

## ASX ANNOUNCEMENT

**BENITEC BIOPHARMA (ASX: BLT; OTC: BTEBD)**

23 June 2015

### **BENITEC ANNOUNCES PLANS FOR AN INITIAL PUBLIC OFFERING IN THE UNITED STATES WITH LISTING ON NASDAQ**

*Not for release in the United States*

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**Sydney, Australia:** Benitec Biopharma Limited (ASX: BLT) is pleased to advise that on 22 June 2015 it filed a registration statement on Form F-1 with the U.S. Securities and Exchange Commission in connection with an initial public offering (*IPO*) in the United States with a listing on the NASDAQ Global Select Market (*NASDAQ*). The registration statement, which is subject to completion and amendment, is attached to this ASX Announcement.

Benitec proposes to raise approximately US\$60 - 70 million under the IPO through the issuance of up to 5,750,000 American Depositary Shares<sup>1</sup> (*ADSs*), representing 115,000,000 fully paid ordinary shares of Benitec (*Shares*). The actual number of ADSs and the issue price will be determined by Benitec in conjunction with the underwriters of the IPO at the conclusion of an investor roadshow for the IPO to be conducted in the United States in late July 2015.

Benitec proposes to undertake the IPO and list the ADSs on NASDAQ in order to access the US public equity market. The United States has the world's largest capital markets and Benitec believes it can most effectively access those markets through an IPO and listing in the United States.

Proceeds from the IPO would primarily be used to advance Benitec's therapeutic programs.

Following Benitec's proposed listing on NASDAQ, Benitec would continue to maintain its primary listing on the ASX with the secondary listing on NASDAQ. Benitec's ordinary shares would continue to trade on ASX in A\$ and its ADSs would trade on NASDAQ in US\$.

The offer of the Shares in connection with the IPO is subject to shareholder approval as well as market conditions and, as a result, there can be no assurance that Benitec will complete the IPO and list ADSs on NASDAQ or, if it does, at what price the ADSs would be sold.

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<sup>1</sup> An American Depositary Share is an instrument that enables non-US companies to list equity securities on a US stock exchange such as NASDAQ. Each ADS represents one or more underlying ordinary shares in the non-US company and confers beneficial rights of ownership to these underlying shares. The underlying shares are held on deposit by a custodian bank in the non-US company's home country.



Benitec has dispatched a Notice of Meeting today for an extraordinary general meeting to be held on 22 July 2015, seeking approval from shareholders under ASX Listing Rules.

*This announcement has been prepared for publication in Australia and may not be released in the United States. This announcement does not constitute an offer to sell, or a solicitation of an offer to buy, securities in the United States or any other jurisdiction. Any securities described in this announcement have not been registered under the US Securities Act of 1933 and may not be offered or sold in the United States absent registration or in transactions exempt from registration under the US Securities Act and applicable US state securities laws. Any public offering of securities to be made in the United States will be made by means of a prospectus that may be obtained from the issuer and that will contain detailed information about the issuer and management, as well as financial statements.*

**About Benitec Biopharma Limited:**

Benitec Biopharma Limited is an ASX-listed biotechnology company (ASX: BLT; OTC: BTEBD) 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](http://www.benitec.com).

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

**FORM F-1  
REGISTRATION STATEMENT**  
*UNDER  
THE SECURITIES ACT OF 1933*

**Benitec Biopharma Limited**  
(Exact name of registrant as specified in its charter)

**Australia**  
(State or other jurisdiction of  
incorporation or organization)

**2834**  
(Primary Standard Industrial  
Classification Code Number)

**Not Applicable**  
(I.R.S. Employer  
Identification Number)

F6A/1-15 Barr Street  
Balmain, NSW, 2041, Australia  
Tel: +61 2 9555 6986  
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Tacere Therapeutics, Inc.  
3940 Trust Way  
Hayward, CA 94545  
Tel: (510) 780-0819  
(Name, address, including zip code, and telephone number, including area code, of agent for service)

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**Approximate date of commencement of proposed sale to the public:**  
As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earliest effective registration statement for the same offering.

**CALCULATION OF REGISTRATION FEE**

Title of Each Class of Securities to be Registered <sup>(1)(2)</sup>	Proposed Maximum Aggregate Offering Price <sup>(3)</sup>	Amount of Registration Fee
Ordinary shares, no par value .....	\$70,000,000	\$8,134

- (1) American depositary shares, or ADSs, issuable upon deposit of the ordinary shares registered hereby will be registered under a separate registration statement on Form F-6 (Registration No. 333-196105). Each ADS represents 20 ordinary shares.
- (2) Includes additional ordinary shares that are issuable upon the exercise of the underwriters' option to purchase additional shares to cover over-allotments, if any.
- (3) Estimated solely for the purpose of determining the amount of registration fee in accordance with Rule 457(o) under the Securities Act of 1933.

**The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.**

The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

American Depositary Shares  
Representing Ordinary Shares



**Benitec Biopharma Limited**  
US\$ per ADS

This is the initial public offering in the United States of Benitec Biopharma Limited, an Australian corporation. We are offering American Depositary Shares, or ADSs. Each ADS will represent 20 ordinary shares. We expect that the initial public offering price will be between US\$ and US\$ per ADS.

Prior to this offering, the ADSs have not been listed on any stock exchange. We have applied for a listing of the ADSs on The NASDAQ Global Select Market under the symbol "BNTC."

Our ordinary shares are listed on the Australian Securities Exchange under the symbol "BLT." On June 22, 2015, the closing price of our ordinary shares on the Australian Securities Exchange was A\$0.78 per ordinary share, equivalent to US\$12.17 per ADS based on an exchange rate of A\$1.00 to US\$0.78 (as published by the Reserve Bank of Australia as of June 22, 2015).

We are an "emerging growth company," as that term is used in the Jumpstart Our Business Startups Act of 2012, and, as such, we have elected to comply with certain reduced public company reporting requirements.

**Investing in the ADSs involves risks. See "Risk Factors" beginning on page 12 of this prospectus.**

	Per ADS	Total
Public offering price	US\$	US\$
Underwriting discounts and commissions	US\$	US\$
Proceeds, before expenses, to us(1)	US\$	US\$

(1) We have agreed to reimburse the underwriters for certain expenses. See "Underwriting."

We have granted the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to additional ADSs from us at the public offering price less the underwriting discounts and commissions. If the underwriters exercise their option in full, the total underwriting discounts and commissions payable by us will be US\$ and the total proceeds to us, before expenses, will be US\$ .

**Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

Delivery of the ADSs will be made against payment in New York, New York, on or about , 2015.

*Sole Bookrunner*

**BMO Capital Markets**

*Lead Manager*

**Maxim Group LLC**

*Co-Manager*

**Roth Capital Partners**

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You may rely only on the information contained in this prospectus. Neither we nor any of the underwriters have authorized anyone to provide information different from that contained in this prospectus. When you make a decision about whether to invest in the ADSs, you should not rely upon any information other than the information in this prospectus. Neither the delivery of this prospectus nor the sale of ADSs means that information contained in this prospectus is correct after the date of this prospectus. This prospectus is not an offer to sell or solicitation of an offer to buy the ADSs in any circumstances under which the offer of solicitation is unlawful.

We have not taken any action to permit a public offering of the ADSs outside the United States or to permit the possession or distribution of this prospectus outside the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about and observe any restrictions relating to the offering of the ADSs and the distribution of this prospectus outside of the United States.

## CONVENTIONS THAT APPLY TO THIS PROSPECTUS

Unless otherwise indicated or the context implies otherwise:

- “we,” “us,” “our” or “Benitec” refers to Benitec Biopharma Limited, an Australian corporation, and its subsidiaries;
- “shares” or “ordinary shares” refers to our ordinary shares;
- “ADSs” refers to American Depositary Shares, each of which represents 20 ordinary shares; and
- “ADRs” refers to American Depositary Receipts, which evidence the ADSs.

Our reporting and functional currency is the Australian dollar. Solely for the convenience of the reader, this prospectus contains translations of some Australian dollar amounts into U.S. dollars at specified rates. Except as otherwise stated in this prospectus, all translations from Australian dollars to U.S. dollars are based on the rate published by the Reserve Bank of Australia on the date indicated. See “Exchange Rate Information.” No representation is made that the Australian dollar amounts referred to in this prospectus could have been or could be converted into U.S. dollars at such rate.

Unless otherwise noted, all industry and market data in this prospectus, including information provided by independent industry analysts, is presented in U.S. dollars. Unless otherwise noted, all other financial and other data related to Benitec Biopharma Limited in this prospectus is presented in Australian dollars. All references to “\$” in this prospectus refer to Australian dollars or U.S. dollars, as the context requires based on the foregoing. All references to “A\$” in this prospectus mean Australian dollars. All references to “US\$” in this prospectus mean U.S. dollars.

Our fiscal year end is June 30. References to a particular “fiscal year” are to our fiscal year ended June 30 of that calendar year.

Unless otherwise indicated, the consolidated financial statements and related notes included in this prospectus have been prepared in accordance with International Accounting Standards and also comply with International Financial Reporting Standards, or IFRS, and interpretations issued by the International Accounting Standards Board, or IASB, which differ in certain significant respects from Generally Accepted Accounting Principles in the United States, or GAAP. See “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Certain Differences Between IFRS and GAAP.”

## INDUSTRY AND MARKET DATA

This prospectus includes information with respect to market and industry conditions and market share from third-party sources or based upon estimates using such sources when available. We believe that such information and estimates are reasonable and reliable. We also believe the information extracted from publications of third-party sources has been accurately reproduced. However, we have not independently verified any of the data from third-party sources. Similarly, our internal research is based upon our understanding of industry conditions, and such information has not been verified by any independent sources.

## TRADEMARKS AND TRADENAMES

We have proprietary and licensed rights to trademarks used in this prospectus which are important to our business, many of which are registered under applicable intellectual property laws. These trademarks are as follows:

- BENITEC BIOPHARMA®™
- SILENCING GENES FOR LIFE®™
- Tribetarna®
- Hepbarna®
- Nervarna®
- Pabparna™

Solely for convenience, trademarks and trade names referred to in this prospectus appear without the “®” or “™” symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent possible under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other companies’ trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other companies. Each trademark, trade name or service mark of any other company appearing in this prospectus is the property of its respective holder.

## PROSPECTUS SUMMARY

*This summary provides a brief overview of information contained elsewhere in this prospectus and is qualified in its entirety by the more detailed information and the financial statements and notes thereto included elsewhere in this prospectus. This summary does not contain all of the information that you should consider before investing in the ADSs. You should read the entire prospectus carefully before making an investment decision, including the information presented under the headings “Risk Factors,” “Cautionary Note Regarding Forward-Looking Statements” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and the historical consolidated financial statements and the related notes to those financial statements included elsewhere in this prospectus.*

## BUSINESS

### Overview

We are a clinical-stage biotechnology company developing a novel, proprietary therapeutic technology platform that combines gene silencing and gene therapy with a goal of providing sustained, long-lasting silencing of disease-causing genes from a single administration. We believe our technology has the potential to be a “one shot” cure for a wide range of diseases that are currently addressed by strict ongoing treatment regimens or that have no effective treatment or only palliative care options. We are using our technology, called DNA-directed RNA interference, or ddRNAi, to develop our pipeline of product candidates for the treatment of numerous chronic and life-threatening human diseases, such as hepatitis C, hepatitis B, age-related macular degeneration, or AMD, drug-resistant non-small cell lung cancer, or NSCLC, and oculopharyngeal muscular dystrophy, or OPMD. These diseases have large patient populations, with the exception of OPMD which is a rare disease. In addition, we have licensed our ddRNAi technology to other biopharmaceutical companies whose pipeline programs are progressing towards, or are in, clinical development for applications including HIV/AIDS, retinitis pigmentosa, Huntington’s disease, cancer immunotherapy and intractable neuropathic pain.

### Our Technology

#### *Standard RNAi approach*

Many diseases are known to be caused by the inappropriate expression of a gene or multiple genes. It has been observed since 1998 that RNA interference, or RNAi, is a mechanism that can potentially be used to specifically turn off, or silence, genes whose sequences are known. Thus, RNAi can potentially be used to treat or cure diseases with a genetic basis by targeting a specific region of the molecular sequence of the disease-causing gene. RNAi is potentially applicable to over 20,000 human genes and a large number of disease-causing microorganism-specific genes. The mechanism of action of RNAi involves the introduction of short interfering RNA, or siRNA, into a cell. The siRNA’s sequence is constructed to match a short region of the target gene. The siRNA is processed by the cell’s own enzymes to destroy the target gene’s messenger RNA, or mRNA, thus preventing the disease-causing gene from being expressed. This occurs as long as the siRNA remains prevalent in the cell.

#### *Our ddRNAi approach*

Our approach differs from the standard RNAi approach, which is commonly referred to as siRNA, which is being developed by several other companies, including Alnylam Pharmaceuticals, Inc., or Alnylam, Tekmira Pharmaceuticals Corporation, or Tekmira, and Dicerna Pharmaceuticals, Inc., or Dicerna. In this standard RNAi approach, double-stranded siRNA is produced synthetically and subsequently introduced into the target cell



either by chemical modification of the RNA or by a range of other delivery methods. While clinical efficacy has been demonstrated for a number of indications utilizing this approach, it has a number of limitations, which include:

- treatment requires repeat administration for multiple cycles in order to maintain its efficacy;
- patient adherence challenges due to dosing frequency and treatment duration;
- therapeutic concentrations of siRNA are not stably maintained because the levels of synthetic siRNA in the cells decrease over time;
- novel chemical modifications or novel delivery materials are typically required to introduce the siRNA into the target cells, making it complicated to develop therapeutics;
- limited ability to target diseases of tissues other than the liver;
- can have an adverse immune response, or interferon response, potentially resulting in serious adverse effects;
- requirement for specialized delivery formulations for those diseases caused by multiple disease-causing genes; and
- siRNA only acts to silence genes, but cannot be used to replace defective genes with normally functioning genes.

