



# Benitec Ltd (ASX:BLT)

AusBiotech October 2007

# Investment Highlights

**International, royalty-generating IP estate covering seminal patents in DNA-directed RNA interference (ddRNAi)**

- ddRNAi: DNA 'mini-gene' transcribed by the cell into double-stranded RNA (dsRNA), which is then cut into guide RNAs
- Mimics natural production of dsRNA
- Introduced into cells with biological vectors

**Focused on commercially attractive, life-threatening diseases in major cancer and infectious disease indications**

**Lead product in human trials targeting HIV/AIDS**

**Third party validation through licensing deals and collaborations with industry-leading partners for research, commercial and therapeutic uses of ddRNAi.**

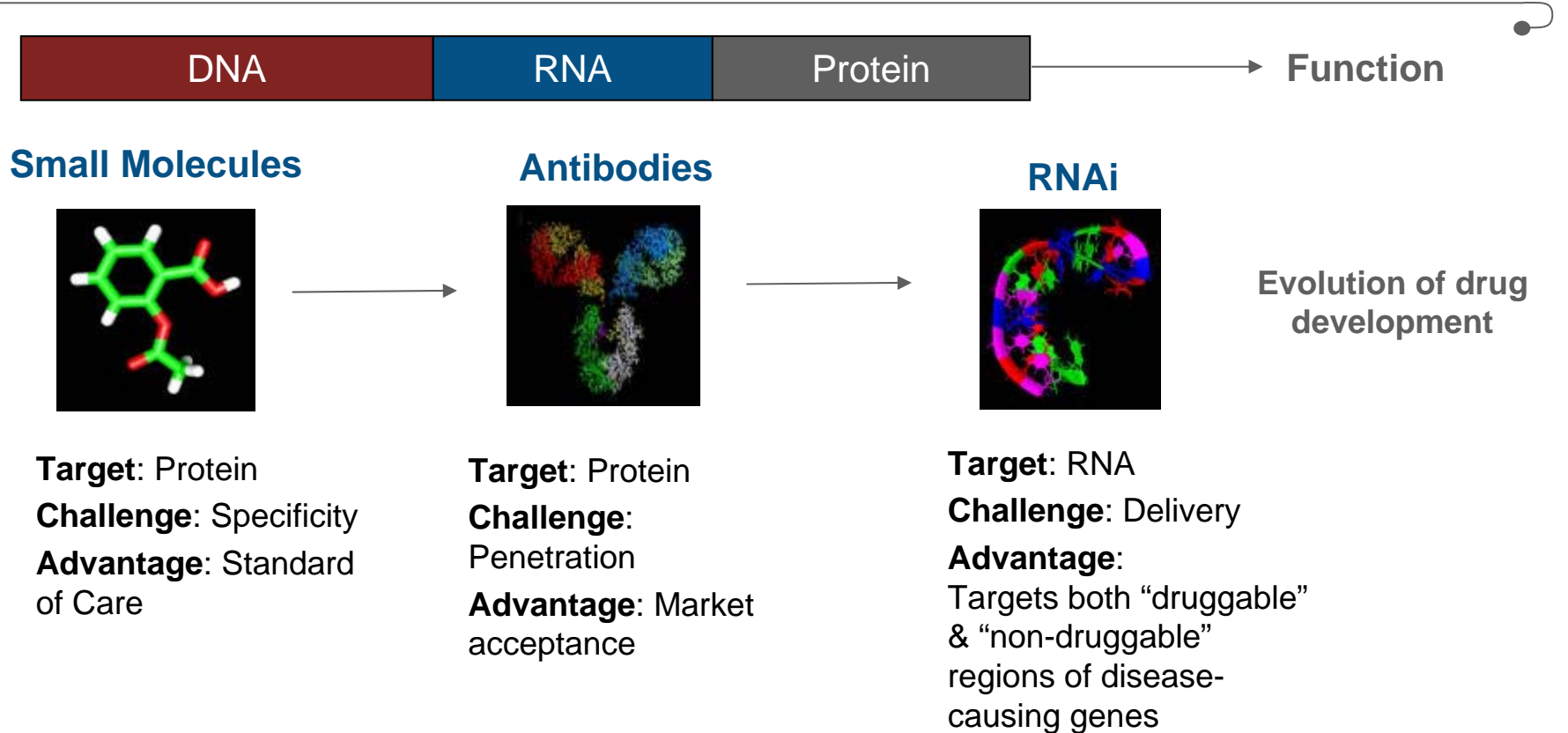
- Sigma Aldrich
- Pfizer Inc
- Merck Inc
- Promega
- Potential for additional ddRNAi and shRNA collaborations

