BENITEC BIOPHARMA LIMITED (ASX: BLT, OTC: BTEBY)

11 March 2015

BENITEC BIOPHARMA PRESENTS AT 27th ANNUAL ROTH CONFERENCE

- **Benitec invited to 27th Roth Conference**
- **Dr. David Suhy, Senior Vice President R&D, presents an update on the company's programs**
- **Roth Conference draws 500 presenting companies and 3,000 attendees**

Sydney, Australia: Benitec Biopharma's Senior Vice President of Research & Development, Dr. David Suhy was invited to present a comprehensive update on the company's extensive pipeline of ddRNAi-based programs at Roth's invitation-only investor conference. The conference is being held at the Ritz-Carlton Hotel at Laguna Beach California USA from 8-11 March.

The presentation was given at 2.30pm local time on 10 March.

A copy of Dr. Suhy's presentation follows.

For further information regarding Benitec and its activities, please contact the persons below, or visit the Benitec website at www.benitec.com

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About Benitec Biopharma Limited

Benitec Biopharma Limited is an ASX-listed biotechnology company (ASX:BLT; OTC:BTEBY) which has developed a 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 C and B, drug resistant lung cancer and wet Age-related Macular Degeneration. Benitec has also licensed ddRNAi to other biopharmaceutical companies for applications including HIV/AIDS, Huntington's Disease, chronic neuropathic pain and retinitis pigmentosa. For more information visit www.benitec.com.



GENE SILENCING: A quiet revolution in healthcare

27th Annual Roth Conference
10 March 2015

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.

This document does not constitute an offer, solicitation or recommendation in relation to the subscription, purchase or sale of securities in any jurisdiction. Neither this presentation nor anything in it will form any part of any contract for the acquisition of securities.

Company Financial Snapshot



Key financial details	ASX:BLT OTC: BTEBY
Share Price as of 2 nd March 2015:	AUD \$0.865
Market Capitalisation as at 9 th January 2015:	AUD \$100M
Issued Securities as at 21 st August 2014:	
Ordinary shares	115,218,993
Options	22,695,098
Cash balance at 31 st December 2014:	AUD \$27.5 M

Strong Investment Case



- Patented approach to utilize RNA Interference technology for the treatment of human diseases
- ddRNAi combines RNAi with gene therapy delivery and results in compounds designed for a 'single shot cure' against human diseases
- Hepatitis C (TT-034) Phase I/IIa trial
- Successful TT-034 trial will validate approach for hepatitis C and other human diseases
- Raised AUD \$31.5m; funding achieved in Feb 2014 will take TT-034 trial to Phase IIb and progress other programs & platform development
- Pipeline of 'company making' programs focused mainly on large indications with a strong technology fit

Value, investment & opportunity



Company	Technology	Stage	Market Cap (US \$M)
Alnylam	siRNA	Phase III	7,820
Isis	Antisense	Phase II/III	8,500
Arrowhead	siRNA	Phase II	436.46
Dicerna	siRNA	Phase I	328.62
Silence	siRNA	Phase II	157.11
Benitec	ddRNAi	Phase I/IIa	95.2*

ddRNAi: the gene-silencing revolution

ddRNAi technology:

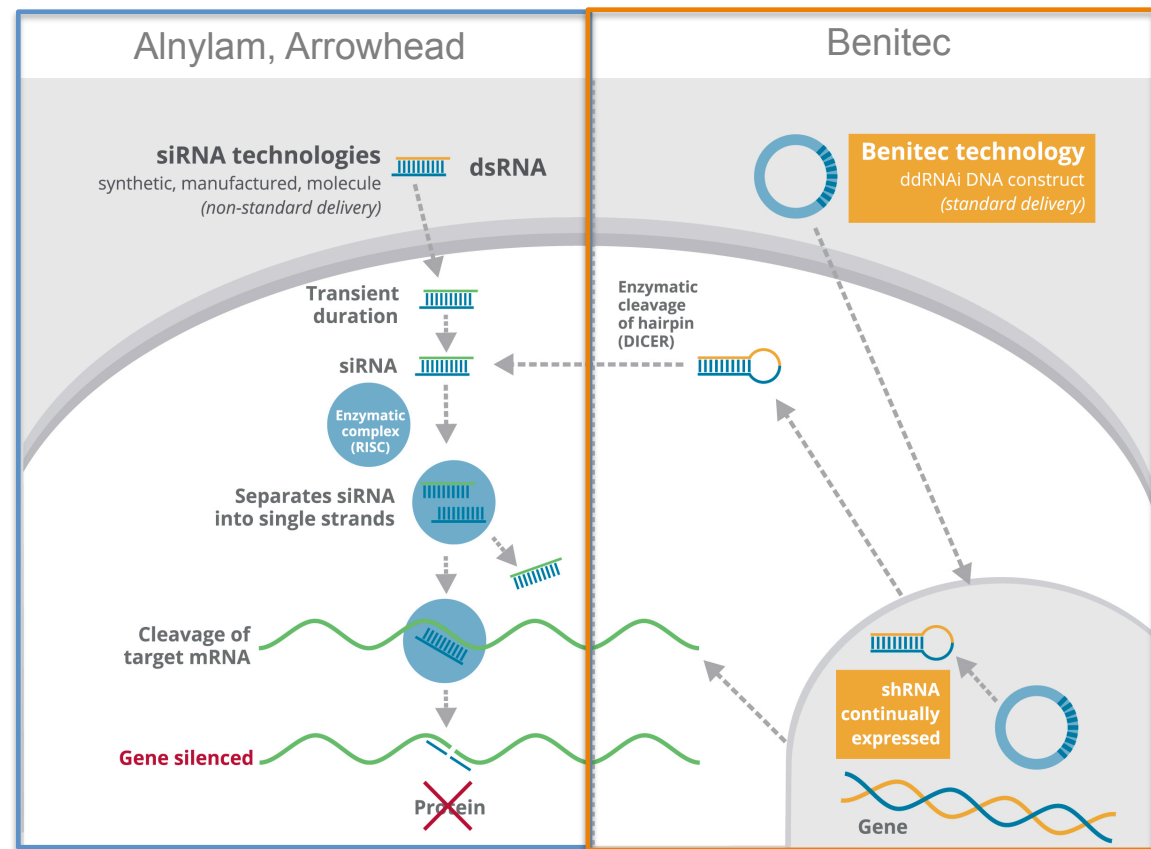
- 'Turns off' disease-associated genes
- Uses power & specificity of RNAi

ddRNAi delivery:

- Uses gene therapy vehicles
- Longer lasting (for life of target cells)
- Avoids Toll-Like Receptor responses

Unique benefits:

- Multiple therapy in one molecule (one gene, multiple sites, multiple genes)
- Protected by over 100 patents (technology & specific diseases)

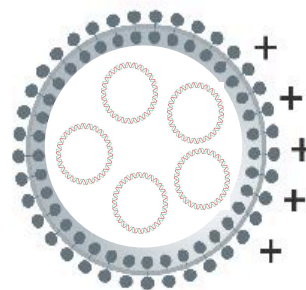


ddRNAi: agnostic on delivery

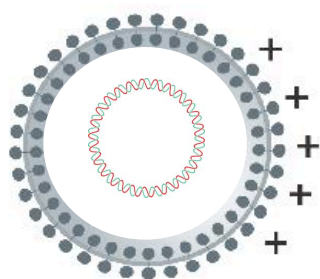
Alternate delivery systems used for the ddRNAi platform