Our ddRNAi technology is designed to utilize the specificity and gene silencing effect of RNA interference while overcoming many of the limitations associated with the ongoing administration of siRNA. Our ddRNAi approach combines RNA interference with gene therapy. Unlike siRNA, our ddRNAi technology starts with a DNA construct. Gene therapy vectors, which are carrier molecules, often viruses, that deliver genetic material into the cell, are used to deliver the DNA construct to the nucleus of the targeted cells. The DNA construct then generates double-stranded short hairpin RNAs, or shRNAs, which are processed by the cell into siRNAs, which in turn silence the disease-associated genes. Advantages of our ddRNAi approach include:

- ddRNAi is designed to produce sustained, long-lasting silencing of the disease-causing gene, following a single administration, leading to the potential for “one shot” cures for a wide range of diseases, which could eliminate the requirement for patient compliance to take regular doses of medicine for long-term management of their disease;
- ddRNAi technology can target a wide range of tissues, including, but not limited to, the liver;
- ddRNAi uses the cell’s own transcriptional mechanisms to produce a constant level of shRNA so that intracellular levels of siRNA do not fall below threshold levels required for disease suppression;
- the level of shRNA in the cells can potentially be fine-tuned to achieve optimal concentrations;
- off-tissue effects can be minimized;
- the DNA constructs are shielded in gene therapy vectors that are designed to avoid activating the interferon response;
- ddRNAi provides the option to both silence the defective gene and replace the defective gene with a normal version;
- ddRNAi can be designed to express multiple siRNAs in the same cell, targeting either a single gene at several different sites to minimize the risk of viral resistance, or multiple genes in distinct cellular pathways, potentially enabling treatment of complex genetic diseases such as cancer, diabetes and heart disease; and
- ddRNAi can elicit long-term response by continued expression of siRNA from a single administration, potentially preventing viral reinfection.

## Our Pipeline

The following table sets forth our current product candidates and out-licensed product candidates and their development status.

Focus	Indication	Product Candidate	Company	Discovery	Preclinical Proof of Concept	Clinical Trials Phase I/IIa	Phase IIb/III
<b><i>In-House Programs</i></b>							
Infectious Disease	Hepatitis C (GT-1)	TT-034	Benitec				
	Hepatitis B	Hepbama	Benitec				
Ocular Disease	AMD	TT-211	Benitec				
Cancer	Drug-Resistant Non-Small Cell Lung Cancer	Tribetama	Benitec				
Genetic Disease	OPMD	Pabpama	Benitec				
<b><i>Out-Licensed Programs</i></b>							
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				

Our lead product candidate, TT-034, which currently is in a Phase I/IIa first-in-human clinical trial, is being developed to treat patients chronically infected with the most common genotype, GT-1, of the hepatitis C virus, or HCV. We expect to receive efficacy data in the fourth quarter of 2015. If the results of the trial are favorable, we anticipate commencing a Phase IIb/III trial in the second quarter of 2017. Of the five patients who have been dosed thus far in the Phase I/IIa trial, there have been no treatment-related serious adverse effects observed. Three of the five patients have been biopsied to date, and we have seen shRNA expression in all three. We believe, based on preliminary results from three patients, that TT-034 has clinical proof of concept for the production of shRNA in the liver from a single administration. According to the World Health Organization, or the WHO, 130 million to 150 million individuals worldwide have chronic hepatitis C. Hepatitis C is a leading cause of cirrhosis and hepatocellular carcinoma, which often requires a liver transplant. Patients suffering from HCV have limited treatment options that require adherence to strict recurrent treatment regimens, cause debilitating side effects that can cause patients to deviate from their prescribed treatment regimen, and lack the ability to prevent reinfection. We believe TT-034 represents the first systemic administration of a ddrRNAi-based therapeutic, making us the only company to date to advance into a clinical trial an RNAi therapeutic for systemic administration by gene therapy vectors.

We are also developing Hepbama, which currently is in preclinical studies, for the treatment of the hepatitis B virus, or HBV. We plan to file an investigational new drug, or IND, application in the first quarter of 2017. HBV is a small DNA virus that, according to the WHO, infects up to 240 million people worldwide, resulting in up to 780,000 deaths per year. Infection with HBV occurs in phases ranging from a silent, acute phase that can be resolved by the immune system, to a persistent chronic infection requiring life-long therapy. In the case of a chronic HBV infection, the presence of viral particles and proteins, particularly the s-antigen, causes hepatic inflammation leading to liver dysfunction, acute hepatic failure, cirrhosis or hepatocellular carcinoma. Patients suffering from HBV have limited treatment options from therapies consisting of antivirals and, less commonly, interferon therapy. These treatments require adherence to strict recurrent treatment regimens, may cause the hepatitis B virus to mutate and develop antiviral drug resistance, and may only provide viral suppression through the course of administration, and not a cure. The long-term use of interferon, particularly in high doses, may also be associated with significant side effects, including nausea, vomiting, shortness of breath, dizziness and fatigue,

that can cause patients to deviate from the course of treatment. Hepbarna is designed to be a single administration ddRNAi-based monotherapy that is delivered using a gene therapy vector that targets the liver and inhibits viral replication and s-antigen production on a long-term basis. As both HBV and HCV replicate in the liver, we have designed Hepbarna to mimic the design elements of TT-034, which we believe could help expedite Hepbarna's regulatory pathway.

In addition to TT-034 for HCV and Hepbarna for HBV, we are focusing on developing product candidates to treat AMD, OPMD and drug-resistant NSCLC. For selected product candidates, at the appropriate stage, we may collaborate with large pharmaceutical companies to further develop and, if approved, commercialize them to achieve broad product distribution. For certain products we deem to be outside of our immediate focus, we will continue to out-license, where appropriate, applications of our ddRNAi technology for the development of a range of therapeutics, which we believe could provide further validation of our technology's potential to address numerous diseases.

### **Our Strategy**

Our objective is to become the leader in discovering, developing, clinically validating and commercializing ddRNAi-based therapeutics for a range of human diseases with high unmet clinical need or large patient populations, and to thereby provide a better life for patients with these diseases. Our strategy to accomplish this goal is to:

- **Progress our pipeline of proprietary ddRNAi-based therapeutics.** Our lead product candidate, TT-034, is a single administration ddRNAi-based therapeutic currently in Phase I/IIa to treat the most common genotype of HCV. We are also pursuing early preclinical research in HBV, AMD, drug-resistant NSCLC and OPMD. We plan to submit IND applications for our drug-resistant NSCLC product candidate in the third quarter of 2016 and for our HBV and AMD product candidates in the first and second quarters of 2017, respectively. We expect to complete preclinical proof-of-concept studies for our OPMD product candidate in the third quarter of 2016.
- **Continue our leadership position in ddRNAi-based therapeutics.** We believe we are the only company to date to advance into a clinical trial an RNAi therapeutic for systemic administration by gene therapy vectors.
- **Further develop and improve our ddRNAi platform technology and its associated intellectual property position.** In addition to progressing our pipeline of product candidates, we will further develop and improve our ddRNAi platform technology and its associated intellectual property through in-house development and in-licensing of complementary technologies.
- **Develop drugs in our core disease areas and partner selectively to commercialize and expand our pipeline.** The adaptability of our platform also presents an opportunity for us to selectively form collaborations to expand our capabilities and product offerings into a range of diseases and potentially to accelerate the development and commercialization of ddRNAi therapeutics more broadly. We will continue to expand our franchise of ddRNAi-based therapeutics by out-licensing, where appropriate, applications of ddRNAi for the development of a range of therapeutics outside of our immediate focus. Once clinical proof of concept has been achieved for a product candidate, we plan, where appropriate, to enter into collaborations with pharmaceutical companies to develop that product candidate and ultimately commercialize it if it receives regulatory approval.
- **Pursue indications with high unmet medical need or large patient populations.** Each of our five current core indications are severe diseases with high unmet medical need or large patient populations. We believe there is a strong rationale for treating these diseases and other diseases that have well-characterized gene targets that can be silenced, thus preventing the disease-causing gene from being

expressed. We also intend to develop ddRNAi applications in novel technologies, including cell therapy and immunotherapy, such as chimeric antigen receptor T cells, or CAR T, for a range of additional disease areas.

Our development team has more than 50 years of combined experience in designing and developing ddRNAi therapeutics and includes founding scientists in the ddRNAi field. Additionally, we have rights to intellectual property that includes a patent portfolio protecting our ddRNAi technology platform in numerous jurisdictions through 2019, and a growing portfolio of patents protecting improvements to our ddRNAi technology and product candidates in numerous jurisdictions through at least 2025.

### **Risk Factors**

You should carefully consider the risks described under the “Risk Factors” section beginning on page 12. Some of these risks are:

- We have incurred significant net losses and anticipate that we will continue to incur significant net losses for the foreseeable future. We may never achieve or maintain profitability.
- We have never generated any revenue from product sales and may never be profitable.
- Even if this offering is successful, we will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or discontinue our product development efforts or other operations.
- Currently, no product candidates utilizing ddRNAi technology have been approved for commercial sale, and our approach to the development of ddRNAi technology may not result in safe, effective or marketable products.
- We are early in our product development efforts and have only one product candidate in early-stage clinical trials. All of our other current product candidates are still in preclinical development. We may not be able to obtain regulatory approvals for the commercialization of some or all of our product candidates.
- Issues which may impact ddRNAi delivery into the cell could limit our ability to develop and commercialize product candidates.
- If other companies develop technologies or product candidates for our target disease indications more rapidly than we do or if their technologies, including delivery technologies, are more effective, our ability to develop and successfully commercialize product candidates may be compromised.
- If we are unable to obtain or protect intellectual property rights related to our product candidates, we may not be able to obtain exclusivity for our product candidates or prevent others from developing similar competitive products.
- If we are classified as a “passive foreign investment company,” our U.S. shareholders could suffer adverse tax consequences as a result.
- Australian takeover laws may discourage takeover offers being made for us or may discourage the acquisition of a significant position in our ordinary shares or ADSs.

These and other risks described in this prospectus could materially and adversely impact our business, financial condition, operating results and cash flow, which could cause the trading price of our ADSs to decline and could result in a loss of your investment.

## **Corporate Information**

Benitec Biopharma Limited was incorporated under the laws of Australia in 1995 and has been listed on the Australian Securities Exchange, or ASX, since 1997.

Our headquarters are located at F6A/1-15 Barr St, Balmain, New South Wales, Australia. Our telephone number is +61 2 9555 6986. Our website address is [www.benitec.com](http://www.benitec.com). Information on our website and the websites linked to it do not constitute part of this prospectus or the registration statement to which this prospectus forms a part. Our agent for service of process in the United States is Tacere Therapeutics, Inc., 3940 Trust Way, Hayward, CA 94545.

### **Implications of Being an Emerging Growth Company**

As a company with less than US\$1.0 billion in revenue during our last fiscal year, with less than US\$1 billion in non-convertible debt securities issued in the past three years, and that is pursuing a first registered equity offering in the United States, we qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may avail itself of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies. For example, we have elected to rely on an exemption from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, relating to internal control over financial reporting, and we will not provide such an attestation from our auditors for as long as we qualify as an emerging growth company. We have also elected to rely on an exemption that permits an emerging growth company to include only two years of audited financial statements and only two years of related management’s discussion and analysis of financial condition and results of operations disclosure, and we have therefore only included two years of audited financial statements and related disclosure in this prospectus.

We will remain an emerging growth company until the earliest of:

- the end of the fiscal year in which the fifth anniversary of the completion of this offering occurs;
- the end of the first fiscal year in which the market value of our ordinary shares held by non-affiliates exceeds US\$700 million as of the end of the second quarter of such fiscal year;
- the end of the first fiscal year in which we have total annual gross revenues of at least US\$1 billion; and
- the date on which we have issued more than US\$1 billion in non-convertible debt securities in any rolling three-year period.

Once we cease to be an emerging growth company, we will not be entitled to the exemptions provided for by the JOBS Act.

### **Implications of Being a Foreign Private Issuer**

We are also considered a “foreign private issuer” pursuant to Rule 405 under the Securities Act of 1933, as amended. In our capacity as a foreign private issuer, we are exempt from certain rules under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that impose certain disclosure obligations and procedural requirements for proxy solicitations under Section 14 of the Exchange Act. In addition, our officers, directors and principal shareholders are exempt from the reporting and “short-swing” profit recovery provisions of Section 16 of the Exchange Act and the rules under the Exchange Act with respect to their purchases and sales of our common shares. Moreover, we are not required to file periodic reports and financial statements with the U.S. Securities and Exchange Commission, or SEC, as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act. In addition, we are not required to comply with Regulation FD, which restricts the selective disclosure of material information.

We may take advantage of these exemptions until such time as we are no longer a foreign private issuer. We would cease to be a foreign private issuer at such time as more than 50% of our outstanding voting securities are held by U.S. residents and any of the following three circumstances applies: (1) the majority of our executive officers or directors are U.S. citizens or residents; (2) more than 50% of our assets are located in the United States; or (3) our business is administered principally in the United States. We are required to determine our status as a foreign private issuer on an annual basis at the end of our second fiscal quarter.

**THE OFFERING**

ADSs offered by us . . . . .	ADSs
ADSs to be outstanding immediately after this offering . . . . .	ADSs
Ordinary shares to be outstanding immediately after this offering, including shares underlying ADSs . . .	ordinary shares
Underwriters' option to purchase additional ADSs . . . . .	ADSs
The ADSs . . . . .	Each ADS represents 20 ordinary shares.