**Fire and Mello Nobel Prize provides scientific boost to RNAi**

**RNAi field validated by recent acquisitions and collaborations with big Pharma**



# RNAi - The next wave of drug development

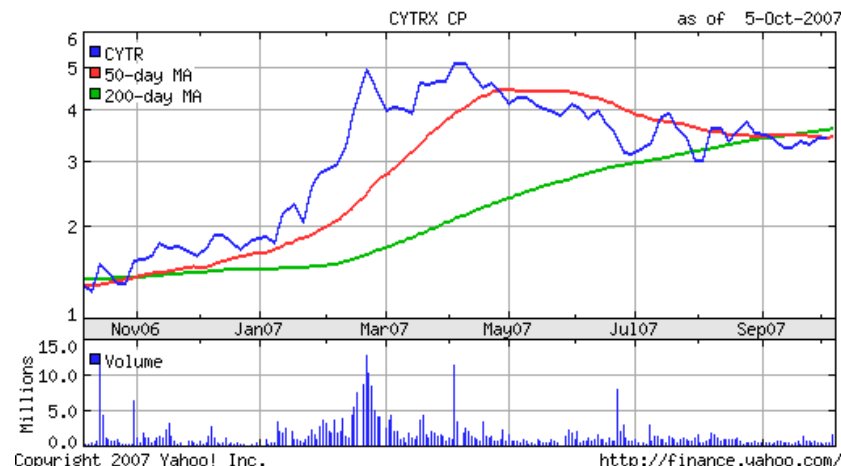
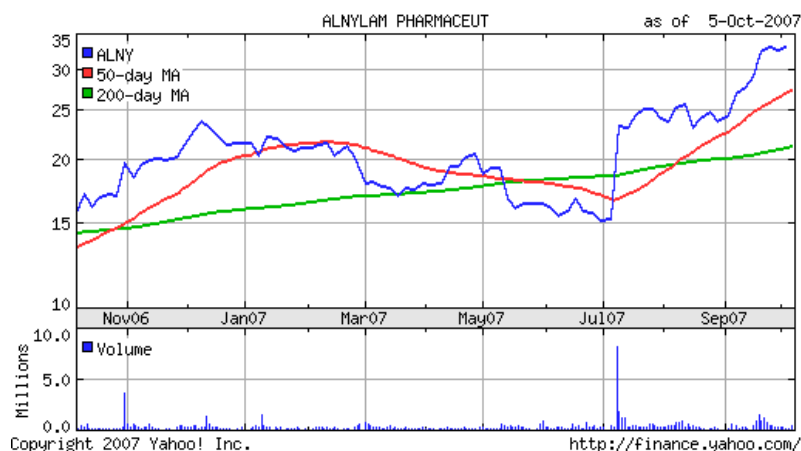


“RNA interference (RNAi) represents the most potent mechanism for target specific knockdown of gene expression discovered to date.”

Dr. John Rossi, City of Hope Comprehensive Cancer Center

“RNA interference (RNAi) has revolutionized biology — it has changed the way in which we view gene regulation and is a heaven-sent tool for studies of gene function” Magdalena Skipper (2003), Nature Reviews Genetics 4, 671

# Market Reward for RNAi



## Anylam Pharmaceuticals

- IPO \$7 (Jun04) now \$32.85 (Oct07) Market cap - 1.24B
- Roche non exclusive \$US300m RNAi alliance/equity investment deal 2007 -share price leapt more than 50 percent, from \$15.20 to \$23.12
- Novartis 2005 US\$700m R&D collaboration