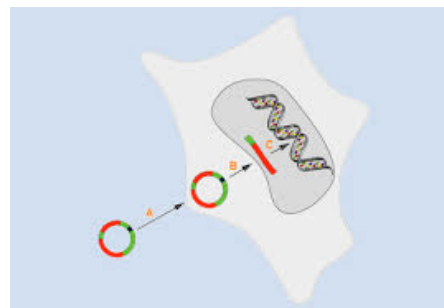
Viral Vectors



Nanoparticle delivery of
mini-circle DNA or mini-
transcription cassettes

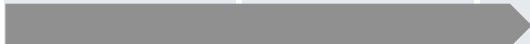
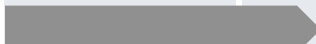
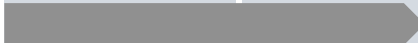

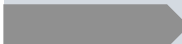


Nanoparticle
delivery of
DNA plasmids





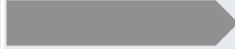


Delivery of transduced
cells expressing shRNA
Including stem cells

Pipeline programs

Focus	Indication	Partners / Collaborators	Discovery	Pre-clinical	Clinical
Infectious Disease	Hepatitis C				
	Hepatitis B	Biomics Biotechnology (JV)			
Cancer	Drug Resistant Lung Cancer	University of New South Wales (RC)			
Ocular Disease	AMD				
Genetic Disease	OPMD	Royal Holloway London University (RC)			

Sub-licensed programs

Focus	Indication	Partners/Collaborators	Discovery	Pre-clinical	Clinical
Infectious Disease	HIV/AIDS	Licensed to Calimmune			
Cancer	Cancer Vaccines	Licensed to Regen BioPharma			
Ocular Disease	Retinitis Pigmentosa	Licensed to Genable			
Genetic Disease	Huntington's Disease	Licensed to UniQure			
Neuropathic Pain	Sodium NAV 1.7 Ion Channel	Licensed to Circuit			

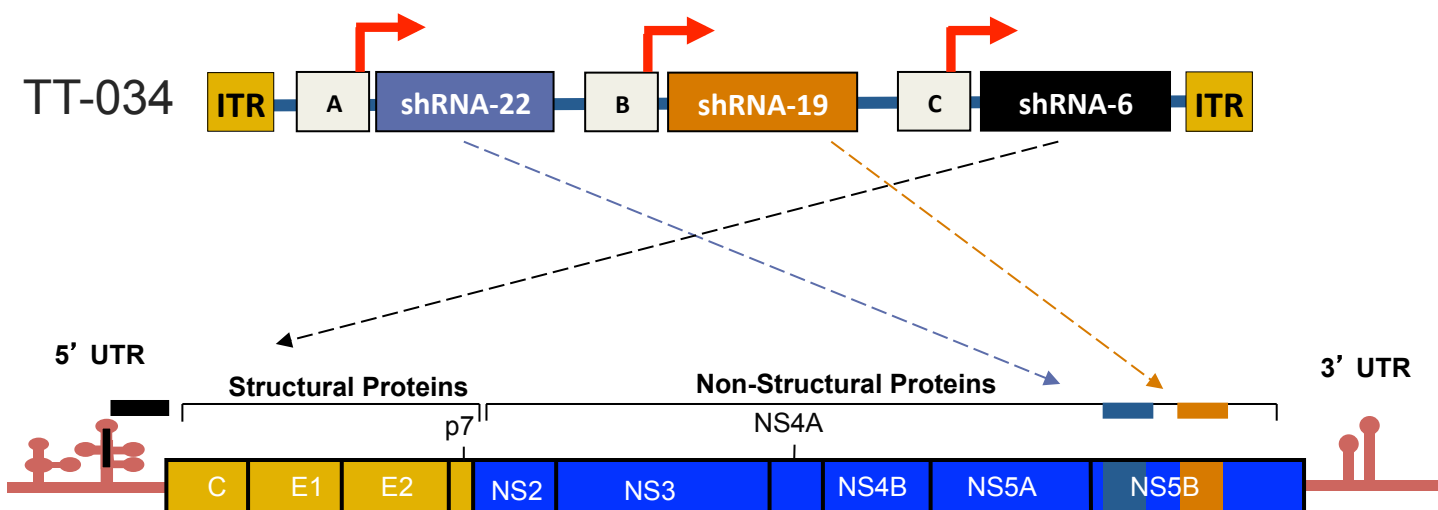
TT-034 is a ddRNAi therapeutic that is intended as a “one-shot-cure”

- Recombinant AAV genome delivered via an AAV8 vector (high liver tropism)
- Continuously produces anti-viral shRNAs for over 180 days
- shRNAs target three separate, well conserved regions of HCV genome
- Near complete liver cell coverage

Goal is to achieve complete and sustained elimination of virus with a single infusion

- Eliminates long treatment courses and patient compliance issues
- Very low toxicity in animal studies
- Potential for combination with small molecule therapies for enhanced efficacy