The depositary (as identified below) will be the holder of the ordinary shares underlying the ADSs and you will have the rights of an ADS holder as provided in the deposit agreement among us, the depositary and holders and beneficial owners of ADSs from time to time.

You may surrender your ADSs to the depositary to withdraw the ordinary shares underlying your ADSs. The depositary will charge you a fee for such an exchange.

We may amend or terminate the deposit agreement for any reason without your consent. Any amendment that imposes or increases fees or charges or which materially prejudices any substantial existing right you have as an ADS holder will not become effective as to outstanding ADSs until 30 days after notice of the amendment is given to ADS holders. If an amendment becomes effective, you will be bound by the deposit agreement as amended if you continue to hold your ADSs.

To better understand the terms of the ADSs, you should carefully read the section in this prospectus entitled "Description of American Depositary Shares." We also encourage you to read the deposit agreement, which is an exhibit to the registration statement to which this prospectus forms a part.

Depositary . . . . . The Bank of New York Mellon.

Shareholder approval of offering . . . . . Under Australian law, certain steps necessary for the consummation of this offering require the approval of our shareholders voting at an extraordinary general meeting of shareholders. We expect to receive all such required approvals from our shareholders prior to the completion of this offering.

Use of proceeds . . . . . We estimate that the net proceeds to us from this offering, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, will be US\$        million, assuming the ADSs are offered at US\$        per ADS, which is the midpoint of the estimated price range set forth on the cover page of this prospectus. We intend to use the net proceeds from this offering to advance the programs for our therapies, for working capital and for general corporate purposes. See "Use of Proceeds."

- Risk factors ..... You should carefully read and consider the information in this prospectus under the heading “Risk Factors” and all other information included in this prospectus before deciding to invest in the ADSs.
- Listing and trading symbol ..... We have applied for the listing of the ADSs on NASDAQ under the symbol “BNTC.”
- Lock-up ..... We and our directors and executive officers have agreed with the underwriters, subject to specified exceptions, not to sell or transfer any ordinary shares or ADSs or securities convertible into or exercisable for ordinary shares or ADSs, for a period of 180 days after the date of this prospectus. See “Underwriting.”

The number of ordinary shares shown above that will be outstanding immediately following the completion of this offering:

- is based on 115,881,763 ordinary shares outstanding as of March 31, 2015; and
- excludes an aggregate of 25,684,481 ordinary shares issuable upon the exercise of options outstanding at March 31, 2015, at a weighted average exercise price of A\$1.27, of which options to purchase 21,172,996 ordinary shares were vested at a weighted average exercise price of A\$1.29.

Except as otherwise indicated herein, all information in this prospectus assumes no exercise by the underwriters of their option to purchase up to additional ADSs.



## SUMMARY HISTORICAL CONSOLIDATED FINANCIAL DATA

The following tables set forth summary historical financial data for the periods indicated.

The consolidated statement of profit or loss and other comprehensive income data and consolidated statement of financial position data for and as of the fiscal years ended June 30, 2013 and 2014 are derived from the audited consolidated financial statements included in this prospectus. The consolidated statement of profit or loss and other comprehensive income data for the six-month periods ended December 31, 2013 and 2014 and the consolidated statement of financial position data as of December 31, 2014 are derived from the unaudited consolidated financial statements that are included in this prospectus. The consolidated statement of financial position data as of December 31, 2013 are derived from the unaudited consolidated statement of financial position as of December 31, 2013 not included in this prospectus.

Our financial statements have been prepared in Australian dollars and in accordance with International Accounting Standards and IFRS, as issued by the IASB.

You should read the summary consolidated financial data in conjunction with our consolidated financial statements and related notes beginning on page F-1 of this prospectus, and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included elsewhere in this prospectus. Our historical results do not necessarily indicate our expected results for any future periods. Financial results for the six months ended December 31, 2014 are not necessarily indicative of the results that may be expected for the full year ended June 30, 2015.

	For the year ended June 30,		For the six months ended December 31,	
	2014	2013	2014 (unaudited)	2013 (unaudited)
<b>Statement of Profit or Loss and Other Comprehensive Income Data:</b>				
Revenue:				
Revenue .....	A\$ 597,940	A\$ 639,849	A\$ 639,167	A\$ 223,917
Other income .....	775,833	824,333	—	—
Total revenue .....	1,373,773	1,464,182	639,167	223,917
Costs and expenses:				
Royalties and license fees .....	(192,753)	(30,000)	(40,000)	(5,596)
Research and development .....	(3,757,869)	(1,280,012)	(2,210,023)	(1,850,012)
Employment related .....	(2,444,015)	(1,832,065)	(2,343,524)	(1,243,816)
Share-based expenses .....	(355,116)	(518,749)	—	—
Impairment costs .....	—	(1,503,296)	—	—
Travel related expenses .....	(585,359)	(345,826)	(516,528)	(209,772)
Consultants costs .....	(652,839)	(336,570)	(400,305)	(304,341)
Occupancy costs .....	(121,582)	(100,153)	(131,364)	(61,785)
Corporate expenses .....	(646,315)	(531,686)	(436,353)	(386,415)
Foreign exchange translation .....	(111,399)	1,526,215	391,955	14,625
Total costs and expenses .....	(8,867,247)	(4,952,142)	(5,686,142)	(4,047,112)
Loss before income tax .....	(7,493,474)	(3,487,960)	(5,046,975)	(3,823,195)
Income tax benefit .....	454,365	—	—	454,365
Loss for the period .....	A\$ (7,039,109)	A\$ (3,487,960)	A\$ (5,046,975)	A\$ (3,368,830)
Loss per share, basic and diluted .....	A\$ (0.0781)	A\$ (0.0825)	A\$ (0.044)	A\$ (0.043)
Weighted-average shares outstanding, basic and diluted .....	90,432,177	41,688,975	115,218,666	78,846,552

	As of June 30,		As of December 31,	
	2014	2013	2014	2013
			(unaudited)	(unaudited)
<b>Statement of Financial Position Data:</b>				
Cash and cash equivalents . . . . .	A\$31,359,199	A\$1,587,299	A\$26,827,488	A\$5,183,854
Total current assets . . . . .	34,447,525	1,722,590	29,917,889	8,071,440
Total assets . . . . .	34,495,202	1,750,710	30,336,095	8,095,936
Total current liabilities . . . . .	954,680	1,110,370	718,850	404,981
Total liabilities . . . . .	954,680	1,110,370	718,850	404,981
Total equity . . . . .	33,540,522	640,340	29,617,245	7,690,955

## RISK FACTORS

*An investment in the ADSs involves significant risks. You should carefully consider the risks described below and the other information in this prospectus, including our consolidated financial statements and related notes included elsewhere in this prospectus, before you decide to invest in the ADSs. If any of the following risks actually occurs, our business, prospects, financial condition and results of operations could be materially and adversely affected, the trading price of the ADSs could decline and you could lose all or part of your investment.*

### **Risks Related to Our Financial Condition and Capital Requirements**

***We have incurred significant net losses. We anticipate that we will continue to incur significant net losses for the foreseeable future and we may never achieve or maintain profitability.***

We are a clinical-stage biotechnology company and have not yet generated significant revenue. We have incurred losses of A\$3.5 million, A\$7.0 million and A\$5.0 million for the fiscal years ended June 30, 2013 and 2014 and the six months ended December 31, 2014, respectively. We have not generated any revenues from sales of any of our product candidates.

As of December 31, 2014, we had accumulated losses of A\$101.3 million. We have devoted most of our financial resources to research and development, including our clinical and preclinical development activities. To date, we have financed our operations primarily through the issuance of equity securities, research and development grants from the Australian government and payments from our collaboration partners. We have not generated, and do not expect to generate, any significant revenue for the foreseeable future, and we expect to continue to incur significant operating losses for the foreseeable future due to the cost of research and development, preclinical studies and clinical trials and the regulatory approval process for product candidates. The amount of our future net losses is uncertain and will depend, in part, on the rate of our future expenditures. Our ability to continue operations will depend on, among other things, our ability to obtain funding through equity or debt financings, strategic collaborations or additional grants.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue our research and preclinical and clinical development of our product candidates;
- expand the scope of our current preclinical studies and clinical trials for our product candidates or initiate additional preclinical, clinical or other studies for product candidates;
- seek regulatory and marketing approvals for any of our product candidates that successfully complete clinical trials;
- further develop the manufacturing process for our product candidates;
- change or add additional manufacturers or suppliers;
- seek to identify and validate additional product candidates;
- acquire or in-license other product candidates and technologies, which may or may not include those related to our ddRNAi technology and delivery vectors for our therapeutic candidates;
- maintain, protect and expand our intellectual property portfolio;
- create additional infrastructure to support our operations as a public company in the United States and our product development and future commercialization efforts; and
- experience any delays or encounter issues with any of the above.

The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause the price of the ADSs to decline.

***We have never generated any revenue from product sales and may never be profitable.***

Our ability to generate significant revenue and achieve profitability depends on our ability to, alone or with strategic collaboration partners, successfully complete the development of and obtain the regulatory approvals for our product candidates, to manufacture sufficient supply of our product candidates, to establish a sales and marketing organization or suitable third-party alternative for the marketing of any approved products and to successfully commercialize any approved products on commercially reasonable terms. All of these activities will require us to raise sufficient funds to finance business activities. We do not expect any milestone payments from our collaborative partners to be significant in the foreseeable future. In addition, we do not anticipate generating revenue from commercializing product candidates for the foreseeable future, if ever. Our ability to generate future revenues from commercializing product candidates depends heavily on our success in:

- establishing proof of concept in preclinical studies and clinical trials for our product candidates;
- successfully completing clinical trials of our product candidates;
- obtaining regulatory and marketing approvals for product candidates for which we complete clinical trials;
- maintaining, protecting and expanding our intellectual property portfolio, and avoiding infringing on intellectual property of third parties;
- establishing and maintaining successful licenses, collaborations and alliances with third parties;
- developing a sustainable, scalable, reproducible and transferable manufacturing process for our product candidates;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide products and services adequate, in amount and quality, to support clinical development and commercialization of our product candidates, if approved;
- launching and commercializing any product candidates for which we obtain regulatory and marketing approval, either by collaborating with a partner or, if launched independently, by establishing a sales, marketing and distribution infrastructure;
- obtaining market acceptance of any product candidates that receive regulatory approval as viable treatment options;
- obtaining favorable coverage and reimbursement rates for our products from third-party payors;
- addressing any competing technological and market developments;
- identifying and validating new product candidates; and
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter.

The process of developing product candidates for ddRNAi-based therapeutics contains a number of inherent risks and uncertainties. For example, it may not be possible to identify a target region of a disease-associated gene that has not been previously identified and/or patented by others, resulting in restrictions on freedom to operate for that target sequence. Silencing the target gene may not ultimately result in curing the disease as there may be more factors contributing to the development of the disease than the target gene. Silencing the target gene using ddRNAi may lead to short- or long-term adverse effects that were not predicted or observed in preclinical studies. The delivery of the DNA construct to the target cells may not be possible, or complete or adequate to provide sufficient therapeutic benefit.

Even if one or more of our product candidates is approved for commercial sale, we may incur significant costs associated with commercializing any approved product candidate. As one example, our expenses could increase beyond expectations if we are required by the Food and Drug Administration, or FDA, or other regulatory agencies, domestic or foreign, to perform clinical and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations, which could have an adverse effect on our business, financial condition, results of operations and prospects.

***Even if this offering is successful, we will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or discontinue our product development efforts or other operations.***

Developing ddRNAi products is expensive, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance our product candidates in preclinical studies and clinical trials and as we undertake preclinical studies of new product candidates.

As of March 31, 2015, our cash and cash equivalents were A\$26.7 million. We estimate that the net proceeds from this offering will be approximately US\$        million, assuming an initial public offering price of US\$        per ADS, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We estimate that these net proceeds, together with our existing cash and cash equivalents, will be sufficient to fund our operations until at least        . However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government grants or other third-party funding, strategic alliances and licensing arrangements or a combination of these approaches. In addition, because the length of time and activities associated with successful development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. In any event, we will require additional capital to obtain regulatory approval for our product candidates and to commercialize any product candidates that receive regulatory approval.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may compromise our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our shareholders, and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our ordinary shares and the ADSs to decline. If we incur indebtedness we may be required to agree to restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could compromise our ability to conduct our business. We could also seek financing through arrangements with collaborative partners at an earlier stage than would otherwise be desirable and we may be required to relinquish rights to some or all of our technologies or product candidates or otherwise agree to terms unfavorable to us.

If we are unable to obtain funding on a timely basis or on acceptable terms, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any approved product candidates.

***We receive Australian government research and development grants. If we lose funding from these research and development grants, we may encounter difficulties in the funding of future research and development projects, which could harm our operating results.***

We have historically received, and expect to continue to receive, grants through the Australian federal government's Research and Development Tax Incentive program, under which the government provides a cash refund for the 45% of eligible research and development expenditures by small Australian entities, which are defined as Australian entities with less than A\$20 million in revenue, having a tax loss. The Research and Development Tax Incentive grant is made by the Australian federal government for eligible research and development purposes based on the filing of an annual application. We received Research and Development Tax Incentive grants in the fiscal years ended June 30, 2013 and June 30, 2014 of A\$824,333 and A\$775,833, respectively. This grant is available for our research and development activities in Australia, as well as activities in the United States to the extent such U.S.-based expenses relate to our activities in Australia, do not exceed half the expenses for the relevant activities and are approved by the Australian government. To the extent our

research and development expenditures are deemed to be “ineligible,” then our grants would decrease. In addition, the Australian government may in the future modify the requirements of, reduce the amounts of the grants available under, or discontinue the Research and Development Tax Incentive program. Any such change in the Research and Development Tax Incentive program would have a negative effect on our future cash flows.