## Sirna Therapeutics

- Merck 2006 US\$1.2B acquisition - 95% premium

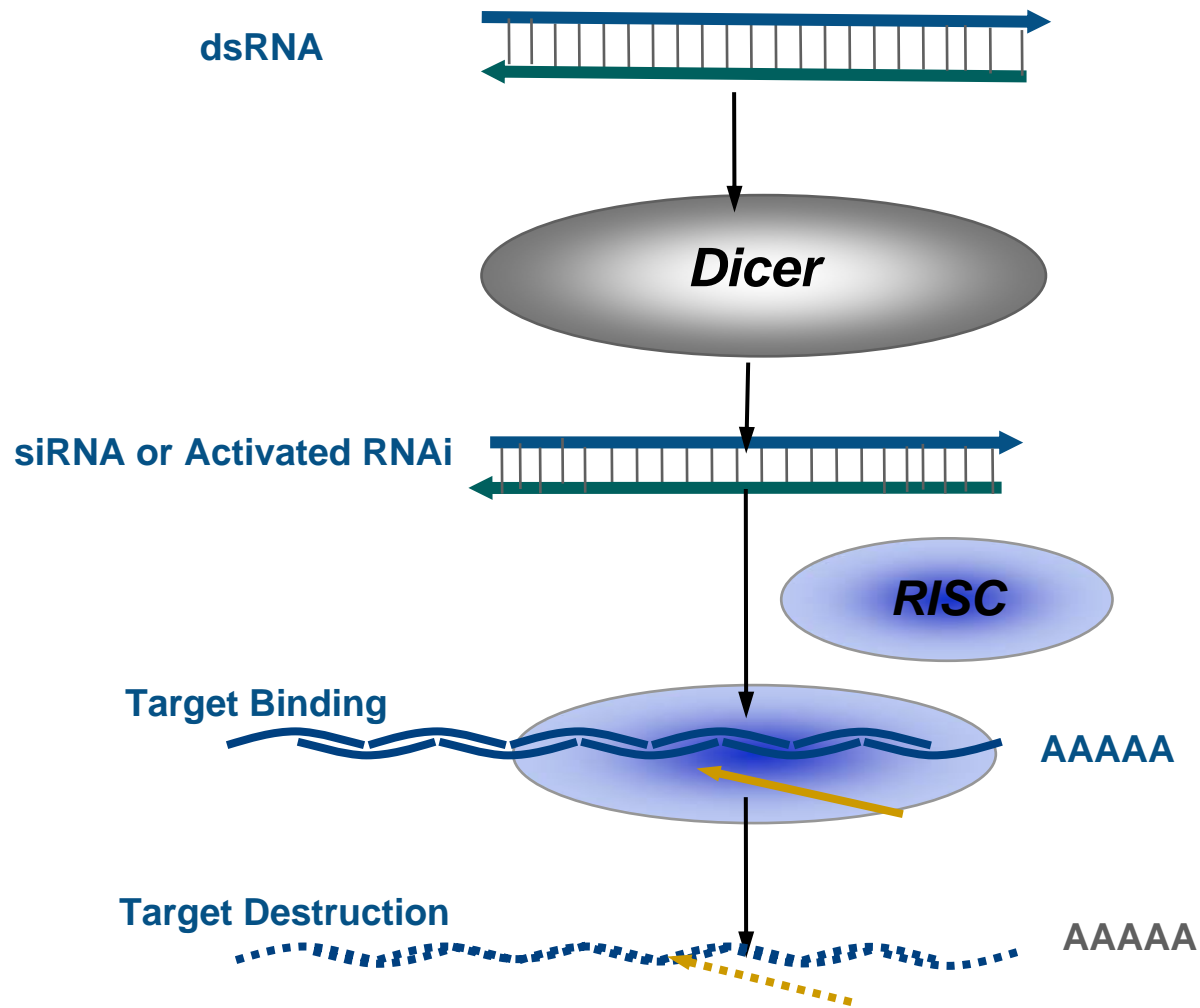
## CytRx

- 5x increase in market cap in 18 months US60M to US300M

**RNAi companies reward investors**

# RNAi Mechanism

Rapid, highly specific mechanism for gene silencing



- Natural mechanism
- Rapidly deployed
- Highly specific
- Catalytic

# Benitec ddRNAi Advantages

## Gene silencing effective at lower doses and longer term than siRNA

- Catalytic dsRNA production potentially critical in targeting infectious agents
- siRNA molecule could become rate-limiting for quickly replicating viruses

## Single payload can target multiple mRNAs

- Particularly relevant to diseases characterized by high mutation rates, i.e. cancers and HIV/AIDS which inevitably result in the emergence of resistance to single drugs.