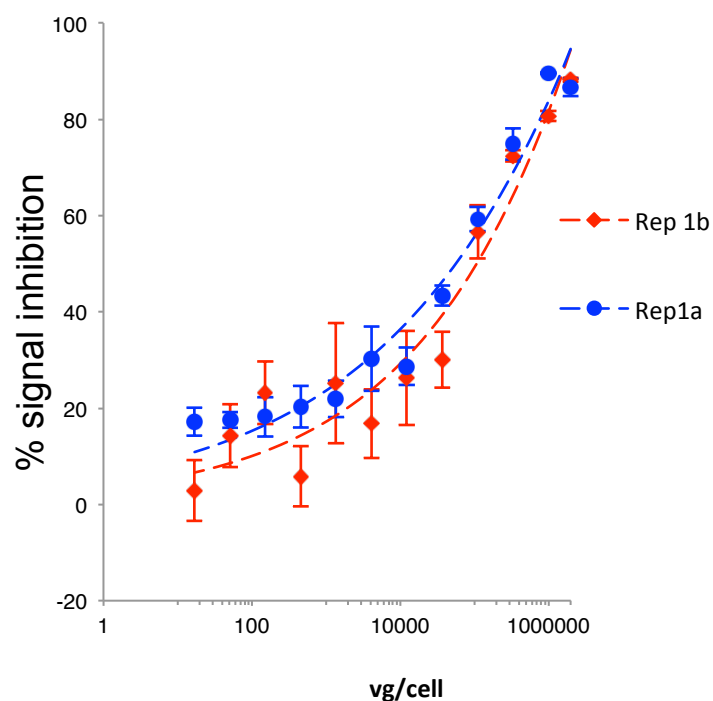
Design of TT-034



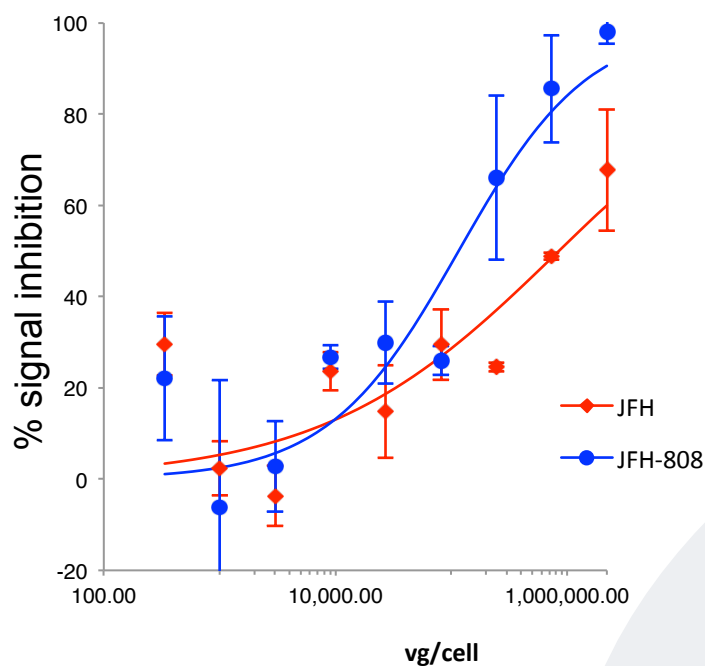
- Three independently transcribed RNAi elements target three separate, well-conserved regions of the HCV genome and helps prevent the generation of viral escape mutants
- Combination drug in one therapeutic entity provides broad patient applicability, while maintaining specificity
- Patent to 2026

TT-034 activity against HCV replicon and HCVcc systems

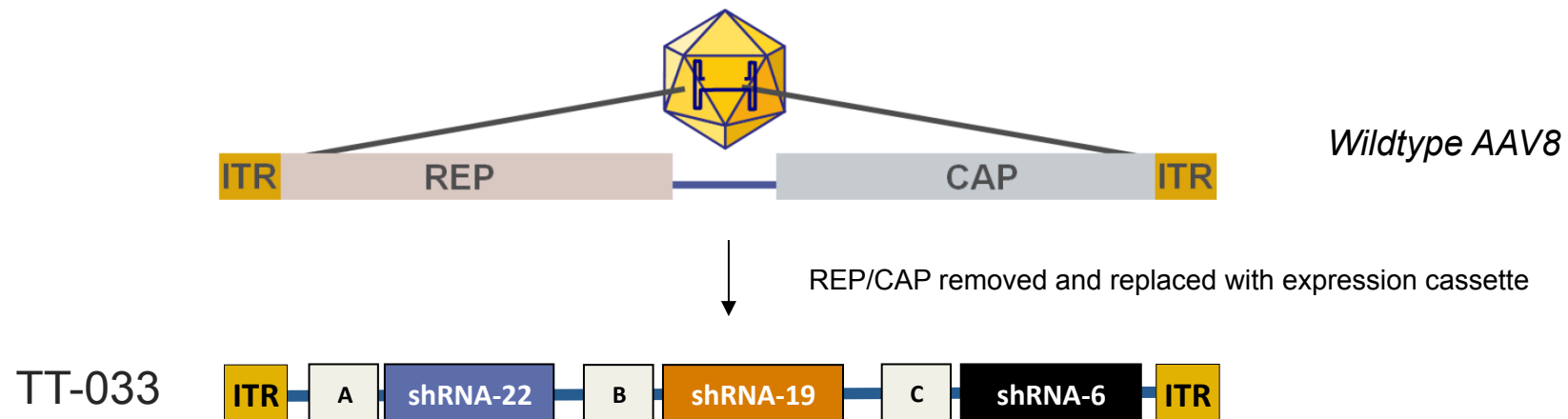
HCV replicon



HCVcc



Use of AAV for delivery



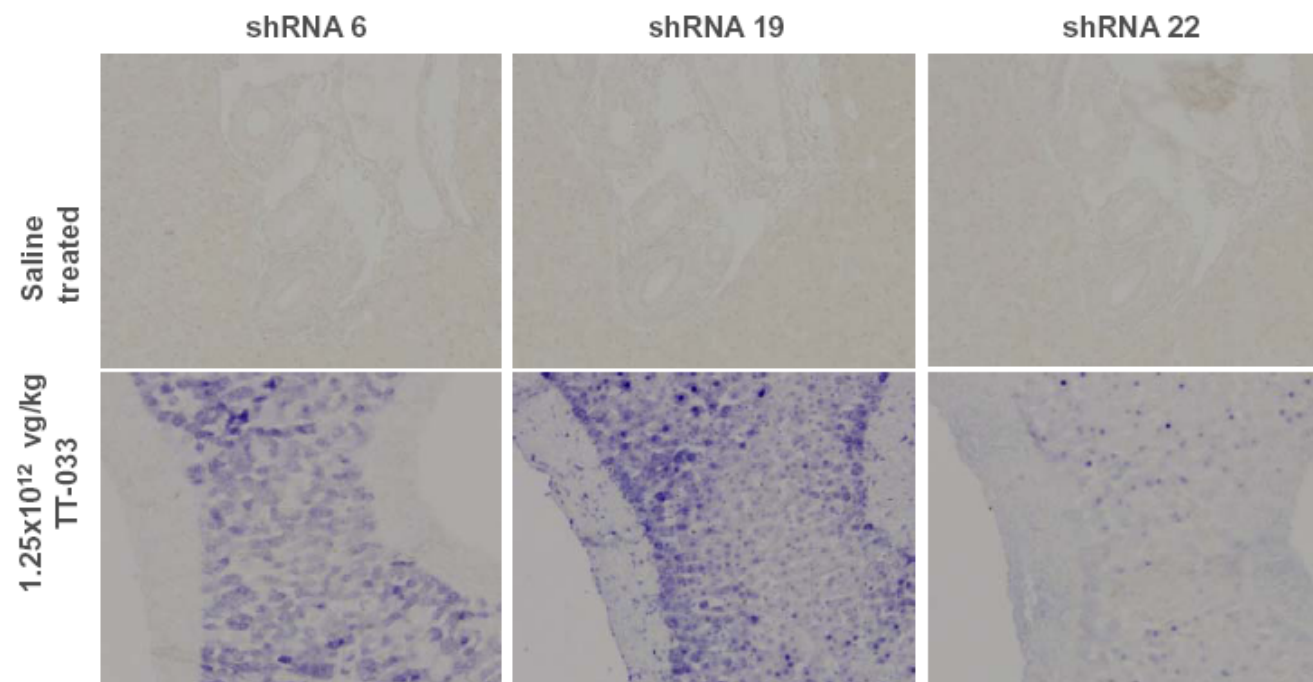
- Non-integrating, non-pathogenic viral delivery system
- Has been used in over 100 clinical trials
- Sustained expression (months/years) of active drug following single injection
- Differing AAV serotype tropisms allow for tissue specific delivery

TT-034: complete hepatocyte transduction in non human primates

animal	SSAN3 Female	
dose	1.25 E12 vg/kg	
	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
Ileum	0.1	0.0
Duodenum	0.1	0.0
Colon	0.1	0.0
Ovary	0.1	0.0
Brain-Diencephalon	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	0.0	0.0
Gallbladder	Tissue NA	
Adrenals	Tissue NA	
LN-axillary	Tissue NA	