### **Risks Related to the Product Development and Regulatory Approval of Our Product Candidates**

***Our product candidates are based on ddRNAi technology. Currently, no product candidates utilizing ddRNAi technology have been approved for commercial sale and our approach to the development of ddRNAi technology may not result in safe, effective or marketable products.***

We have concentrated our product research and development efforts on our ddRNAi technology, and our future success depends on successful clinical development of this technology. We plan to develop a pipeline of product candidates using our ddRNAi technology and deliver therapeutics for a number of chronic and life-threatening conditions, including hepatitis C, hepatitis B, age-related macular degeneration, drug-resistant non-small cell lung cancer and OPMD.

The scientific research that forms the basis of our efforts to develop product candidates is based on the therapeutic use of ddRNAi, and the identification, optimization and delivery of ddRNAi-based product candidates is relatively new. The scientific evidence to support the feasibility of successfully developing therapeutic treatments based on ddRNAi is preliminary and limited. There can be no assurance that any development and technical problems we experience in the future will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may be unable to reach agreement on favorable terms, or at all, with providers of vectors needed to optimize delivery of our product candidates to target disease cells and we may also experience unanticipated problems or delays in expanding our manufacturing capacity or transferring our manufacturing process to commercial partners, any of which may prevent us from completing our clinical trials or commercializing our products on a timely or profitable basis, if at all.

Only a few product candidates based on RNAi or ddRNAi have been tested in either animals or humans, and a number of clinical trials conducted by other companies using other forms of RNAi technologies have not been successful. We may discover that application of ddRNAi does not possess properties required for a therapeutic benefit, such as the ability to continually express shRNAs for the period of time required to be maximally effective or the ability of viral vectors or other technologies to effectively deliver ddRNAi constructs to target cells in therapeutically relevant concentrations. In addition, application of ddRNAi-based products in humans may result in safety problems. We currently have only limited data, and no conclusive evidence, to suggest that we can effectively produce effective therapeutic treatments using our ddRNAi technology.

***We are early in our product development efforts and have only one product candidate in early-stage clinical trials. All of our other current product candidates are still in preclinical development. We may not be able to obtain regulatory approvals for the commercialization of some or all of our product candidates.***

The research, testing, manufacturing, labeling, approval, selling, marketing and distribution of biologics is subject to extensive regulation by the FDA and other regulatory authorities, and these regulations differ from country to country. We do not have any products on the market and are early in our development efforts. We have only one product candidate in clinical trials and all of our other product candidates are in preclinical development. All of our current and future product candidates are subject to the risks of failure typical for development of biologics. The development and approval process is expensive and can take many years to complete, and its outcome is inherently uncertain. In addition, the outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results.

We have not submitted an application, or received marketing approval, for any of our product candidates and will not submit any applications for marketing approval for several years. We have limited experience in

conducting and managing clinical trials necessary to obtain regulatory approvals, including approval by the FDA. To receive approval, we must, among other things, demonstrate with evidence from clinical trials that the product candidate is both safe and effective for each indication for which approval is sought, and failure can occur in any stage of development. Satisfaction of the approval requirements typically takes several years and the time needed to satisfy them may vary substantially, based on the type, complexity and novelty of the pharmaceutical product. We cannot predict if or when we might receive regulatory approvals for any of our product candidates currently under development.

The FDA and foreign regulatory authorities also have substantial discretion in the pharmaceutical product approval process. The numbers, types and sizes of preclinical studies and clinical trials that will be required for regulatory approval varies depending on the product candidate, the disease or condition that the product candidate is designed to address and the regulations applicable to any particular product candidate. Approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, and there may be varying interpretations of data obtained from preclinical studies or clinical trials, any of which may cause delays or limitations in the approval or the decision not to approve an application. Regulatory agencies can delay, limit or deny approval of a product candidate for many reasons, including:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory authorities for approval;
- the patients recruited for a particular clinical program may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- the results of clinical trials may not confirm the positive results from earlier preclinical studies or clinical trials;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to the satisfaction of FDA or comparable foreign regulatory authorities to support the submission of a biologics license application, or BLA, or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may only agree to approve a product candidate under conditions that are so restrictive that the product is not commercially viable;
- regulatory agencies might not approve or might require changes to our manufacturing processes or facilities; or
- regulatory agencies may change their approval policies or adopt new regulations in a manner rendering our clinical data insufficient for approval.

Any delay in obtaining or failure to obtain required approvals could materially and adversely affect our ability to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact the price of the ADSs. Furthermore, any regulatory approval to market a product may be subject to limitations on the indicated uses for which we may market the product. These limitations may limit the size of the market for the product.

We are not permitted to market our product candidates in the United States or in other countries until we receive approval of a BLA from the FDA or marketing approval from applicable regulatory authorities outside the United States. Obtaining approval of a BLA can be a lengthy, expensive and uncertain process. If we fail to obtain FDA approval to market our product candidates, we will be unable to sell our product candidates in the United States, which will significantly impair our ability to generate any revenues. In addition, failure to comply with FDA and non-U.S. regulatory requirements may, either before or after product approval, if any, subject us to administrative or judicially imposed sanctions, including:

- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- restrictions on the products, manufacturers or manufacturing process;
- warning letters;
- civil and criminal penalties;
- injunctions;
- suspension or withdrawal of regulatory approvals;
- product seizures, detentions or import bans;
- voluntary or mandatory product recalls and publicity requirements;
- total or partial suspension of production;
- imposition of restrictions on operations, including costly new manufacturing requirements; and
- refusal to approve pending BLAs or supplements to approved BLAs.

Even if we do receive regulatory approval to market a product candidate, any such approval may be subject to limitations on the indicated uses for which we may market the product. It is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain the appropriate regulatory approvals necessary for us or our collaborators to commence product sales. Any delay in obtaining, or an inability to obtain, applicable regulatory approvals would prevent us from commercializing our product candidates, generating revenues and achieving and sustaining profitability.

***Because our product candidates are based on a novel technology, it is difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval.***

The clinical trial requirements of the FDA and comparable foreign regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of such product candidates. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other pharmaceutical product candidates. The FDA and comparable foreign regulatory authorities have relatively limited experience with ddRNAi-based therapeutics, which makes it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the United States or other countries. We and our current collaborators, or any future collaborators, may never receive approval to market and commercialize any product candidate. Even if we or a collaborator obtain regulatory approval, the approval may be for disease indications or patient populations that are not as broad as we intended or desired and may require labeling that includes significant use or distribution restrictions or safety warnings.

Regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. For example, the FDA has established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the United States National Institutes of Health, or the NIH, are also subject to review by the NIH



Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or the RAC. Although the FDA decides whether individual gene therapy protocols may proceed, the RAC review process can delay the initiation of a clinical trial, even if the FDA has reviewed the trial design and details and approved its initiation. Conversely, the FDA can put a proposed biological product on clinical hold even if the RAC has provided a favorable review of the product. Also, before a clinical trial can begin at any institution, that institution's institutional review board, or IRB, and its institutional biosafety committee, or IBC, if it has one, have to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or comparable foreign regulatory bodies to change the requirements for approval of any of our product candidates.

These committees and advisory groups and the new guidelines they promulgate and new requirements they may impose may lengthen the clinical development and regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory committees and advisory groups, and comply with applicable guidelines and requirements as they may change from time to time. If we fail to do so, we may be required to delay or discontinue development of our product candidates. These additional processes may result in a development, review and approval process that is longer than we otherwise would have expected for our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market would delay or prevent us from commercializing our product candidates, generating revenues and achieving and sustaining profitability.

***Preliminary positive results from the clinical trial of our leading product candidate are not necessarily predictive of the final results of the trial, and positive results from preclinical studies of our product candidates are not necessarily predictive of the results of our planned clinical trials of our product candidates.***

As of April 2015, five patients have been dosed and three of those have been biopsied in our Phase I/IIa clinical trial for TT-034 and in those biopsied patients we have observed shRNA expressions in the patients' liver cells. The preliminary results from this trial are not necessarily predictive of the final results of the trial. The biological effect observed in this trial has been observed in only the three patients who have been biopsied to date, is not statistically significant and might not be observed in any other patients treated with TT-034. It is also important to note that in these first two dose cohorts, the biological response was designed to be, and was observed to be, lower than the level required to achieve a therapeutic effect in those patients.

In addition, positive results in preclinical proof-of-concept and animal studies of our product candidates may not result in positive results in clinical trials in humans. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical trials after achieving positive results in preclinical development or early stage clinical trials, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway or safety or efficacy observations made in clinical trials, including adverse events. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or other regulatory authority approval. If we fail to produce positive results in our clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be negatively impacted.

***Issues that may impact ddRNAi delivery to the cell could adversely affect or limit our ability to develop and commercialize product candidates.***

Successful clinical development of ddRNAi-based therapeutics is largely dependent on using the appropriate vectors to obtain therapeutically relevant concentrations of the DNA constructs that express the

shRNAs in the appropriate target cells. To develop effective product candidates, we will need to license delivery technologies from third parties or develop delivery technologies with research collaborators. Although delivery technologies, including AAV vectors, have been identified and are well defined for specific tissue types, we continue to seek vectors with ideal delivery properties for other indications we are pursuing, including OPMD. The tissue tropism and other physical properties of AAV vectors are limited and may not be effective for other product candidates or delivery into a wide array of tissues types. AAV vectors can also trigger immune responses in some patients, and those patients will not derive clinical benefit from administration of a product candidate unless steps are taken to clinically address the issue. If we or our collaborators are not successful in identifying effective vectors for our product candidates, we may not succeed in developing marketable products. In addition, if we are unable to reach agreement on favorable terms, or at all, with providers of any effective vectors that we do identify, we may not succeed in completing our clinical trials or commercializing our products on a timely or profitable basis, if at all. We have only one such agreement in place that allows us to use a vector both for clinical trials and for commercialization, and that agreement is with respect to our program for the treatment of AMD.

We use AAV vectors as part of our ddRNAi approach for several indications. As such, we require licenses and the ability to manufacture large quantities of AAV particles under the FDA's current good manufacturing practices, or cGMP, requirements and those of comparable foreign regulatory authorities in order to commercialize a product candidate using an AAV vector.

***We may find it difficult to enroll patients in our clinical trials, and patients could discontinue their participation in our clinical trials, which could delay or prevent clinical trials of our product candidates and make those trials more expensive to undertake.***

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on the speed at which we can recruit patients to participate in testing our product candidates. Patients may be unwilling to participate in our clinical trials because of negative publicity from adverse events in the biotechnology, RNAi or gene therapy industries. Patients may be unavailable for other reasons, including competitive clinical trials for similar patient populations, and the timeline for recruiting patients, conducting trials and obtaining regulatory approval of potential products may be delayed. If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or discontinue ongoing or planned clinical trials. Clinical trial delays could result in increased costs, slower product development, setbacks in testing the effectiveness of our technology or discontinuation of the clinical trials altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a trial, to complete our clinical trials in a timely manner. Patient enrollment is affected by factors including:

- finding and diagnosing patients;
- severity of the disease under investigation;
- design of the clinical trial protocol;
- size and nature of the patient population;
- eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under study;
- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials;
- clinicians' and patients' perceptions of the potential advantages of the product being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating;

- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

For example, we have experienced some difficulties in enrolling patients in our clinical trial of TT-034. This has been due to several factors, including sudden changes in patients' viral load, liver enzymes and other clinical parameters immediately prior to their dosing, as well as late withdrawal due to personal reasons. We believe the increased availability of new and effective therapies such as Sovaldi and Harvoni, which were recently approved for treatment of the hepatitis C virus, and the fact that the early lower-dose cohort patients receive a sub-therapeutic dose of TT-034, may also be contributing factors. We may continue to face difficulties enrolling patients in our clinical trials for TT-034 for these and other reasons that may arise as we proceed.

We or our collaborators plan to seek initial marketing approval for our product candidates in the United States, Australia and Europe. We may not be able to initiate or continue clinical trials in a timely manner if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by the FDA or comparable foreign regulatory agencies. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with contract research organizations, or CROs, clinical sites and physicians;
- different standards for the conduct of clinical trials;
- our inability to locate and engage qualified local consultants, physicians and partners; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatments.

In addition, patients enrolled in our clinical trials may discontinue their participation at any time during the trial as a result of a number of factors, including experiencing adverse events, which may or may not be judged related to our product candidates under evaluation. The discontinuation of patients in any one of our trials may cause us to delay or discontinue our clinical trial, or cause the results from that trial not to be positive or sufficient to support either partnering with a pharmaceutical company to further develop and commercialize the product candidate or filing for regulatory approval of the product candidate.

***We may encounter substantial delays in our clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.***

We are currently in Phase I/IIa clinical trials for TT-034 for the treatment of hepatitis C. None of our other proprietary product candidates is currently in clinical trials. Before obtaining marketing approval from regulatory authorities for the sale of TT-034 or any other product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical trials are expensive and time-consuming, and their outcome is uncertain. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include:

- inability to generate sufficient preclinical, toxicology or other data to support the initiation of human clinical trials;
- delays in reaching consensus with regulatory agencies on trial design;
- identifying, recruiting and training suitable clinical investigators;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- delays in obtaining required IRB or IBC approval at each clinical trial site;
- delays in recruiting suitable patients to participate in our clinical trials;

- imposition of a clinical hold by regulatory agencies, including after an inspection of our clinical trial operations or trial sites;
- failure by our CROs, other third parties or us to adhere to clinical trial requirements;
- failure to perform in accordance with the FDA's good clinical practices, or GCP, or applicable regulatory requirements in other countries;
- inability to manufacture, test, release, import or export for use sufficient quantities of our product candidates for use in clinical trials;
- failure to manufacture our product candidate in accordance with cGMP requirements or applicable regulatory guidelines in other countries;
- delays in the testing, validation and manufacturing of our product candidates;
- delays in the delivery of our product candidates to the clinical trial sites;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- clinical trial sites dropping out of a trial;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical trial protocols; or
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or discontinue product development programs.