## Flexible delivery options

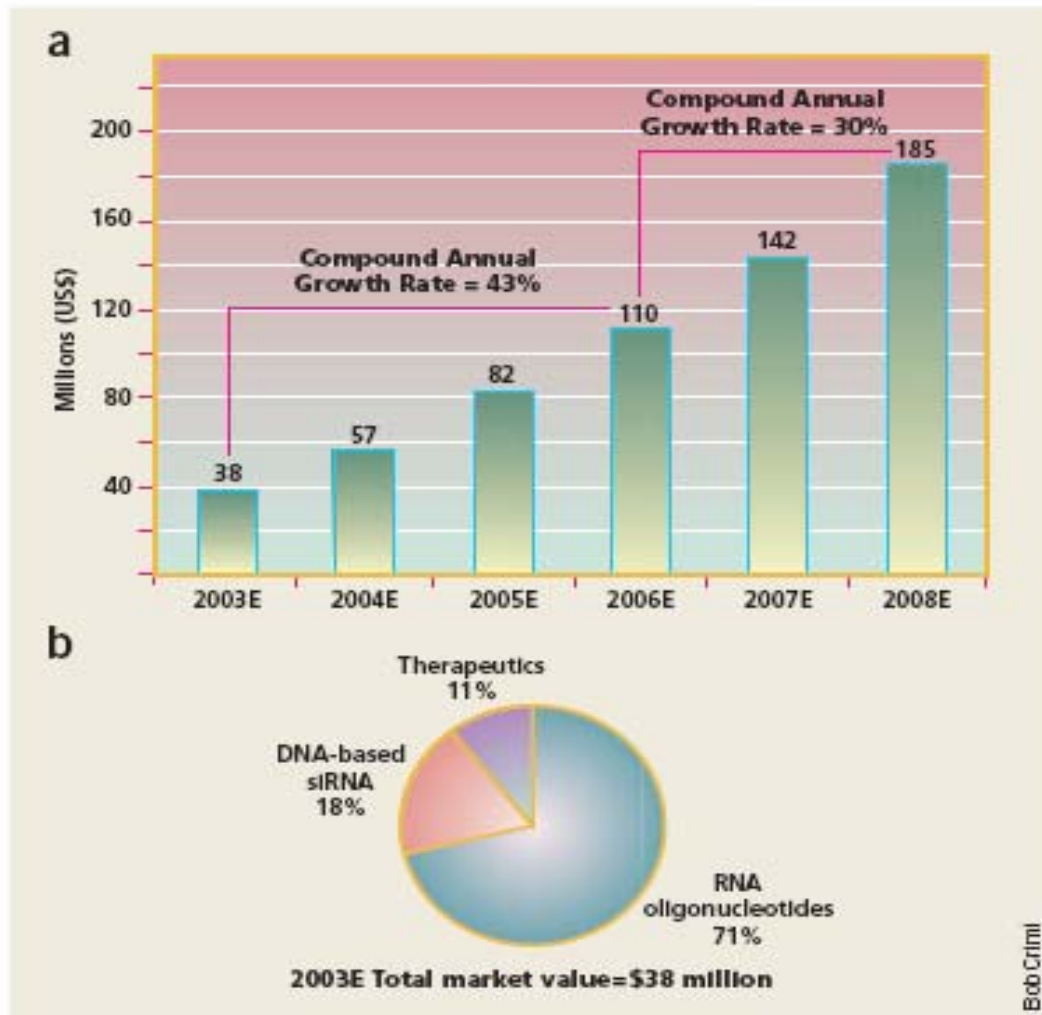
- Plasmid in liposome
- Viral vectors
- Stem cells