Biodistribution Analysis

In Situ Hybridization

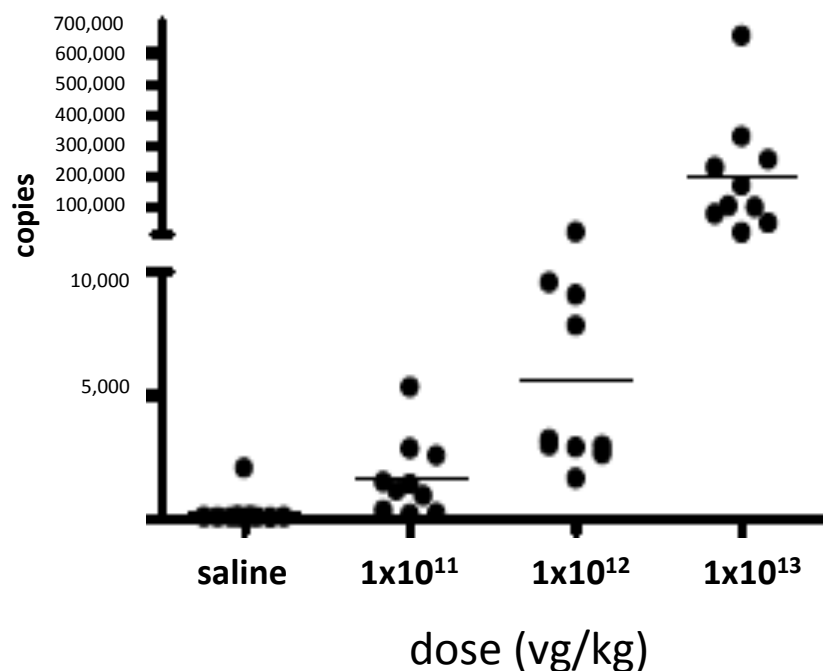


TT-034: Durability of shRNA expression in liver from a single IV administration

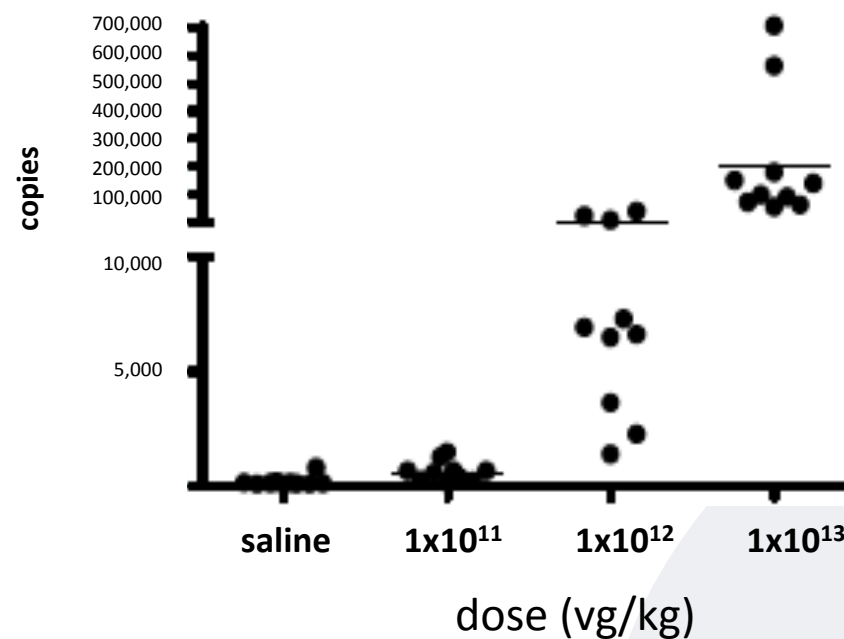


Levels of shRNA22 in murine hepatic tissues

60 days post dosing



180 days post dosing



Hepatitis C – TT-034 update



Open-label dose-escalation Phase I/IIa trial underway:

- Protocol reviewed, approved by NIH RAC, unanimous panel support
- FDA released IND January 2014
- Patient dosing commenced May 2014
- 4th and 5th patients to be dosed March 2015

US-based trial sites:

- Duke Clinical Research Unit, North Carolina - Keyur Patel, MD
- University of California, San Diego – David Wyles, MD

TT-034 clinical trial: Phase I/Ia dose 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	4.00×10^{10}	Starting dose	2	Sequential (1+1)	6 weeks
2	1.25×10^{11}	0.5	3	Sequential and parallel (1+2)	6 weeks
3	4.00×10^{11}	0.5	3	Sequential and parallel (1+2)	6 weeks
4	1.25×10^{12}	0.5	3	Sequential and parallel (1+2)	10 weeks
5	4.00×10^{12}	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

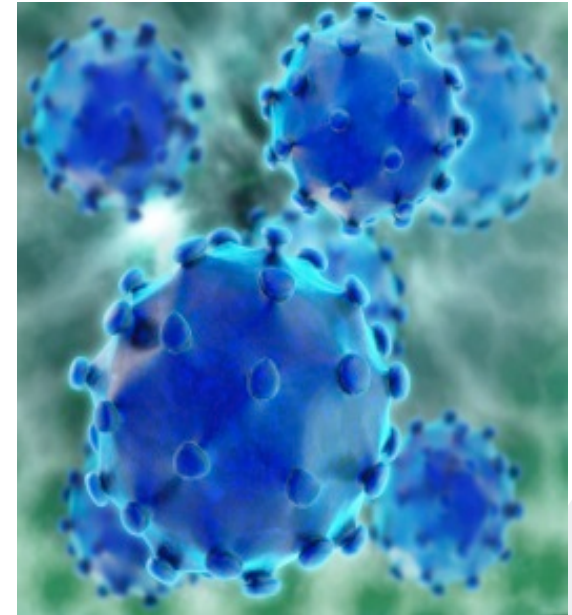
TT-034 trial endpoints

Primary Endpoints (Safety):

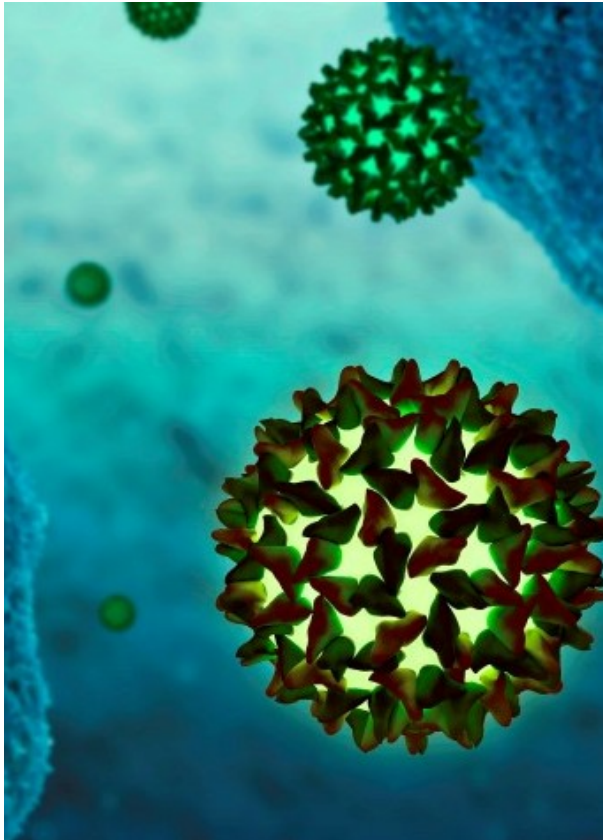
- Incidence of adverse events
- Changes in clinical parameters