Further, a clinical trial may be suspended or discontinued by us, our collaborators, the IRBs or the IBCs at the sites in which such trials are being conducted, the data safety monitoring board, or DSMB, for such trial, or by the FDA or comparable foreign regulatory authorities due to a number of factors, including the imposition of a clinical hold or termination of a trial due to failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, unforeseen safety issues or adverse side effects of our product candidate, or a product candidate from another company that shares similar properties, failure to demonstrate adequate benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience discontinuation of, or delays in the completion of, any clinical trial of our product candidates, the commercial prospects of our product candidates may be harmed, and our ability to generate product revenues from any of these product candidates may be eliminated or delayed. Furthermore, many of the factors that lead to a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

In addition, if we or our third-party collaborators make significant manufacturing or formulation changes to our product candidates, we or they may need to conduct additional studies to bridge the modified product candidates to earlier versions to ensure comparability and safety of the two different product candidates.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to commercialize our programs and product candidates. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates.

If the results of our clinical trials are inconclusive or if there are safety concerns or adverse events associated with our product candidates, we may:

- fail to obtain, or be delayed in obtaining, marketing approval for our product candidates;

- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- need to change the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw their marketing approval of the product after granting it;
- have regulatory authorities impose restrictions on distribution of the product in the form of a risk evaluation and mitigation strategy, or REMS, or modified REMS, that limit our ability to commercialize the product;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued and held liable for harm caused to patients; or
- experience damage to our reputation.

Any of these events could prevent us from achieving or maintaining market acceptance of our product candidates and impair our ability to commercialize our product candidates.

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of any particular study, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any BLA we submit to the FDA or any comparable foreign regulating authorities. Any such delay or rejection could prevent us from commercializing our product candidates.

***Our product candidates and the process for administering our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following any potential marketing approval.***

Treatment with our product candidates may produce undesirable side effects or adverse reactions or events. For example, the AAV vector and related capsid protein, which we are currently using to deliver most of our ddRNAi product candidates, could cause adverse immunological side effects due to preexisting and/or recall responses to the naturally occurring virus from which the vector is engineered, or to the DNA construct product itself. These responses may also interfere with therapeutic efficacy if not identified and managed optimally. Preexisting immune responses to AAV manifesting as neutralizing antibodies are common within the general population and may be a limitation to the enrollment of patients in gene therapy clinical trials using AAV vectors, the successful use of AAV vectors in gene therapy clinical trials and the market acceptance of product candidates, if approved, that are delivered using AAV vectors. Patients with neutralizing antibodies to AAV will not derive clinical benefit from administration of such a product candidate unless steps are taken to clinically address the issue and those treatments themselves may cause adverse effects. In previous clinical trials undertaken by other companies involving systemic administration of AAV viral vectors for gene therapy, some subjects experienced adverse events, including the development of a negative T cell response against the AAV capsid protein. If our vectors cause similar adverse events, we may be required to delay or discontinue further clinical development of our product candidates. It is also possible that we may discover new adverse events related to AAV or other vectors, which could potentially enhance the risk to patients who use our product candidates delivered with that vector.

If any such adverse events occur, our clinical trials could be suspended or discontinued and the FDA or comparable foreign regulatory authorities could order us to cease further development or deny approval of our

product candidates for any or all targeted indications. The product-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial. If we elect or are required to delay, suspend or discontinue any clinical trial of any of our product candidates, the commercial prospects of such product candidates will be harmed and our ability to generate product revenues from any of these product candidates will be delayed or eliminated. Any of these occurrences may harm our business, financial condition and prospects significantly.

Additionally, if any of our product candidates receive marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits of the product outweigh its risks, which may include, among other things, a medication guide outlining the risks of gene therapies for distribution to patients and a communication plan to patients and healthcare practitioners. Other elements to assure safe use in a mandated REMS could include, but are not limited to, restrictions upon distribution and prescribing, additional prescriber training, establishment of patient registries and other measures that could limit commercialization of the product. Comparable foreign regulating authorities might require adoption of measures similar to a REMS. Furthermore, if we or others later identify undesirable side effects caused by our product candidate, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way a product candidate is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our product candidates and could significantly harm our business, prospects, financial condition and results of operations.

***If we are unable to successfully develop related diagnostics for our therapeutic product candidates, or experience significant delays in doing so, we may not achieve marketing approval or realize the full commercial potential of our therapeutic product candidates.***

We plan to develop related diagnostics for some of our therapeutic product candidates, including Tribetarna targeting drug-resistant non-small cell lung cancer. Such related diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as medical devices and require separate regulatory approval or clearance prior to commercialization. Marketing approval or clearance of the diagnostic will require sufficient data to support its safety and efficacy. In addition, at least in some cases, the FDA and comparable foreign regulatory authorities may require the development and regulatory approval or clearance of a related diagnostic as a condition to approving our therapeutic product candidates. While we have some, limited experience in developing diagnostics, we plan to rely in large part on third parties to perform these functions. We may seek to enter into arrangements with one or more third parties to create a related diagnostic for use with our current or future product candidates.

If we, or any third parties that we engage to assist us, are unable to successfully develop or obtain marketing approval or clearance for related diagnostics for our therapeutic product candidates, or experience delays in doing so:

- the development of Tribetarna and potentially other product candidates may be delayed or impaired altogether if we are unable to appropriately select patients for enrollment in our clinical trials;
- our relevant therapeutic product candidate may not receive marketing approval if its effective use depends on a related diagnostic in the regulatory authority's judgment; and

- we may not realize the full commercial potential of any therapeutic product candidates that receive marketing approval if, among other reasons, we are unable to appropriately identify patients with the specific genetic alterations targeted by our therapeutic product candidates.

If any of these events were to occur, our business would be harmed.

***Even if we complete the necessary preclinical studies and clinical trials, we cannot predict when or if we will obtain regulatory approval to commercialize a product candidate or the approval may be for a more narrow indication than we expect.***

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in clinical trials, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or comparable foreign regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process. Regulatory agencies also may approve a treatment candidate for fewer or more limited indications than requested, may not approve the price we intend to charge for our product candidate, may limit our ability to promote the product, may impose significant limitations upon the approval of the product, including, but not limited to, narrow indications, significant warnings, precautions or contraindications with respect to conditions of use, or may grant approval subject to the performance of post-marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. The FDA or comparable foreign regulatory authorities may impose a REMS or other conditions upon our approval that limit our ability to commercialize the product candidate.

***Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny.***

Even if we obtain regulatory approval in a jurisdiction, the regulatory authority may still impose significant restrictions on the indicated uses or marketing of our product candidates, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. For example, the holder of an approved BLA is obligated to monitor and report to the FDA adverse events and any failure of a product to meet the specifications in the BLA. FDA guidance advises that patients treated with some types of gene therapy undergo follow-up observations for potential adverse events for as long as 15 years. The holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable foreign, federal and state laws.

In addition, product manufacturers and their establishments, products and applications are subject to payment of user fees and continual review and periodic inspections by the FDA and comparable foreign regulatory authorities for compliance with cGMP and comparable foreign requirements, and adherence to commitments made in the BLA. If we or a regulatory agency discover previously unknown problems with a product such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of any of our product candidates, a regulatory agency may:

- issue a warning letter asserting that we are in violation of the law;

- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to permit government reimbursement of our product by government-sponsored third-party payors;
- refuse to approve a pending BLA or supplements to a BLA submitted by us for other indications or new product candidates;
- seize our product; or
- refuse to allow us to enter into or continue supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenues.

***Even if we obtain and maintain approval for our product candidates from the FDA, we may never obtain approval for our product candidates outside of the United States, which would limit our market opportunities and adversely affect our business.***

Approval of a product candidate in the United States by the FDA does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Sales of our product candidates outside of the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries must also approve the manufacturing and marketing of the product candidates in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval. Even if a product candidate is approved, the FDA or comparable regulatory authorities in other countries, as the case may be, may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the United States also have requirements for approval of product candidates with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries.

Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Regulatory approval of a product candidate in one country does not ensure approval in any other country, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in other countries. Also, regulatory approval for any of our product candidates may be withdrawn based on adverse events reported or regulatory decisions made in other countries. If we fail to comply with the regulatory requirements in international markets and/or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be compromised and our business may be adversely affected.

***Our future prospects are also dependent on our or our collaborators' ability to successfully develop a pipeline of additional product candidates, and we and our collaborators may not be successful in efforts to use our platform technologies to identify or discover additional product candidates.***

The success of our business depends primarily upon our ability to identify, develop and commercialize products based on our platform technology. We only have one product candidate currently in clinical development.



Our other product candidates derived from our platform technology may not successfully complete IND-enabling studies, and our research programs may fail to identify other potential product candidates for clinical development for a number of reasons. Our and our collaborators' research methodology may be unsuccessful in identifying potential product candidates, our potential product candidates may not demonstrate the necessary preclinical outcomes to progress to clinical studies, or our product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

If any of these events occur, we may be forced to discontinue our development efforts for a program or programs. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

***We may not be able to obtain orphan drug exclusivity for our product candidates.***

Of our current product candidates, the only one designed for treatment of an indication that would likely qualify for rare disease status is Pabparna for the treatment of OPMD. Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs or biological products for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a product intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. The FDA may also designate a product as an orphan drug if it is intended to treat a disease or condition of more than 200,000 individuals in the United States and there is no reasonable expectation that the cost of developing and making a drug or biological product available in the United States for this type of disease or condition will be recovered from sales of the product candidate. Under the European Union orphan drug legislation, a rare disease or condition means a disease or condition which affects not more than five in ten thousand persons in the European Union at the time of the orphan drug designation application.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug for that time period. During the marketing exclusivity period, in the European Union, the European Medicines Agency, or the EMA, is precluded from approving a similar drug with an identical therapeutic indication. The applicable period is seven years in the United States and ten years in the European Union. The European Union exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition, and the same drug could be approved for a different condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug, made by a competitor, for the same condition if the FDA concludes that the competitive product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In the European Union, the EMA can approve a competitive product if the orphan drug no longer meets the criteria for orphan designation (including sufficient profitability), if the competitive product is safer, more effective or otherwise clinically superior, or if the orphan drug cannot be supplied in sufficient quantities.

**Risks Related to Our Reliance on Third Parties**

***Our prospects for successful development and commercialization of our products are dependent to varying degrees upon the research, development, commercialization, and marketing efforts of our collaborators.***

We rely on third parties for certain aspects of the research, development, commercialization and marketing of our current and any future product candidates. Other than as provided for in our collaboration agreements, we

have no control over the resources, time and effort that our collaborators may devote to the development of product candidates using our ddRNAi technology. We are dependent on our collaborators to conduct some aspects of the research and development of each of our product candidates, and expect to need access to them to facilitate and/or to complete the regulatory process. We will likely rely on a pharmaceutical company for the successful marketing and commercialization of any such product candidates for which they/we receive approval, if any. There can be no guarantee at this stage that we will conclude a partnership with such a company on favorable terms, or at all, nor even if we do so, that success will be achieved.

Our ability to recognize revenues from successful collaborations may be impaired by multiple factors including:

- a collaborator may shift its priorities and resources away from our programs due to a change in business strategies, or a merger, acquisition, sale or downsizing of its company or business unit;
- a collaborator may cease development in an area that is the subject of a collaboration agreement;
- a collaborator may change the success criteria for a particular program or product candidate in development, thereby delaying or ceasing development of such program or product candidate in development;
- a collaborator with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;
- a collaborator with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- a collaborator may exercise its rights under the agreement to discontinue our collaboration;
- a dispute may arise between us and a collaborator concerning the development and commercialization of a product candidate in development, resulting in a delay in milestones, royalty payments, or discontinuation of a program and possibly resulting in costly litigation or arbitration that may divert management attention and resources;
- a collaborator may not adequately protect the intellectual property rights associated with a product candidate; and
- a collaborator may use our proprietary information or intellectual property in such a way as to expose us to litigation from a third party.

If our collaborators do not perform in the manner we expect or fulfill their responsibilities in a timely manner, or at all, the development, regulatory and commercialization process could be delayed or discontinued or otherwise be unsuccessful. Conflicts between us and our collaborators may arise. In the event of discontinuation of one or more of our collaboration agreements, it may become necessary for us to assume the responsibility for any such product candidates at our own expense or seek new collaborators. In that event, we likely would be required to limit the size and scope of one or more of our independent programs or increase our expenditures and seek additional funding, which may not be available on acceptable terms or at all, and our business may be harmed.

***We rely on third parties to conduct our preclinical studies and clinical trials. If these third parties do not meet our deadlines or otherwise conduct the studies as required, we may be delayed in progressing, or ultimately may not be able to progress, product candidates to clinical trials, our clinical development programs could be delayed or unsuccessful, and we may not be able to commercialize or obtain regulatory approval for our product candidates when expected, or at all.***

We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. We are dependent on third parties to conduct the clinical trials for TT-034, and preclinical studies for our other product candidates, and therefore the timing of the initiation and completion of these trials and studies is reliant on third parties and may occur at times substantially different from our estimates or expectations.

In the case of clinical trials, we rely on CROs and third-party collaborators to conduct our clinical trials in accordance with our clinical protocols and regulatory requirements. Our CROs, investigators and third-party collaborators play a significant role in the conduct of these trials and subsequent collection and analysis of data. There is no guarantee that any CROs, investigators or the other third-party collaborators on which we rely for administration and conduct of our clinical trials will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fails to meet expected deadlines, fails to adhere to our clinical protocols, fails to meet regulatory requirements or otherwise performs in a substandard manner, our clinical trials may be extended, delayed or terminated. If any of our clinical trial sites terminates for any reason, we may lose all of the information on subjects enrolled in our ongoing clinical trials.

