- Secure funding to accelerate the clinical development of Benitec's programs. The $31.5 million capital raise finalised in April is enabling the Company to:
  - Fund TT-034 into Phase I/II(b) and to advance other programs in the Company's pipeline with particular emphasis on lung cancer, AMD and HBV.
  - Expand the Company's in-house capability with the opening of its own laboratory in northern California.
  - Appoint key personnel: Benitec has recruited a number of experienced and highly qualified scientific, program management and Intellectual Property resources to support the accelerated clinical development of the Company's programs.

Successful execution of these elements is enhancing Benitec's opportunities to engage with the pharmaceutical industry and achieve successful commercial outcomes for the Company's programs.

Strategic Advantage

Benitec's ddRNAi technology is a form of RNA interference (RNAi) that can 'silence' or shut down disease-causing genes. Recently there has been an increasing awareness of the value of gene silencing and RNAi as a therapeutic modality; Companies operating in this segment – such as Alnylam, Arrowhead, Dicerna, Tekmira, Bluebird Bio and Isis – have seen significant increases in their valuation. In particular, Alnylam has grown its company's market capitalisation from around $1 Billion to over $4 Billion over the last two years. Benitec's ddRNAi technology has a number of differential advantages over RNAi: the most important is its ability to silence a disease-causing gene for long periods with a single administration, whereas conventional RNAi requires continuous administration.

Big pharma is demonstrating a renewed interest in RNAi and gene therapy. Benitec's ddRNAi technology offers an optimised combination of these approaches, and the TT-034 clinical trial, if successful, will provide validation of the technology for treating a wide range of diseases.

In-house Programs

Focus	Indication	Partners/Collaborators	Discovery	Pre-clinical	Clinical
Infectious Disease	Hepatitis C				
	Hepatitis B	Biomics Biotechnology (JV)			
Cancer	Non Small Cell* Lung Cancer	University of New South Wales (RC)			
	Cancer Associated Pain	Stanford University (RC)			
Ocular Disease	AMD**	Stanford University (RC)			
Genetic Disease	OPMD***	Royal Holloway London University (RC)			

RC = research collaboration
JV = joint venture

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

Benitec has six in-house development programs underway. Following the acquisition of Tacere in November 2012, the Company decided to put most of these programs on hold whilst focusing on advancing the hepatitis C therapeutic, TT-034, towards the clinic. With the securing of the major fund raising in April 2014, the Company is re-activating the other pipeline programs. Highlights over the previous 12 months include:

- **Hepatitis C – "TT-034".** In 2014 TT-034 became Benitec's first clinical stage treatment achieving the following key milestones:
  - Allowance by the FDA to proceed with a clinical trial for TT-034 was received in mid-January. Of particular note, the New Drug Application (NDA) was accepted by the Agency within 30 days of receipt with no significant changes.
  - Commencement of screening and patient recruitment at Duke Medical Research Unit.
  - The first patient was dosed in late May.
  - The first patient experienced no treatment-related adverse events and, importantly, there was evidence of liver transduction and production of short hairpin RNAs (shRNA).
  - Approval by the Data Safety Monitoring Board (DSMB) to proceed with the clinical trial with no modification following review of the safety parameters of the first patient after 6 weeks following the single administration.
  - A paper describing TT-034 was accepted for publication in the prestigious scientific journal Nature Molecular Therapy Nucleic Acids.
  - University of California San Diego (UCSD) has joined the Duke Clinical Research Unit to concurrently screen and enrol patients, boosting patient recruitment.
- **Chemotherapy-resistant lung cancer – "Tribetarna™".** Benitec's lung cancer program targeting the gene responsible for chemotherapy resistance, beta III tubulin, has made encouraging progress toward the clinic. Significant milestones in the last 12 months include:
  - Significantly increased survival observed in a preclinical in vivo model of lung cancer following intravenous administration of the ddRNAi-based therapeutic, Tribetarna™ in combination with cisplatin, confirming previously reported results.
  - Dr Craig Lewis appointed Chief Medical Adviser. Dr Lewis is a medical oncologist at Sydney's Prince of Wales Hospital; he has a major interest in clinical trial research in lung cancer, breast cancer and sarcoma.
  - Professor Maria Kavallaris (Benitec's collaborator on Tribetarna™) was acknowledged by the prestigious National Health and Medical Research Council (NHMRC)'s List of High Achievers in Health and Medical Research Award.
  - Pre-pre IND submission filed with the US FDA and a teleconference held to discuss guidance on appropriate toxicology studies to be conducted for this first-in-man therapeutic approach.
- **Wet age-related macular degeneration (AMD)**. A focus of Benitec's US laboratory has been the testing and optimisation of suitable vectors to deliver ddRNAi constructs to the retina. In parallel the Company has identified suitable animal models to complete the validation of this therapy. The single-administration approach permits the possibility of use as a prophylactic, preventing any development of retinal damage before AMD develops thus offering both a treatment and a preventative solution to this important healthcare problem.