## High target affinity to specific tissues addresses limitations of siRNA by allowing for specific inactivation of key genes in a diseased tissue

## Potential for lower cost of goods and easier manufacturing compared with siRNA

- siRNA requires modifications to produce more stable RNA and avoid off target effects

# RNAi market opportunity



Global RNAi sales projected to reach US\$6.65 Billion by 2010 and 12 Billion by 2015 (Therapeutic 1.5B, Research 1.2B, Reagent Use 9.3B)\*

Competitive and dynamic market

\* RNAi technologies, companies and markets (2006) Jain K.K. Pharmaceutical report)

# Dominant International RNAi IP Position

*“Most of the IP in (RNAi) is owned by Benitec...Benitec lays claim to a seminal US patent... that describes ‘genetic constructs for delaying or repressing the expression of a target gene’”*

-Nature Biotechnology, “Negotiating the RNAi patent thicket” (March 2007)

**First company to demonstrate RNAi in human cells as ddRNAi pioneer**

**Dominant international IP position in RNAi human therapeutics**

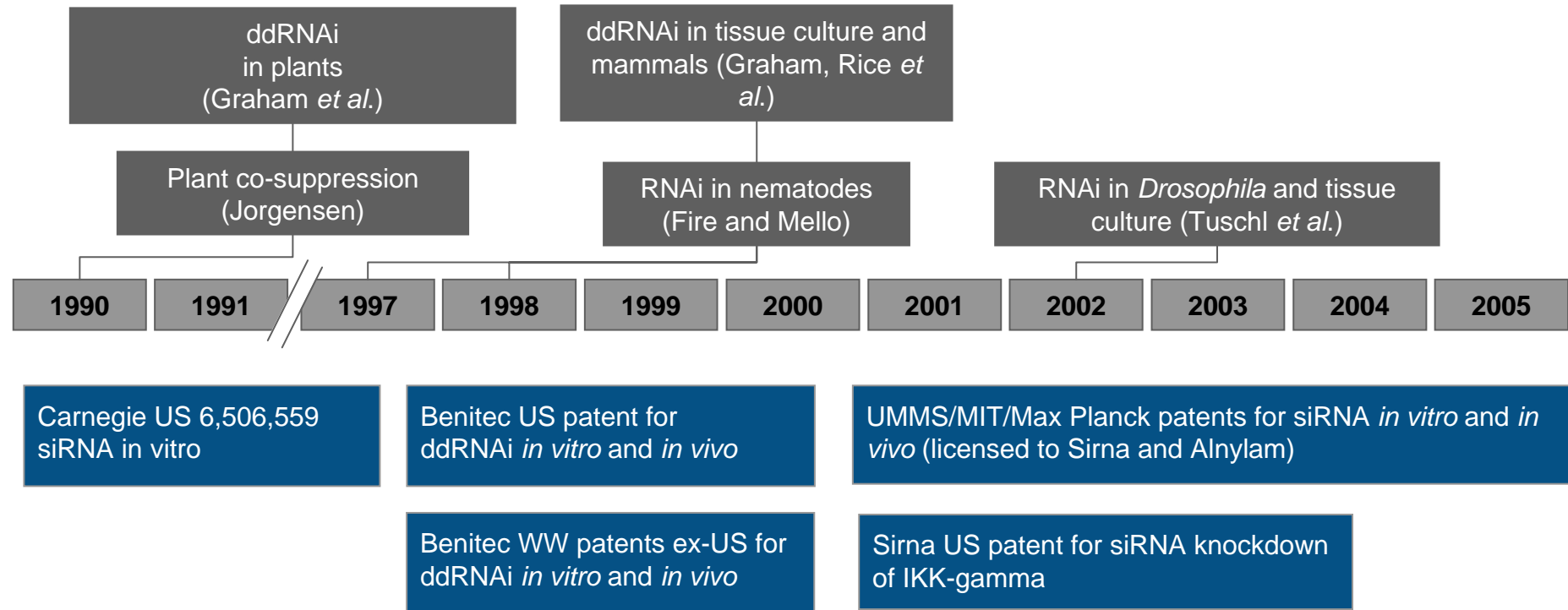
**Core U.S. and U.K. technology patents granted in 2003**