If we cannot contract with acceptable third parties on commercially reasonable terms, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed or discontinued.

In all events, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. The FDA requires clinical trials to be conducted in accordance with current GCP, including for conducting, recording and reporting the results of preclinical studies and clinical trials to assure that data and reported results are credible and accurate and that the rights and confidentiality of clinical trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements, and any failure to satisfy these responsibilities and requirements, whether caused by us or by third parties upon whom we rely, could have a material adverse effect on our business, financial condition, results of operations and prospects.

***Because we rely on third-party manufacturing and supply partners, our supply of research and development, preclinical and clinical development materials may become limited or interrupted or may not be of satisfactory quantity or quality.***

We rely on third-party supply and manufacturing partners to manufacture and supply the materials for our research and development and preclinical and clinical study supplies. We do not own manufacturing facilities or supply sources for such materials.

There can be no assurance that our supply of research and development, preclinical and clinical development biologics and other materials will not be limited, interrupted or restricted in certain geographic regions, be of satisfactory quality or continue to be available at acceptable prices. Replacement of a third-party manufacturer could require significant effort, cost and expertise because there may be a limited number of qualified replacements.

The manufacturing process for a product candidate is subject to FDA and foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as cGMP. In the event that any of our suppliers or manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves or enter into an agreement with another third party, which would be costly and delay clinical trials.

In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills or technology to another third party. These factors increase our reliance on our manufacturers and may require us to obtain a license from a manufacturer in order to

have another third-party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines of the FDA and comparable foreign regulatory authorities. The delays and costs associated with the verification of a new manufacturer could increase our costs and delay the development of our product candidates.

We expect to continue to rely on third-party manufacturers for preclinical and clinical grade product candidates and if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements could adversely affect our business in a number of ways, including:

- an inability to conduct necessary preclinical studies to progress our product candidates to clinical trials;
- an inability to initiate or continue clinical trials of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- loss of the cooperation of a collaborator;
- subjecting our product candidates to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

***We and our collaborators may disagree over our right to receive payments under our collaboration agreements, potentially resulting in costly litigation and loss of reputation.***

Our ability to receive payments under our collaboration agreements depends on our ability to clearly delineate our rights under those agreements. We have out-licensed portions of our intellectual property to our collaborators with the intent that our collaborators will develop product candidates based on our ddRNAi technology to address specific conditions, including HIV/AIDS, certain cancers, ocular diseases and genetic diseases and intractable neuropathic pain. However, a collaborator may use our intellectual property without our permission, dispute our ownership of intellectual property rights, or argue that our intellectual property does not cover, or add value to, any product candidates they develop. If a dispute arises, it may result in costly patent office procedures and litigation, and our collaborator may refuse to pay us while the dispute is ongoing. Furthermore, regardless of any resort to legal action, a dispute with a collaborator over intellectual property rights may damage our relationship with that collaborator and may also harm our reputation in the industry. Even if we are entitled to payments from our collaborators, we may not actually receive these payments, or we may experience difficulties in collecting the payments to which we believe we are entitled. After our collaborators launch commercial products containing our licensed traits, we will need to rely on the good faith of our collaborators to report to us the sales they earn from these products and to accurately calculate the payments we are entitled to, a process that will involve complicated and difficult calculations. Although we seek to address these concerns in our collaboration agreements by reserving our right to audit financial records, such provisions may not be effective.

***We have only limited experience in regulatory affairs and intend to rely on consultants and other third parties for regulatory matters, which may affect our ability or the time we require to obtain necessary regulatory approvals.***

We have limited experience in filing and prosecuting the applications necessary to gain regulatory approvals for gene therapy or ddRNAi product candidates. Moreover, the product candidates that are likely to result from

our development programs are based on novel technologies that have not been extensively tested in humans. The regulatory requirements governing these types of product candidates may be less well defined or more rigorous than for conventional products. As a result, we may experience a longer regulatory process in connection with obtaining regulatory approvals of any products that we develop. We intend to rely on independent consultants for purposes of our regulatory compliance and product development and approvals in the United States and elsewhere. Any failure by our consultants to properly advise us regarding, or properly perform tasks related to, regulatory compliance requirements could compromise our ability to develop and seek regulatory approval of our product candidates.

***Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.***

Because we rely on third parties to manufacture our product candidates, and because we collaborate with various organizations and academic institutions on the advancement of our technology and product candidates, we may, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite these contractual provisions, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by potential competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, discovery by a third party of our trade secrets or other unauthorized use or disclosure would impair our intellectual property rights and protections in our product candidates.

In addition, these agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us. In other cases we may share these rights with other parties. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication.

### **Risks Related to Commercialization of Our Product Candidates**

***We have not entered into agreements with any third-party manufacturers to support commercialization of our product candidates. Additionally, no manufacturers have experience producing our product candidates at commercial levels, and any manufacturer that we work with may not achieve the necessary regulatory approvals or produce our product candidates at the quality, quantities, locations and timing needed to support commercialization.***

We have not yet secured manufacturing capabilities for commercial quantities of our product candidates or established facilities in the desired locations to support commercialization of our product candidates. We intend to rely on third-party manufacturers for commercialization, and currently we have only entered into agreements with such manufacturers to support our clinical trials for TT-034. We may be unable to negotiate agreements with third-party manufacturers to support our commercialization activities on commercially reasonable terms.

We may encounter technical or scientific issues related to manufacturing or development that we may be unable to resolve in a timely manner or with available funds. Currently, we do not have the capacity to manufacture our product candidates on a commercial scale. In addition, our product candidates are novel, and no manufacturer currently has experience producing our product candidates on a large scale. If we are unable to engage manufacturing partners to produce our product candidates on a larger scale on reasonable terms, our commercialization efforts will be harmed.

Even if we timely develop a manufacturing process and successfully transfer it to the third-party manufacturers of our product candidates, if such third-party manufacturers are unable to produce the necessary quantities of our product candidates, or do so in compliance with cGMP or with pertinent foreign regulatory requirements, and within our planned time frame and cost parameters, the development and sales of our product candidates, if approved, may be impaired.

***If we are unable to enter into agreements with third parties to commercialize our product candidates or establish sales and marketing capabilities to market and sell our product candidates, we may be unable to generate any revenues.***

We currently have no sales and marketing organization and have no experience selling and marketing pharmaceutical products. To successfully commercialize any product candidates that may be approved, we will need to develop these capabilities, either through our relationships with collaborators or our own. We may seek to enter into collaborations with other entities to utilize their marketing and distribution capabilities, but we may be unable to enter into marketing agreements on favorable terms, if at all. If our future collaborators do not commit sufficient resources to commercialize our future products, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. The establishment and development of our own sales force or the establishment of a contract sales force to market any products we may develop will be expensive and time-consuming and could delay any product launch. Moreover, we cannot be certain that we will be able to successfully develop this capability. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations to recruit, hire, train and retain marketing and sales personnel. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

***Physicians, patients, third-party payors or others in the medical community may not be receptive to our product candidates, and we may not generate any future revenue from the sale or licensing of our product candidates.***

Even if we obtain approval for a product candidate, we may not generate or sustain revenue from sales of the product if the product cannot be sold at a competitive cost or if it fails to achieve market acceptance by physicians, patients, third-party payors or others in the medical community. These market participants may be hesitant to adopt a novel treatment based on ddRNAi technology, and we may not be able to convince the medical community and third-party payors to accept and use, or to provide favorable reimbursement for, any product candidates developed by us or our existing or future collaborators. Market acceptance of our product candidates will depend on, among other factors:

- the safety and efficacy of our product candidates;
- our ability to offer our products for sale at competitive prices;
- the relative convenience and ease of administration of our product candidates;
- the prevalence and severity of any adverse side effects associated with our product candidates;
- the terms of any approvals and the countries in which approvals are obtained;
- limitations or warnings contained in any labeling approved by the FDA or comparable foreign regulatory authorities;
- conditions upon the approval imposed by FDA or comparable foreign regulatory authorities, including, but not limited to, a REMS;
- the willingness of patients to try new treatments and of physicians to prescribe these treatments;

- the availability of government and other third-party payor coverage and adequate reimbursement; and
- availability of alternative effective treatments for the disease indications our product candidates are intended to treat and the relative risks, benefits and costs of those treatments.

Since we are focused on the emerging therapeutic modality of ddRNAi, these risks may increase if new competitors are able to market ddRNAi-based therapeutics or if these treatments become less favored in the commercial marketplace. In addition, we believe that one of the benefits of our ddRNAi technology is the expected length of time of its effect. If our treatments do not have a long-term effect after administration, such a development would likely significantly and adversely affect market acceptance of our product candidates, if approved.

Additional risks apply in relation to any disease indications we pursue which are classified as rare diseases and allow for orphan drug designation by regulatory agencies in major commercial markets, such as the United States or European Union. If pricing is not approved or accepted in the market at an appropriate level for any approved product for which we pursue and receive an orphan drug designation, such product may not generate enough revenue to offset costs of development, manufacturing, marketing and commercialization despite any benefits received from the orphan drug designation, such as market exclusivity, for a period of time. Orphan exclusivity could temporarily delay or block approval of one of our products if a competitor obtains orphan drug designation for its product first. However, even if we obtain orphan exclusivity for one of our products upon approval, our exclusivity may not block the subsequent approval of a competitive product that is shown to be clinically superior to our product.

Market size is also a variable in disease indications not classified as rare. Our estimates regarding potential market size for any indication may be materially different from what we discover to exist at the time we commence commercialization, if any, for a product, which could result in significant changes in our business plan and have a material adverse effect on our business, financial condition, results of operations and prospects.

***We face competition from entities that have developed or may develop product candidates for our target disease indications, including companies developing novel treatments and technology platforms based on modalities and technology similar to ours. If these companies develop technologies or product candidates more rapidly than we do or their technologies, including delivery technologies, are more effective, our ability to develop and successfully commercialize product candidates may be compromised.***

The development and commercialization of pharmaceutical products is highly competitive. We compete with a variety of multinational pharmaceutical companies and specialized biotechnology companies, as well as technology being developed at universities and other research institutions. Our competitors have developed, are developing or could develop product candidates and processes competitive with our product candidates. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community, patients and third-party payors, and any new treatments that enter the market.

We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we are developing, and may in the future try to develop, product candidates. We are aware of multiple companies that are working in the field of RNAi therapeutics, including Alnylam, Tekmira, Arrowhead, Silence Therapeutics plc, RXi Pharmaceuticals Corporation, Quark Pharmaceuticals, Inc., Marina Biotech, Inc. and Dicerna. Arrowhead, Tekmira and Alnylam are all developing siRNA-based therapeutics for HBV.

All of our current product candidates, if approved, would compete with approved and currently marketed treatments. For example, with respect to hepatitis C, our product candidate would compete with small molecule treatments such as Sovaldi and Harvoni, each of which was developed by Gilead Sciences, Inc., and Viekira Pak, a regimen consisting of four medications developed by Abbvie Inc.

In addition, our product candidates would compete with antisense and other RNA-based pharmaceutical products currently under development. Like RNAi therapeutics, antisense products target mRNA with the objective of suppressing the activity of specific genes. The development of antisense products is more advanced than that of RNAi therapeutics, and antisense technology may become the preferred technology for products that target mRNAs.

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources and experience than we have. If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position.

Competing products could present superior treatment alternatives, including by being more effective, safer, less expensive or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or non-competitive before we recover the expense of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan.

***A variety of risks associated with international operations could hurt our business.***

If any of our product candidates are approved for commercialization, it is our current intention to market them on a worldwide basis, either alone or in collaboration with others. In addition, we conduct development activities in various jurisdictions throughout the world. We expect that we will be subject to additional risks related to engaging in international operations, including:

- different regulatory requirements for approval of pharmaceutical products in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in Australia or the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

***The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain coverage and adequate reimbursement for any of our product candidates that are approved could limit our ability to market those products and compromise our ability to generate revenue.***

The availability of coverage and adequate reimbursement by governmental and private payors is essential for most patients to be able to afford expensive treatments. Sales of our product candidates will depend substantially, both in the United States and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by third-party payors. If reimbursement is not available, or is available only to



limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the reimbursement amounts approved by third-party payors may not be high enough to allow us to establish or maintain pricing sufficient to realize a return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these new products.

The intended use of a pharmaceutical product by a physician can also affect pricing. For example, CMS could initiate a National Coverage Determination administrative procedure, by which the agency determines which uses of a therapeutic product would and would not be reimbursable under Medicare. This determination process can be lengthy, thereby creating a long period during which the future reimbursement for a particular product may be uncertain.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada and other countries is likely to put pressure on the pricing and usage of any of our product candidates that may be approved for marketing in the future. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems can be substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and other third-party payors, in the United States and abroad, to cap or reduce healthcare costs, resulting in legislation and reforms such as, in the United States, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care Education Reconciliation Act, or the ACA. The ACA may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. In addition, other legislative changes have been adopted since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year effective April 2013 that, due to subsequent legislative amendments to the statute, will stay in effect through 2024 unless additional Congressional action is taken. Additionally, in January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could negatively affect coverage or reduce the reimbursement for any of our product candidates that receive regulatory approval.

We expect to experience pricing pressures in connection with the sale of any of our product candidates, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription pharmaceutical products and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. We cannot predict what healthcare reform initiatives may be adopted in the future. Further federal, state and foreign legislative and regulatory

developments are likely, and we expect ongoing initiatives to increase pressure on pharmaceutical product pricing. Such reforms could depress pricing for any product candidates that we may successfully develop and for which we may obtain regulatory approval and may negatively affect our overall financial condition and ability to develop additional product candidates.