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
- shRNA expression levels in serum (exosomes)



Hepatitis B (HBV)



Context

- 350 million infected worldwide, major unmet medical need
- Substantial interest from several large pharma programs

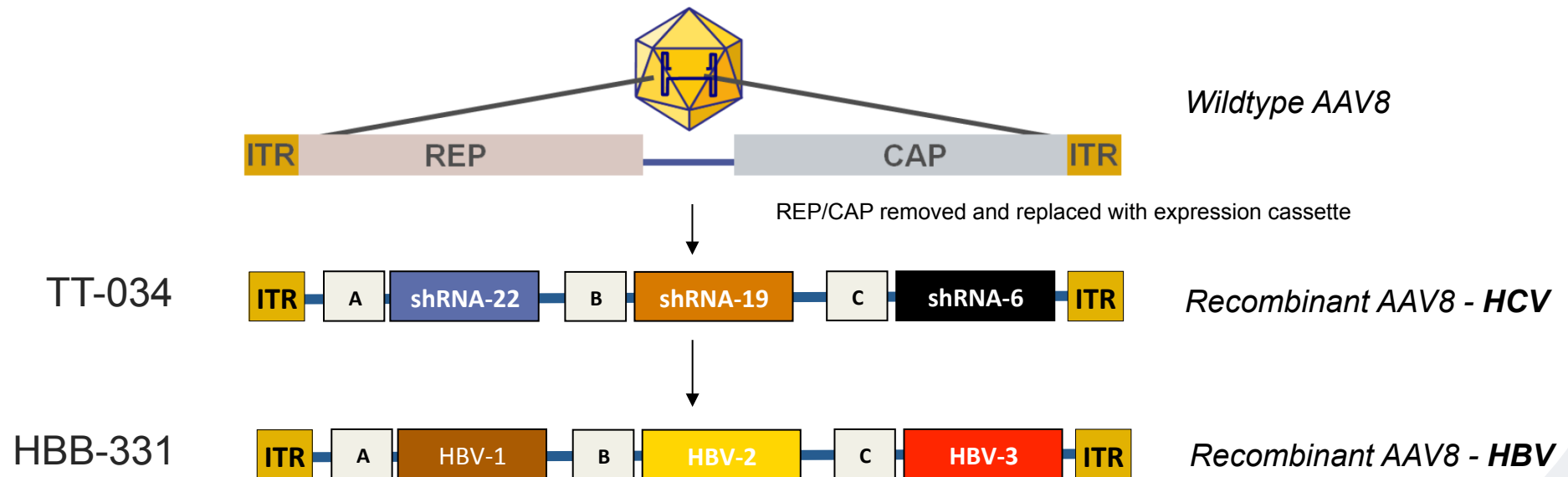
Approach

- Replicate and leverage HCV approach
- TT-034 clinical data provides guidance for HBV development
- Leverage RNAi success, add extra benefits of ddRNAi

Status

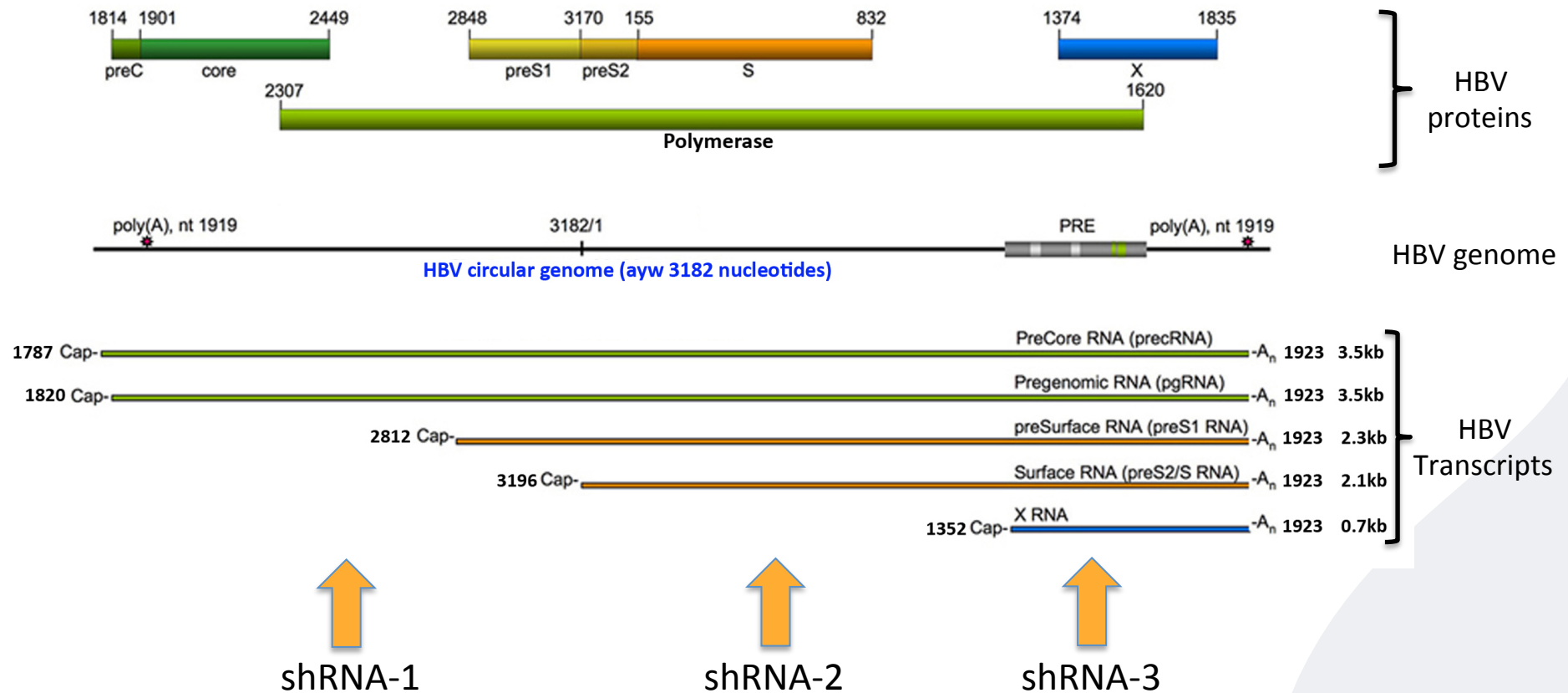
- Testing of clinical construct in HBV cellular and in vivo models ongoing