- Cover method for silencing any gene in any cell using ddRNAi
- World’s first claims describing RNAi effects in human cells and DNA constructs that trigger RNAi

**Patents granted in Australia, Canada, Czech Republic, Great Britain, Hong Kong, New Zealand, Singapore, South Africa, and United States (under re-exam)**

**Ownership assigned to CSIRO while Benitec retains a WW non-revocable right to all human therapeutic applications**

# Core Platform Intellectual Property Rights



# Licenseses and strategic partners

Licensing deals and collaborations with industry-leading partners with potential for additional ddRNAi and shRNA collaborations

**Therapeutic use of ddRNAi**






**Research reagent or transgenic animal product development and sales**













**Research freedom to operate**

**Strategic cross-licensing**

Carnegie Institute






## Molecular targets rHIV7-shI-TAR-CCR5RZ

- HIV genome
- Cell-surface receptor
- Replication machinery
- Vector manufactured by City of Hope's Center for Biomedicine and Genetics, BLT's collaborative partner

Published in *Nature Reviews*, *PNAS* and *Molecular Therapy*

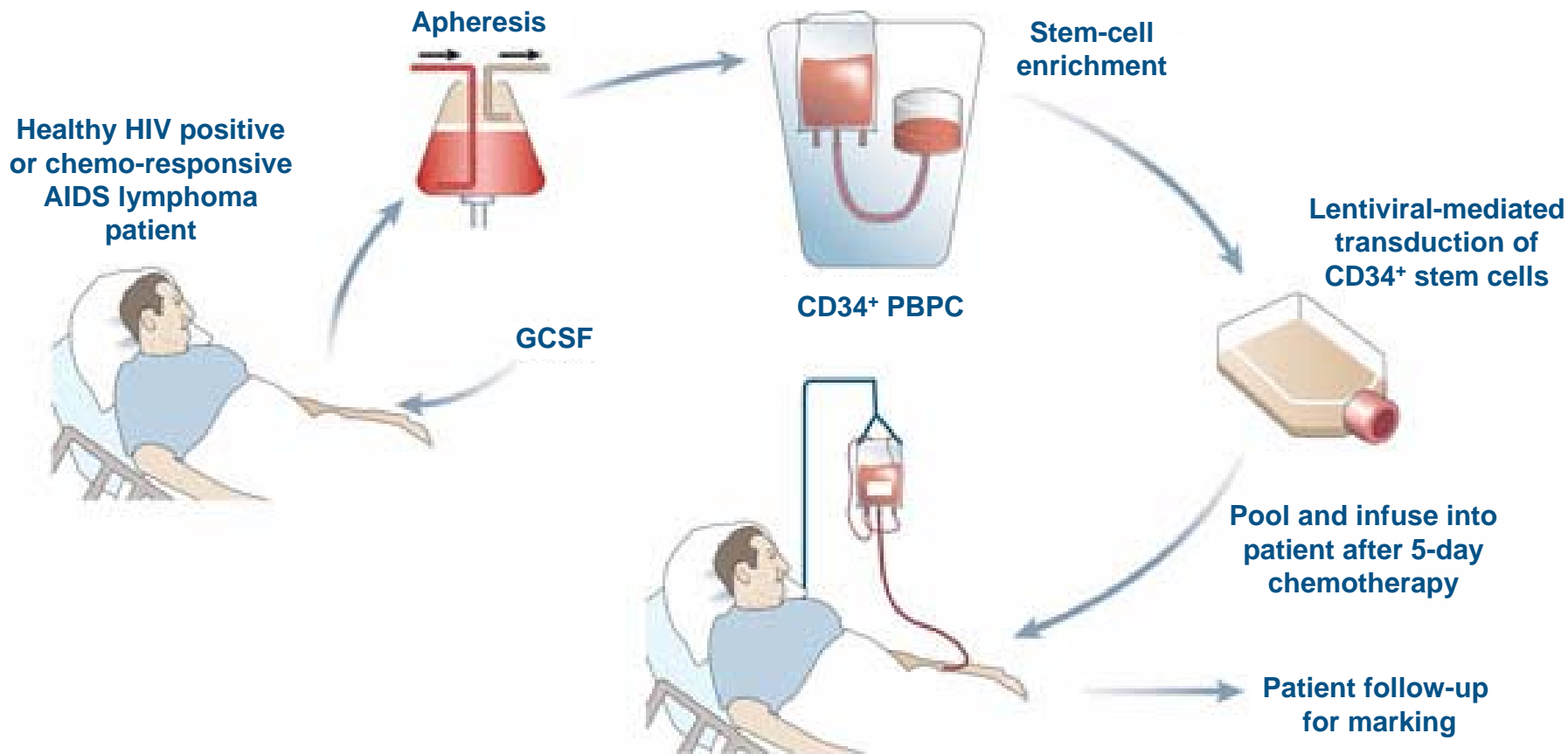
## Ongoing safety and feasibility pilot study in AIDS lymphoma