A facsimile of TT-034: same capsid, same expression cassette, new anti-HBV shRNA



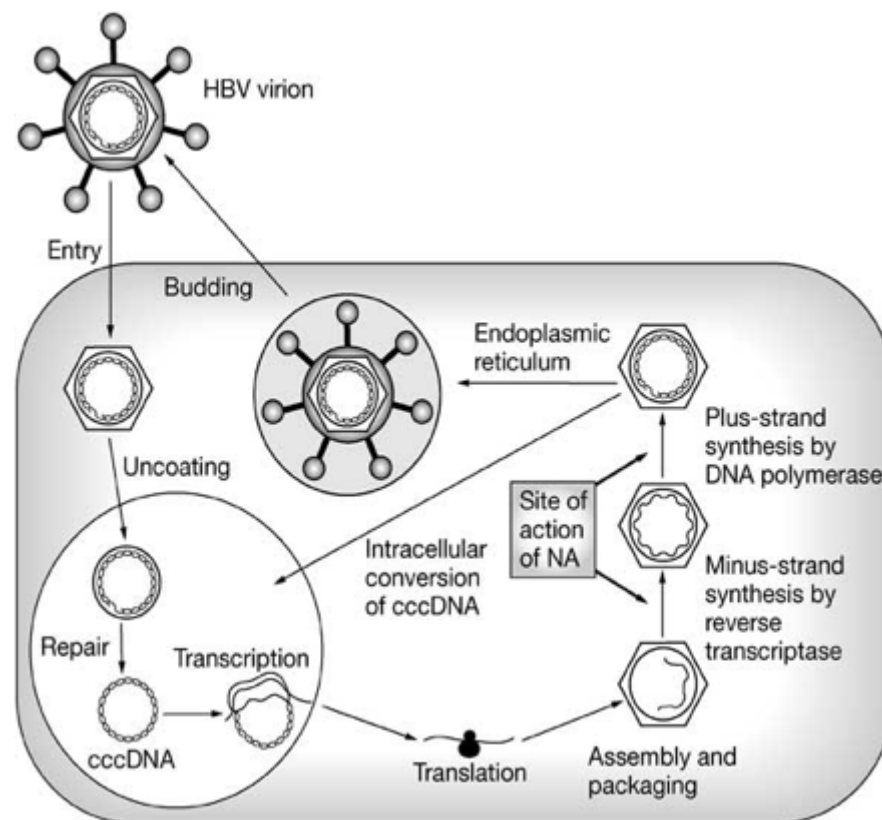
- Swap of 3 anti-HBV shRNA into anti-HCV shRNA position
- Keeps the same AAV8 capsid – identical biodistribution as TT-034
- Keep the same expression cassette – identical expression properties
- May be able to fast track REG/TOX studies using TT-034 data as part of IND package
- TT-034 clinical data guides HBV Protocol development and provides simpler regulatory path

Positioning of anti-HBV shRNA against the HBV genome



The rationale for RNAi in HBV therapy

- HBV is susceptible to RNAi because it replicates via an **RNA intermediate**.
- siRNA needs repeated doses indefinitely.
- ddRNAi can provide a single dose treatment to silence HBV mRNA long term.
- cccDNA will likely persist for quite some time, thus HBB-331 may need to be paired with a NUC



Drug resistant lung cancer



- Lung cancer is the most common cancer worldwide
- With around 65% of patients dying within one year of diagnosis, non-small cell lung cancer is the leading cause of cancer-related deaths worldwide (1.3 million deaths p.a.)
- The rapid emergence of drug resistance cancer cells provides a major challenge in the treatment of non small cell lung cancer.
- The efficiency of existing chemotherapeutic agents is restricted by dose limiting systemic toxicity. A significant opportunity therefore exists for treatments that enhance the effect of therapeutic drugs and are capable of reducing side effects.

A significant need exists for a therapy capable of restoring and/or improving the effect of therapeutic drugs in resistant cell lines and minimizing side effects associated with chemotherapy treatment.

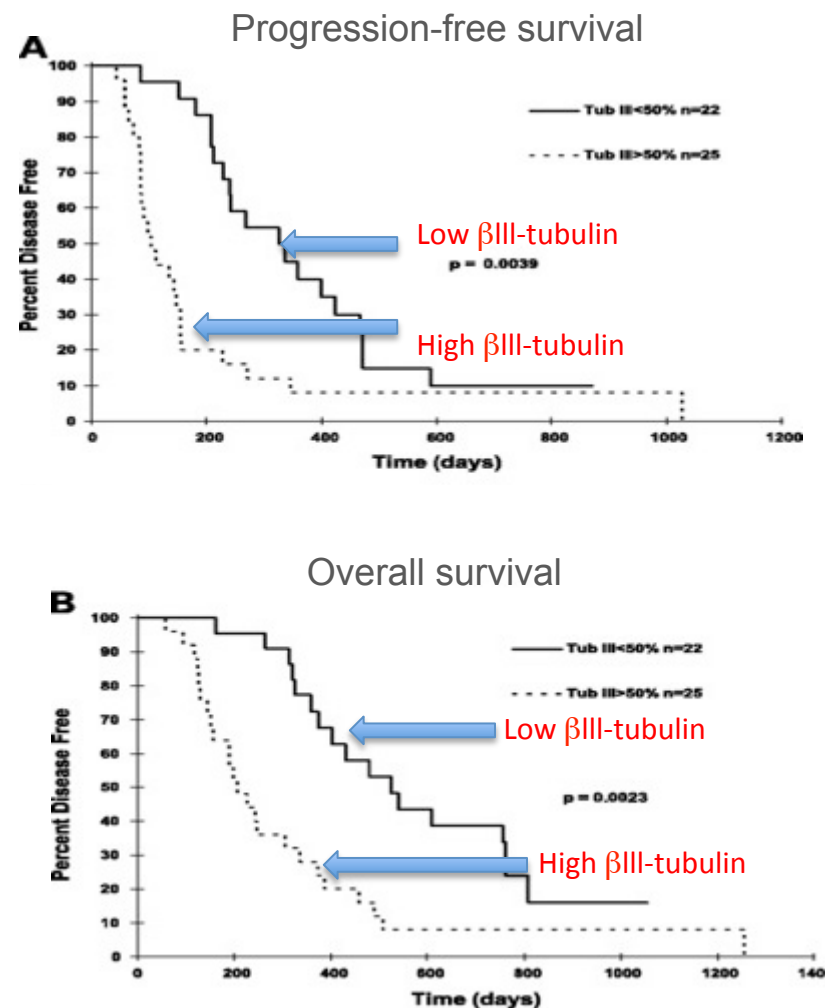
Target: β III-tubulin gene

Resistance to chemotherapy drugs is strongly associated with over-expression of β III-tubulin which appears to act as a tumour pro-survival factor.

Patients with high levels of β III-tubulin show significantly decreased survival.

Inhibition of β III-tubulin by RNAi can restore chemosensitivity.