- Evaluating stem cells treated with lentivirus vector-encoding multiple anti-HIV RNA's

## Development milestones

- ✓ IND filed (Jan 2007)
- ✓ First Human clinical trial (initiated Q307)

# AIDS / lymphoma clinical trial design



# HIV/AIDS T-cell program

## T-Cell therapy for HIV/AIDS

- Inclusion of selective marker into clinical vector rHIV7-shI-TAR-CCR5RZ protected >80% of T-cells from HIV infection in macaques
- Collaborative partners: City of Hope, Fred Hutchinson Cancer Research Center, Colorado State University and U Penn
- US\$7.5 million NIH grant covering development through end of Phase I

## Development Milestones

- ✓ Pre-IND meeting (Feb 2007)
- IND submission (late 2007)
- Phase I initiation in Q1/Q2 2008

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Dr. John Rossi, City of Hope  
Comprehensive Cancer Center

# HCV Program



Licensed to Tacere Therapeutics Inc.

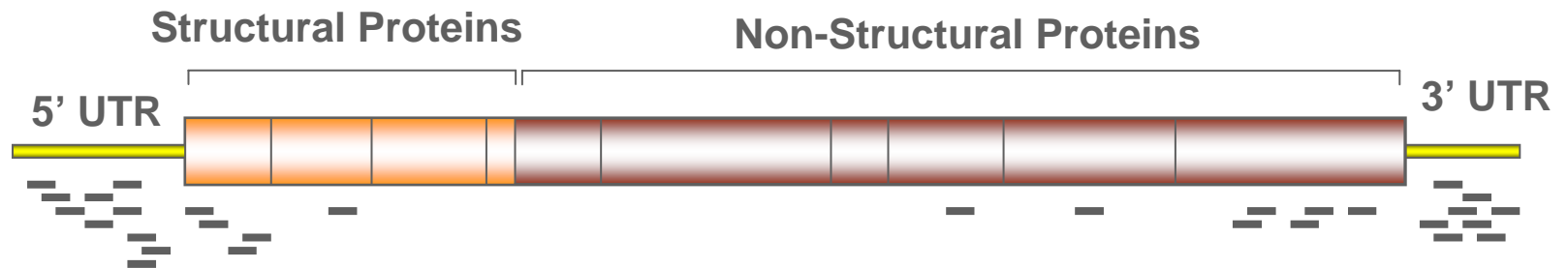
## RNAi Therapeutics targeting Hepatitis C virus genome

- Multi-targeted to prevent viral escape
- Single drug “Cocktail”

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Results published in *Nature* and *Nature Biotech*



# Corporate strategy

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**Further develop proprietary RNAi position in infectious diseases and cancer**