IP licensed from UNSW



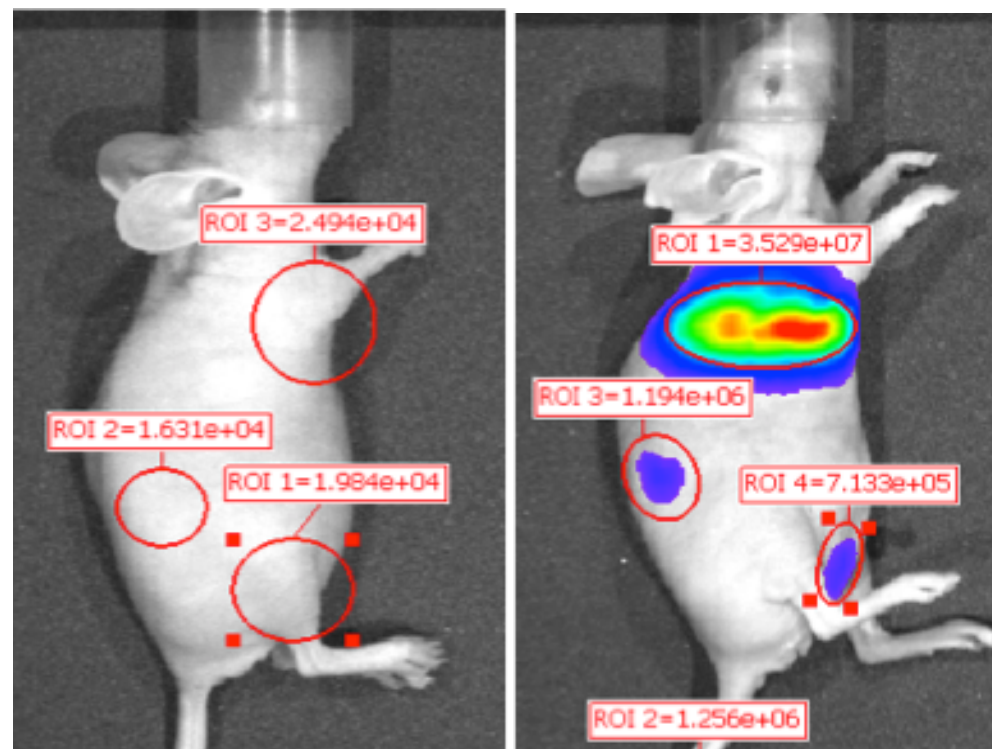
Delivery to lung tumors

Jet-PEI-based complexes can deliver DNA constructs to tumours with very high efficiency

Jet-PEI nanoparticles efficiently deliver plasmid constructs to tumours *in vivo*. Mice were injected i.v. with Jet-PEI complexed with a luciferase-expressing plasmid.

Strong *luc* activity is apparent in tumour-bearing animals (right) but not control animals (left).

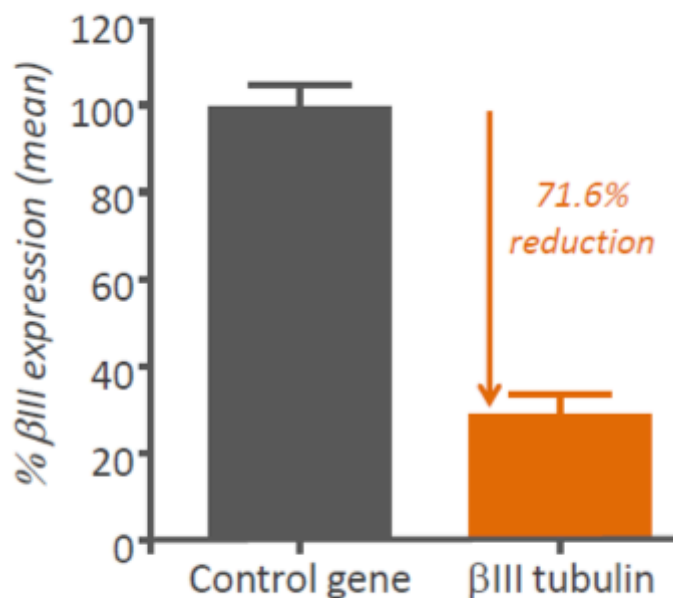
Quantification indicates 1,000-fold higher *luc* activity in tumours compared to non-involved tissues.



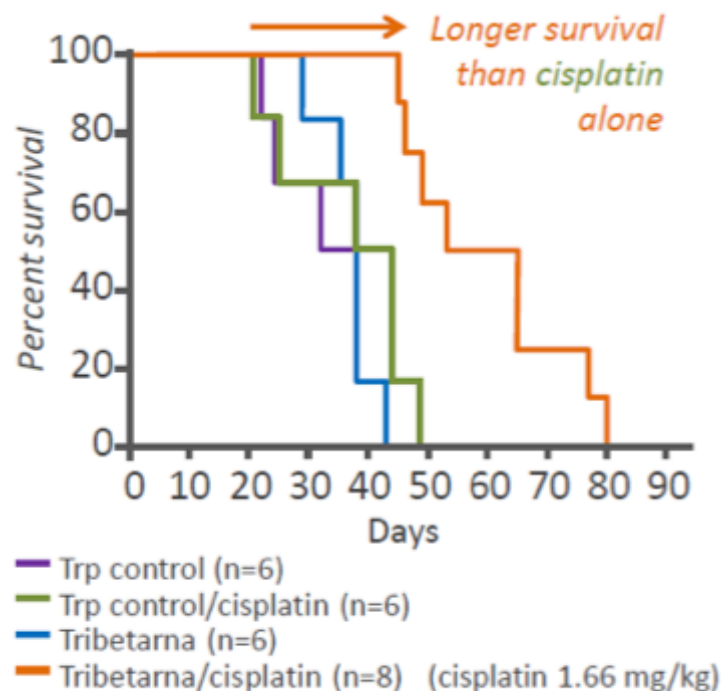
Knockdown of β III-tubulin expression extends survival

Proof-of-principle is established:

A single injection of Tribetarna effectively silences the β III tubulin gene in vivo and in vitro



Tribetarna™ significantly enhances survival in a preclinical model of lung cancer in combination with chemotherapy



Tribetarna™ - next steps

A Phase I/IIa clinical trial of Tribetarna™ in conjunction with cisplatin is planned

Benitec is committed to conducting a Phase I/IIa clinical trial of Tribetarna™ in combination with cisplatin in patients with advanced NSCLC in Europe.

Pre-Pre IND meeting held with FDA Q2 2014.

Patients will receive up to 4 cycles of Tribetarna™ + cisplatin following which tumor growth and survival will be assessed.

To achieve this, preclinical safety and toxicity studies will be conducted in 2015.



With clinical success in lung cancer, this approach can be developed to target other cancers that express high β III tubulin (pancreas, renal, breast, ovarian & gastric)

Age-related Macular Degeneration (AMD)

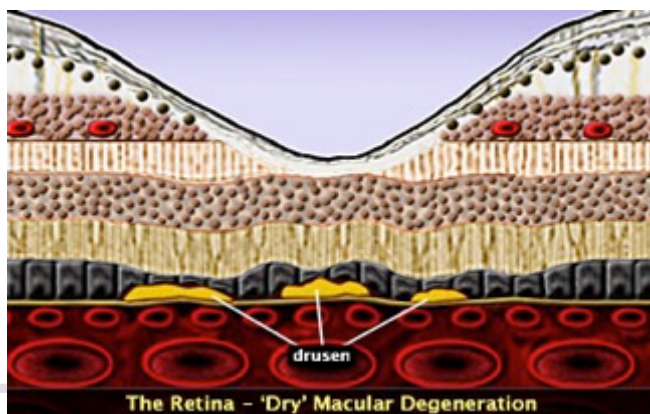


AMD is the leading cause of irreversible vision loss in the US – estimated 1.75M people

Age related – 10% of people between 60 and 75 and 25% of people >75 years old

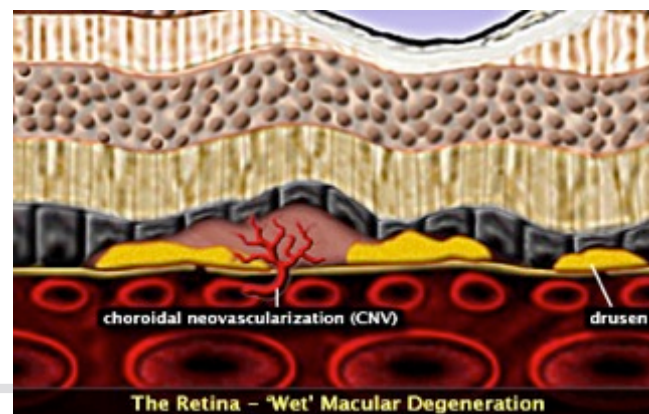


In Dry AMD, drusen deposits start to degrade vision



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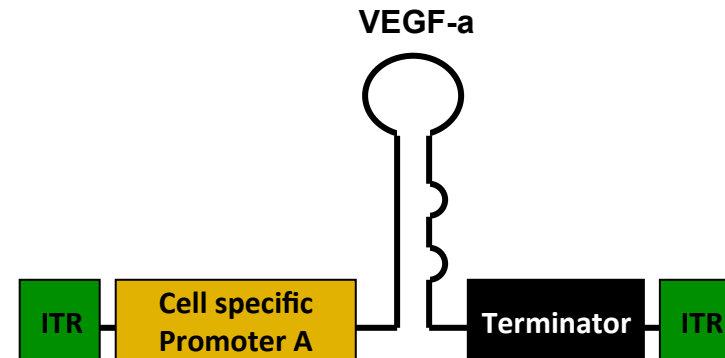
In Wet AMD, an inflammatory response sets off a cascade on events that further degrades vision through neovascularization



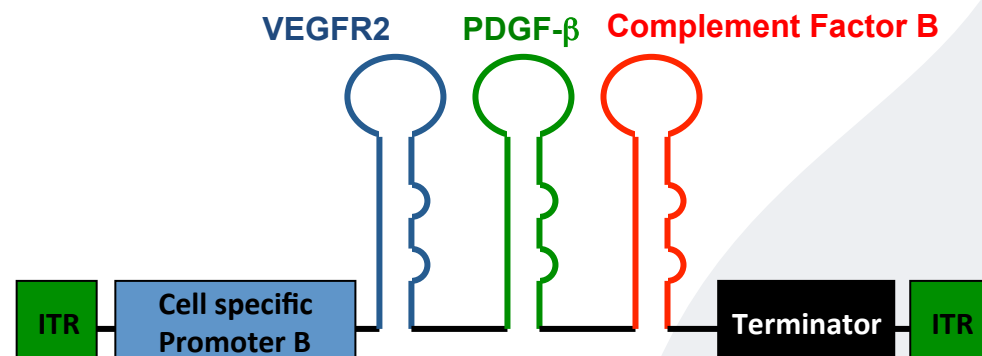
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AMD: 2 shots on goal

TT-211 – An AAV-encapsidated construct that expresses a single shRNA modeled into a miRNA backbone that inhibits the expression of VEGF-A

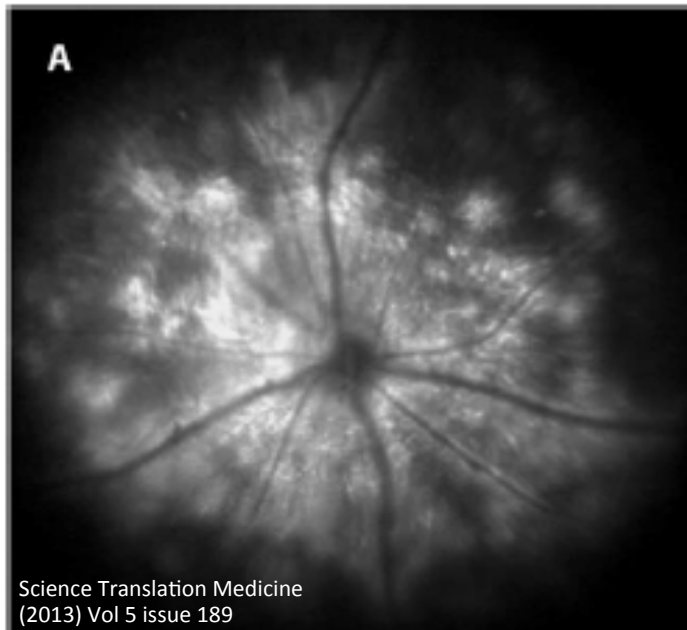


TT-231 – A follow-on product in which an AAV-encapsidated construct expresses three shRNA modeled into three miRNA backbones and inhibit the expression of VEGFR2, PDGF- β and Complement Factor B for the treatment of wet and dry AMD

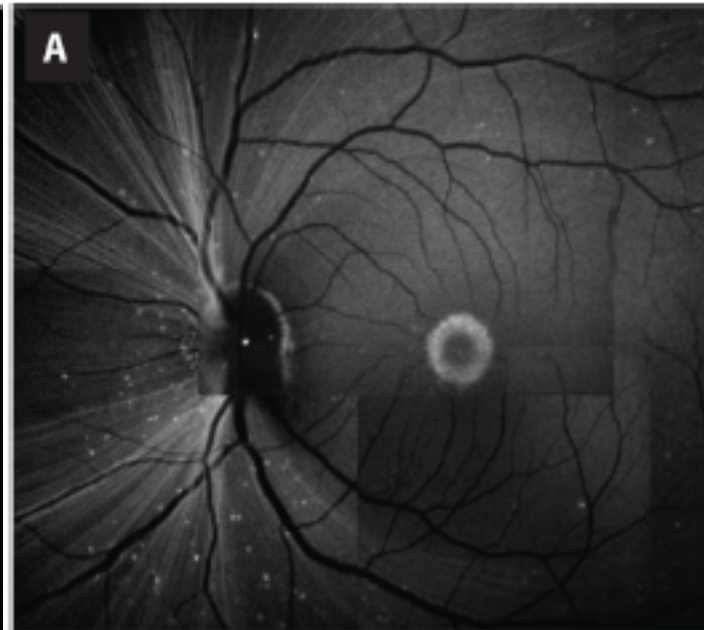


Development of new AAV vectors for therapeutic RNAi applications

AAV 7m8 in mouse



AAV 7m8 in Non Human Primate



First generation 7m8 vector appears to have limited transduction in the more complex primate eye

- Benitec has an exclusive license to ocular vectors from 4D Molecular Therapeutics for use in RNAi applications as well as in silence & replace strategies
- New selection in NHP to identify vectors with pan-retinal expression following intravitreal injection
- Generation and characterization of novel AAV vectors to be completed by Q3 2015.
- Animal model testing to be undertaken directly in NHP model of AMD.
- Once a vector with pan-retinal expression is developed, can be used for a wide variety of ocular diseases.

Commercially-focused Management and Board



BOARD

Chairman:

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

Directors:

John Chiplin, PhD
Polynoma, Arana, ITI Life Science Fund

Iain Ross, BSc, CH.D.
Silence Therapeutics, Tissue Therapies,
Ark Therapeutics, Anatara

Kevin Buchi
Cephalon, Teva, Mesoblast, Tetralogic

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

Summary



- Developing RNAi (Nobel Prize-winning technology)
- ddRNAi can provide a 'single shot cure' for many human diseases
- Over 100 patents, patent applications for ddRNAi
- Extensive pipeline of 'company making' programs
- Clinical stage programs (HCV & HIV/AIDS) poised to validate ddRNAi for other diseases
- Well funded (over \$30M from 10 US institutional investors in Feb 2014)
- Internationally credible, experienced Board and Management

Contact Information



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