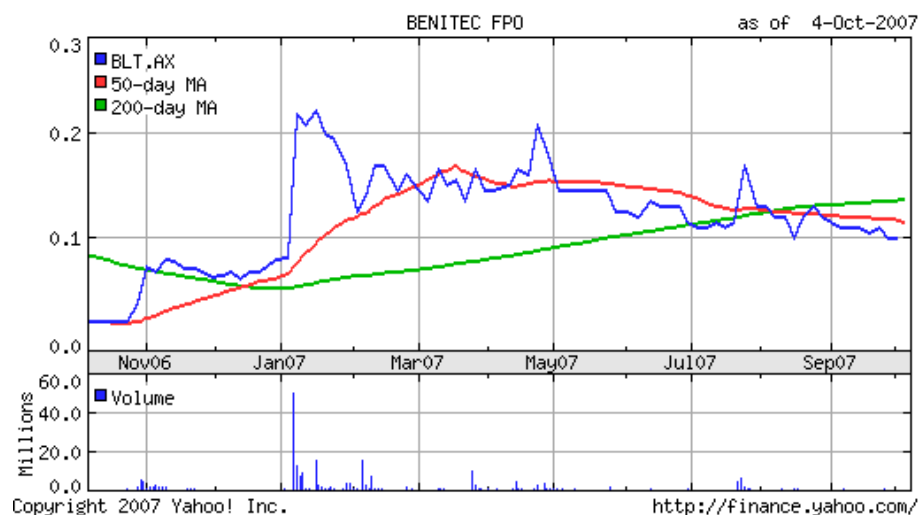
**Strengthen IP underpinning partnerships, collaborations and potential M&A activities**

- Continue to prosecute core patent claims globally (USPTO re-exam)
- Patent prosecution and maintenance on supporting IP Increase therapeutic licenses for non-core areas

**Assist current licensees to increase product revenue**

**Evaluate trade sale and exit opportunities on ongoing basis**

# Capital structure



<b>Share price</b>	\$0.1250* per share
<b>Market Cap:</b>	\$36.05 million*
<b>Issued equity:</b>	288,431,353
<b>Options:</b>	111,362,631
<b>Cash position:</b>	\$4.960 million (6/30/07)
<b>Avg. Daily Volume:</b>	1,182,938 shares
<b>Convertibles:</b>	\$52,980: Chris Bremner

## Key shareholders:

• Dr. Christopher Bremner	19.09%
• Artemis (Rothschild Family)	8.53%
• Sigma Aldrich	6.77%
• Thorney Investments	5.89%
• Promega Corp	6.15%

New capital structure to be in place in 2008. Benitec Inc, Benitec LLC and Benitec Limited UK to be incorporated into Benitec Limited  
 \* As at 5<sup>th</sup> October 2007

# Board, SAB and senior managers

## **Peter Francis – Chairman**

Boron Molecular P/L, Xceed Biotechnology, PolyNovo Biomaterials P/L

## **Dr Ken Reed – Director**

QABC, Advanced Breeding Tech P/L, Australian Biotech Advisory Council, Australian Government's Genetic Manipulation Advisory Committee & Australian Genome Research Facility.

## **Dr Michael Dalling - Director**

Biomedical Imaging Development CRC, Biomass Conversion Technologies P/L, Neural Diagnostics P/L, General Division of the Order of Australia

## **Sue MacLeman – CEO and MD**

Schering Plough, Amgen, Bristol Myers Squibb Pharmaceuticals, Agenix Ltd, EQiTX Ltd, Australia Institute of Company Directors, AusBiotech Limited, PIWG, PIC, PIDT

## **John Rawling – CFO, Company Secretary**

Polynovo Biomaterials Pty Limited, EQiTX Ltd, Kentor Gold Ltd, Terrain Australia Ltd, Online Trading Systems Ltd., Australian Grand Prix Corporation.

## **Dr Jason Smythe – CSO**

NH&MRC C.J. Martin Fellow and then an Irvington Institute (New York USA) ,Postdoctoral Fellow in Immunology (Dr Robert C. Gallo lab), National Cancer Institute USA, Johnson & Johnson Research, Gene Therapy Research Unit at the Children's Medical Research Institute (CMRI), Westmead, CSIRO Division of Molecular Science Chief Scientific Officer of the Australian Tissue Engineering Centre Limited in Melbourne.

## **Scientific Advisory Board**

Dr John Rossi – City of Hope Duarte California USA

Dr Bryan Williams – Monash Medical Research Centre – Victoria, Australia

Dr Cy Stein – Albert Einstein College of Medicine NYC USA

Dr David Crump – PD&C consultant Australia

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# Thank you

**Sue MacLeman**

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