***Our relationships with third-party payors, healthcare professionals and customers in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security and other healthcare laws and regulations, which could expose us to significant penalties.***

Our relationships with third-party payors, healthcare professionals and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act, that may constrain the business or financial arrangements and relationships through which we sell, market and distribute any pharmaceutical products for which we obtain marketing approval. In addition, we may be subject to transparency laws and patient privacy regulation by the federal government and by the U.S. states and foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include, but are not limited to, the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, which impose criminal and civil penalties, including civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose obligations on covered healthcare providers, health plans and healthcare clearinghouses, as well as their business associates that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Open Payments program, created under the ACA, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the CMS information related to payments or other transfers of value made to physicians and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by the physicians and their immediate family members by the 90<sup>th</sup> day of each subsequent calendar year, and disclosure of such information will be made by CMS on a publicly available website; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance

guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require pharmaceutical manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, which could have a material adverse effect on our business. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government healthcare programs, which could also materially affect our business.

***Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our product candidates or compromise our ability to conduct our business or obtain regulatory approvals for our product candidates.***

Gene therapy remains a novel technology and no gene therapy product utilizing ddRNAi has been approved to date in the United States. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians specializing in the treatment of those diseases that our product candidates target prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments they are already familiar with and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. Our product candidates, including our viral delivery systems, could produce adverse events. Adverse events in our clinical trials or following approval of any of our product candidates, even if not ultimately attributable to our product candidates, could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

### **Risks Related to Our Business Operations**

***We may not successfully engage in strategic transactions or enter into new collaborations, which could adversely affect our ability to develop and commercialize product candidates, impact our cash position, increase our expenses and present significant distractions to our management.***

From time to time, we may consider additional strategic transactions, such as collaborations, acquisitions, asset purchases or sales and out- or in-licensing of product candidates or technologies. In particular, we will evaluate and, if strategically attractive, seek to enter into additional collaborations, including with major biotechnology or pharmaceutical companies. The competition for collaborators is significant, and the negotiation process is time-consuming and complex. Any new collaboration may be on terms that are not optimal for us, and we may not be able to maintain any new or existing collaboration if, for example, development or approval of a product candidate is delayed, sales of an approved product candidate do not meet expectations or the collaborator

discontinues the collaboration. Any such collaboration, or other strategic transaction, may require us to incur non-recurring or other charges, increase our expenditures, pose significant integration or implementation challenges or disrupt our management or business.

These transactions would entail numerous operational and financial risks, including exposure to unknown liabilities, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration, acquisition or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business.

Accordingly, although there can be no assurance that we will undertake or successfully complete any additional transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and have a material adverse effect on our business, results of operations, financial condition and prospects. Conversely, any failure to enter any collaboration or other strategic transaction that would be beneficial to us could delay and make more expensive the development and potential commercialization of our product candidates and have a negative impact on the competitiveness of any product candidate that reaches market.

***Any inability to attract and retain qualified key management and technical personnel would impair our ability to implement our business plan.***

Our success largely depends on the continued service of key management and other specialized personnel, including Dr. Peter French, PhD, our Chief Executive Officer, Mr. Gregory West, our Chief Financial Officer, Dr. David Suhy, PhD, our Chief Scientist, Mr. Carl Stubbings, our Chief Business Officer, and Ms. Georgina Kilfoil, our Chief Clinical Officer. The loss of one or more members of our management team or other key employees or advisors could delay or increase the cost of our research and development programs and materially harm our business, financial condition, results of operations and prospects. The relationships that our key managers have cultivated within our industry make us particularly dependent upon their continued employment with us. We are dependent on the continued service of our technical personnel because of the highly technical nature of our product candidates and the specialized nature of the regulatory approval process for our product candidates. Because our management team and key employees are not obligated to provide us with continued service, they could terminate their employment with us at any time without penalty. We do not maintain key person life insurance policies on any of our management team members or key employees. Our future success will depend in large part on our continued ability to attract and retain other highly qualified scientific, technical and management personnel, as well as personnel with expertise in clinical testing, manufacturing, governmental regulation and commercialization. We face competition for personnel from other companies, universities, public and private research institutions, government entities and other organizations.

***Our collaborations with outside scientists and consultants may be subject to restriction and change.***

We work with medical experts, chemists, biologists and other scientists at academic and other institutions, and consultants who assist us in our research, development and regulatory efforts, including the members of our scientific advisory board. In addition, these scientists and consultants have provided, and we expect that they will continue to provide, valuable advice regarding our programs and regulatory approval processes. These scientists and consultants are not our employees and may have other commitments that would limit their future availability to us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. In addition, we are limited in our ability to prevent them from establishing competing businesses or developing competing products. For example, if a key scientist acting as a principal investigator in any of our clinical trials identifies a potential product or compound that is more scientifically interesting to his or her professional interests, his or her availability to remain involved in our clinical trials could be restricted or eliminated.

***We may experience difficulties in managing our growth and expanding our operations.***

We have limited experience in development and commercialization of pharmaceutical products. As our product candidates continue to advance through preclinical studies and clinical trials and potentially toward regulatory approval and commercial sale, we will need to expand our development, regulatory, manufacturing and sales capabilities or contract with other organizations to provide these capabilities for us. In the future, we expect to have to manage additional relationships with collaborators or partners, suppliers and other organizations. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls.

***Our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and insider trading.***

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, principal investigators, CROs, consultants, commercial partners and vendors. Misconduct by these parties could include intentional failures to comply with the regulations of the FDA and comparable foreign regulators, provide accurate information to the FDA and comparable foreign regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

***We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability and costs. If the use of our product candidates harms patients, or is perceived to harm patients even when such harm is unrelated to our product candidates, our regulatory approvals could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims.***

The use of our product candidates in clinical trials and the sale of any products for which we may in the future obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our product candidates. There is a risk that our product candidates may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;
- withdrawal of clinical trial participants;

- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our product candidates;
- decreased demand for our product candidates, if approved for commercial sale; and
- increased cost, or impairment of our ability, to obtain or maintain product liability insurance coverage.

We carry combined public and products liability (including human clinical trials extension) insurance of A\$10 million per occurrence with a A\$10 million aggregate limit. We believe our product liability insurance coverage is sufficient in light of our current clinical programs. However, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain marketing approval for any product candidates, we intend to expand our insurance coverage to include the sale of commercial products, but we may not be able to obtain or maintain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded against other pharmaceutical companies in class action lawsuits based on pharmaceutical products, or medical treatments that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause the price of the ADSs to decline and, if judgments exceed our insurance coverage, could materially and adversely affect our financial position.

During the course of treatment, patients may suffer adverse events, including death, for reasons that may be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our products, or require us to suspend or discontinue our commercialization efforts. Even in a circumstance in which we do not believe that an adverse event is related to our product candidate, the investigation into the circumstance may be time-consuming or inconclusive. These investigations may harm our reputation, delay our regulatory approval process, limit the type of regulatory approvals our product candidates receive or maintain, and compromise the market acceptance of any of our product candidates that may in the future receive regulatory approval. As a result of these factors, a product liability claim, even if successfully defended, could hurt our business and impair our ability to generate revenue.

***We and our development partners, third-party manufacturers and suppliers use biological materials and may use hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly.***

We and our development partners, third-party manufacturers and suppliers may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety or the environment. Our operations and the operations of our third-party manufacturers and suppliers also produce hazardous waste products. National, state and local laws and regulations in the United States, Australia and other countries govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development and commercialization efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials, regulatory approvals or product commercialization progress could be suspended.

***We may use our limited financial and human resources to pursue a particular research program or product candidate and fail to capitalize on programs or product candidates that may be more profitable or for which there is a greater likelihood of success.***

Because we have limited resources, we may forego or delay pursuit of opportunities with certain programs or product candidates or for indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for product candidates may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a collaboration arrangement.

***Our internal computer and information technology systems, or those of our collaborators and other development partners, third-party CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a disruption of our product development programs.***

Despite the implementation of security measures, our internal computer and information technology systems and those of our current and any future CROs and other contractors, consultants and collaborators are vulnerable to damage from computer viruses, cyber-attacks, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such events could cause interruptions of our operations. While we have not experienced any material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other similar disruptions. For example, the loss of clinical trial data from ongoing or future clinical trials or data from preclinical studies could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture our product candidates and conduct clinical trials, and similar events relating to their computer systems could also have similar consequences to our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed and become more expensive.

***Our current laboratory operations are concentrated in one location and any events affecting this location may seriously compromise our ability to operate our business and continue the development of our product candidates.***

Our current laboratory operations are located in our facility situated in Hayward, California. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, power shortage, telecommunication failure or other natural or manmade accidents or incidents that result in us being unable to fully utilize the facility, may compromise our ability to operate our business, particularly on a daily basis, cause us financial losses and inhibit or delay our continued development of our product candidates. Loss of access to this facility may result in increased costs, delays in the development of our product candidates or interruption of our business operations. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at this facility, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facility is unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption may have a material adverse effect on our business, financial position, results of operations and prospects.

***The investment of our cash and cash equivalents is subject to risks which may cause losses and affect the liquidity of these investments.***

As of March 31, 2015, we had A\$26.7 million in cash and cash equivalents. We historically have invested substantially all of our available cash and cash equivalents in cash deposits meeting the criteria of our investment policy, which is focused on the preservation of our capital. Pending use in our business, we expect to invest the net proceeds of this offering in substantially the same manner. These investments are subject to general credit, liquidity, market and interest rate risks. We may realize losses in the fair value of these investments, which would have a negative effect on our financial results. In addition, should our investments cease paying or reduce the amount of interest paid to us, our interest income would suffer. The market risks associated with our investment portfolio may have an adverse effect on our results of operations, liquidity and financial condition.

***Our ability to utilize our net operating losses and certain other tax attributes may be limited.***

We have substantial carried forward tax losses which may not be available to offset any future assessable income. In order for an Australian corporate taxpayer to carry forward and utilize tax losses, the taxpayer must pass either the continuity of ownership test, or COT, or, if it fails the COT, the same business test, or SBT, in respect of relevant tax losses.

We have not carried out any analysis as to whether we have met the COT or, failing the COT, the SBT over relevant periods. In addition, shareholding changes, including changes resulting from this offering, may result in a significant ownership change for us. It is therefore uncertain as to whether any of our A\$45,132,359 losses carried forward as of June 30, 2014 will be available to be carried forward and available to offset our assessable income, if any, in future periods.

### **Risks Related to Our Intellectual Property**

***If we are unable to obtain or protect intellectual property rights related to our product candidates, we may not be able to obtain exclusivity for our product candidates or prevent others from developing similar competitive products.***

We rely upon a combination of patents, know-how, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates.

The patent application process, also known as patent prosecution, is expensive and time-consuming, and we and our current or future licensors and licensees may not be able to prepare, file, and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our current licensors or licensees, or any future licensors or licensees, will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, our patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, patent term adjustments, etc., although we are unaware of any such defects. If we or our current licensors or licensees, or any future licensors or licensees, fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our current licensors or licensees, or any future licensors or licensees, are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents



with claims that cover our product candidates in the United States or other jurisdictions. In addition, we cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents cover our product candidates, third parties may initiate opposition, interference, re-examination, post-grant review, inter partes review, nullification or derivation action in court or before patent offices or similar proceedings challenging the validity, enforceability or scope of such patents, which may result in the patent claims being narrowed or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates or prevent others from designing around our claims. Any of these outcomes could impair our ability to prevent competition from third parties.

If the patent applications we hold or have in-licensed with respect to our programs or product candidates fail to issue, if the breadth or strength of our patent protection is threatened, or if our patent portfolio fails to provide meaningful exclusivity for our product candidates, it could dissuade companies from collaborating with us to develop product candidates and threaten our ability to commercialize future products. Any successful opposition to any patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our licensors were the first to file any patent application related to a product candidate. Furthermore, if third parties have filed such patent applications before March 16, 2013, an interference proceeding in the United States can be initiated by such third parties to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. If third parties have filed such applications on or after March 16, 2013, a derivation proceeding in the United States can be initiated by such third parties to determine whether our invention was derived from theirs. Even where we have a valid and enforceable patent, we may not be able to exclude others from practicing our invention where the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license. In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from competitive medications, including biosimilar or generic medications. This risk is material in light of the length of the development process of our products and lifespan of our current patent portfolio.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect. What constitutes a trade secret and what protections are available for trade secrets varies from state to state in the United States and country by country worldwide. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. Security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. Although we expect all of our employees and consultants to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or

unauthorized disclosure of our trade secrets can be difficult to detect, could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all.

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our markets.

***We rely on license relationships with a number of third parties for portions of our intellectual property, including platform technology patents relating to our ddRNAi technology. This arrangement could restrict the scope and enforcement of our intellectual property rights and limit our ability to successfully commercialize current and future product candidates.***

We have in-licensed certain ddRNAi-related intellectual property from third-party licensors. We rely on some of these third parties to file and prosecute patent applications and maintain patents and otherwise protect the intellectual property we license. We have not had and do not have primary control over these activities for certain of our patents or patent applications and other intellectual property rights we license, and therefore cannot guarantee that these patents and applications will be prosecuted or enforced in a manner consistent with the best interests of our business. We cannot be certain that such activities by third parties have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. Additionally, we may not be able to control the publication or other disclosures of research carried out by our licensors relating to technology that could otherwise prove patentable. Pursuant to the terms of some of our license agreements with third parties, some of our third-party licensors have the right, but not the obligation, to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents. Even if we are permitted to pursue such enforcement or defense, we will require the cooperation of our licensors, and cannot guarantee that we would receive it and on what terms. We cannot be certain that our licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. If we cannot obtain patent protection, or enforce existing or future patents against third parties, our competitive position and our financial condition could suffer.

***Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.***

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and inter partes review proceedings before the USPTO, and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture

or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may be accused of infringing. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any DNA constructs formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we may be unable to effectively market product candidates based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations.

***We may not be successful in obtaining or maintaining necessary rights to gene therapy product components and processes for our development pipeline through acquisitions and in-licenses.***

Presently we have rights to intellectual property to develop our gene therapy product candidates. However, our product candidates may require specific formulations to work effectively and efficiently and rights to such formulations may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify on terms that we find acceptable, or at all. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

For example, we sometimes collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such right of first negotiation for intellectual property, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to required third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

***We may enter into license agreements with third parties, and if we fail to comply with our obligations in such agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.***

We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates.

In many cases, patent prosecution of our in-licensed technology is controlled solely by the licensor. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using the intellectual property. In some cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under any collaboration relationships we might enter into in the future;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

***We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful, and issued patents covering our product candidates could be found invalid or unenforceable if challenged in court.***

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

For example, in patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld

relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, and equivalent proceedings in foreign jurisdictions, such as opposition proceedings. Such proceedings could result in revocation, amendments to our patent claims or statements being made on the record such that our claims may no longer be construed to cover our product candidates. Outcomes or statements on the record in one country could have a disadvantageous effect on prosecution or enforcement of a patent or patent application in another country. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that no invalidating prior art exists or that the patent examiner was aware of all material prior art during prosecution. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain, enforce or defend the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be prosecuted, enforced and defended in a manner consistent with the best interests of our business. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our products or certain aspects of our platform technology. Such a loss of patent protection could have a material adverse impact on our business. Patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without legally infringing our patents or other intellectual property rights. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, enforcement of a favorable decision by a court can depend on cooperation of a governmental authority which may or may not be available in every jurisdiction. There could be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could depress the market price of our ADSs. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

For our patents and patent applications filed in the United States before March 16, 2013, interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Litigation or interference proceedings may result in a decision adverse to our interests and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could cause the trading price of our ADSs to fall.

***Our results of operations will be affected by the level of royalty payments that we are required to pay to third parties.***

We are a party to license agreements that require us to remit royalty payments and other payments related to in-licensed intellectual property. Under our in-license agreements, we may pay up-front fees and milestone payments and be subject to future royalties. We cannot precisely predict the amount, if any, of royalties we will owe in the future, and if our calculations of royalty payments are incorrect, we may owe additional royalties,

which could negatively affect our results of operations. As our product sales increase, we may, from time to time, disagree with our third-party collaborators as to the appropriate royalties owed, and the resolution of such disputes may be costly, may consume management's time, and may damage our relationship with our collaborators. Furthermore, we may enter into additional license agreements in the future, which may also include royalty, milestone and other payments.

***The licenses we grant to our collaborators to use our ddRNAi technology are exclusive to the development of product candidates for certain conditions.***

Some of the out-licenses we grant to our collaborators to use our ddRNAi technology are exclusive to the development of product candidates for certain conditions, so long as our collaborators comply with certain requirements. That means that once our ddRNAi technology is licensed to a collaborator for a specified condition, we are generally prohibited from developing product candidates for that condition and from licensing the ddRNAi to any third party for that condition. The limitations imposed by these exclusive licenses could prevent us from expanding our business and increasing our development of product candidates with new collaborators, both of which could adversely affect our business and results of operations.

***We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.***

Certain of our key employees and personnel are or were previously employed at universities, medical institutions or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee's former employer or other third parties. Litigation may be necessary to defend against these claims. Furthermore, universities or medical institutions who employ some of our key employees and personnel in parallel to their engagement by us may claim that intellectual property developed by such person is owned by the respective academic or medical institution under the respective institution intellectual property policy or applicable law. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs, be a distraction to management and other employees, and damage our relationships with the academic and medical institutions.

***We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.***

We may be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. We may in the future have ownership disputes arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

***Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.***

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications are required to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and applications. The USPTO and various corresponding governmental patent agencies outside of the United States require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and after a patent has issued. There are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction.

***Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.***

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and it therefore is costly, time-consuming and inherently uncertain. In addition, on September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation.

An important change introduced by the Leahy-Smith Act is that, as of March 16, 2013, the United States transitioned to a “first-to-file” system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. It is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

Among some of the other changes introduced by the Leahy-Smith Act are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal court necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action.

Recent U.S. Supreme Court rulings such as *Association for Molecular Pathology v. Myriad Genetics, Inc.* (Myriad I); *BRCA1- & BRCA2-Based Hereditary Cancer Test Patent Litig.* (Myriad II); and *Promega Corp. v. Life Technologies Corp.* have also narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in some situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

***Our success depends, in part, on our ability to protect our intellectual property and our technologies outside the United States. We may not be able to protect our intellectual property rights throughout the world.***

Our commercial success depends, in part, on our ability to obtain and maintain patent and trade secret protection for our technologies, our traits, and their uses, as well as our ability to operate without infringing upon the proprietary rights of others outside the United States. If we do not adequately protect our intellectual property, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability.

Filing, prosecuting and defending patents on product candidates in all countries around the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. In addition, we may at times in-license third-party technologies for which limited international patent protection exists and for which the time period for filing international patent applications has passed. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Potential competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product candidates, if approved, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

### **Risks Related to the ADSs and this Offering**

***The market price and trading volume of the ADSs may be volatile and may be affected by economic conditions beyond our control.***

The market price of the ADSs may be highly volatile and subject to wide fluctuations. In addition, the trading volume of the ADSs may fluctuate and cause significant price variations to occur. If the market price of the ADSs declines significantly, you may be unable to resell your ADSs at or above the purchase price, if at all. We cannot assure you that the market price of the ADSs will not fluctuate or significantly decline in the future.

Some specific factors that could negatively affect the price of the ADSs or result in fluctuations in their price and trading volume include:

- actual or expected fluctuations in our operating results;
- changes in market valuations of similar companies;
- changes in our key personnel;
- changes in financial estimates or recommendations by securities analysts;



- trading prices of our ordinary shares on the ASX;
- changes in trading volume of ADSs on The NASDAQ Global Market, or NASDAQ, and of our ordinary shares on the ASX;
- sales of the ADSs or ordinary shares by us, our executive officers or our shareholders in the future; and
- conditions in the financial markets or changes in general economic conditions.

***An active trading market for the ADSs may not develop or be liquid enough for you to sell your ADSs quickly or at market price.***

Prior to this offering, there has been only a limited public market in the United States for the ADSs. If an active public market in the United States for the ADSs does not develop after this offering, the market price and liquidity of the ADSs may be adversely affected. While we have applied for the listing of the ADSs on NASDAQ, a liquid public market in the United States for the ADSs may not develop or be sustained after this offering. The initial public offering price for the ADSs will be determined by negotiation among us and the underwriters, and the price at which the ADSs are traded after this offering may decline below the initial public offering price, which means you may experience a decrease in the value of your ADSs regardless of our operating performance or prospects. In the past, following periods of volatility in the market price of a company's securities, shareholders often instituted securities class action litigation against that company. If we were involved in a class action suit, it could divert the attention of senior management and, if adversely determined, could have caused us significant financial harm.

***Investors purchasing the ADSs will suffer immediate and substantial dilution.***

The public offering price for the ADSs will be substantially higher than the net tangible book value per ADS of the underlying ordinary shares immediately after this offering. If you purchase ADSs in this offering, you will incur substantial and immediate dilution in the net tangible book value of your investment. Net tangible book value per ADS represents the amount of total tangible assets less total liabilities, divided by the number of ordinary shares then outstanding, multiplied by 20, the number of ordinary shares underlying each ADS. To the extent that options that are currently outstanding are exercised, there will be further dilution to your investment. We may also issue additional ordinary shares, ADSs, performance rights, options and other securities in the future that may result in further dilution of your ADSs. See "Dilution" for a calculation of the extent to which your investment will be diluted.

***The dual listing of our ordinary shares and the ADSs following this offering may adversely affect the liquidity and value of the ADSs.***

Following this offering and after the ADSs are listed on NASDAQ, our ordinary shares will continue to be listed on the ASX. We cannot predict the effect of this dual listing on the value of our ordinary shares and ADSs. However, the dual listing of our ordinary shares and ADSs may dilute the liquidity of these securities in one or both markets and may impair the development of an active trading market for the ADSs in the United States. The trading price of the ADSs could also be adversely affected by trading in our ordinary shares on the ASX.

***Future sales of our ordinary shares or ADSs, or the perception that such sales may occur, could depress the trading price of our ordinary shares and ADSs.***

After the completion of this offering, we expect to have                    ADSs outstanding and                    ordinary shares outstanding, including the shares underlying the ADSs we are selling in this offering, which may be resold in the public market immediately after this offering. We and all of our directors and executive officers have signed lock-up agreements for a period of 180-days following the date of this prospectus, subject to specified exceptions. See "Underwriting."

The underwriters may, in their sole discretion and without notice, release all or any portion of the ordinary shares or ADSs subject to lock-up agreements. As restrictions on resale end, the market price of our ADSs and ordinary shares could drop significantly if the holders of these ADSs or ordinary shares sell them or are perceived by the market as intending to sell them. These factors could also make it more difficult for us to raise additional funds through future offerings of our ordinary shares, ADSs or other securities.

***As a foreign private issuer, we are permitted and we expect to follow certain home country corporate governance practices in lieu of certain NASDAQ requirements applicable to domestic issuers. This may afford less protection to holders of the ADSs.***

As a foreign private issuer whose ADSs will be listed on NASDAQ, we will be permitted to follow certain home country corporate governance practices in lieu of certain NASDAQ requirements. For example, we may follow home country practice with regard to the composition of the board of directors and quorum requirements applicable to shareholder meetings. A foreign private issuer must disclose in its annual reports filed with the SEC the requirements with which it does not comply followed by a description of its applicable home country practice. The Australian home country practices described above may afford less protection to holders of the ADSs than that provided under NASDAQ rules. See “Description of Share Capital—Exemptions from Certain NASDAQ Corporate Governance Rules.”

***As a foreign private issuer, we are permitted to file less information with the SEC than a company incorporated in the United States. Accordingly, there may be less publicly available information concerning us than there is for companies incorporated in the United States.***

As a foreign private issuer, we are exempt from certain rules under the Exchange Act, that impose disclosure requirements as well as procedural requirements for proxy solicitations under Section 14 of the Exchange Act. In addition, our officers, directors and principal shareholders are exempt from the reporting and “short-swing” profit recovery provisions of Section 16 of the Exchange Act. Moreover, we are not required to file periodic reports and financial statements with the SEC as frequently or as promptly as a company that files as a U.S. company whose securities are registered under the Exchange Act, nor are we required to comply with the SEC’s Regulation FD, which restricts the selective disclosure of material non-public information. Accordingly, there may be less information publicly available concerning us than there is for a company that files as a domestic issuer.

***We are an emerging growth company as defined in the JOBS Act and the reduced disclosure requirements applicable to emerging growth companies may make the ADSs less attractive to investors and, as a result, adversely affect the price of the ADSs and result in a less active trading market for the ADSs.***

We are an emerging growth company as defined in the JOBS Act, and we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies. For example, we have elected to rely on an exemption from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act relating to internal control over financial reporting, and we will not provide such an attestation from our auditors for so long as we qualify as an emerging growth company. We have also elected to rely on an exemption that permits an emerging growth company to include only two years of audited financial statements and only two years of related management’s discussion and analysis of financial condition and results of operations disclosure, and we have therefore only included two years of audited financial statements, selected financial data and management’s discussion and analysis of financial condition and results of operations in this prospectus.

We may avail ourselves of these disclosure exemptions until we are no longer an emerging growth company. We cannot predict whether investors will find the ADSs less attractive because of our reliance on some or all of these exemptions. If investors find the ADSs less attractive, it may cause the trading price of the ADSs to decline and there may be a less active trading market for the ADSs.

We will cease to be an emerging growth company upon the earliest of:

- the end of the fiscal year in which the fifth anniversary of completion of this offering occurs;
- the end of the first fiscal year in which the market value of our ordinary shares held by non-affiliates exceeds US\$700 million as of the end of the second quarter of such fiscal year;
- the end of the first fiscal year in which we have total annual gross revenues of at least US\$1 billion; and
- the date on which we have issued more than US\$1 billion in non-convertible debt securities in any rolling three-year period.

***If we fail to establish and maintain proper internal financial reporting controls, our ability to produce accurate financial statements or comply with applicable regulations could be impaired.***

Section 404(a) of the Sarbanes-Oxley Act requires that, beginning with our second annual report after the completion of this offering, our management assess and report annually on the effectiveness of our internal controls over financial reporting and identify any material weaknesses in our internal controls over financial reporting. Although Section 404(b) of the Sarbanes-Oxley Act requires our independent registered public accounting firm to issue an annual report that addresses the effectiveness of our internal controls over financial reporting, we have opted to rely on the exemptions provided in the JOBS Act, and consequently will not be required to comply with SEC rules that implement Section 404(b) of the Sarbanes-Oxley Act until such time as we are no longer an emerging growth company.

Our first Section 404(a) assessment will take place beginning with our second annual report after the completion of this offering. The presence of material weaknesses could result in financial statement errors which, in turn, could lead to errors in our financial reports and/or delays in our financial reporting, which could require us to restate our operating results. We might not identify one or more material weaknesses in our internal controls in connection with evaluating our compliance with Section 404(a) of the Sarbanes-Oxley Act. In order to maintain and improve the effectiveness of our disclosure controls and procedures and internal controls over financial reporting, we will need to expend significant resources and provide significant management oversight. Implementing any appropriate changes to our internal controls may require specific compliance training of our directors and employees, entail substantial costs in order to modify our existing accounting systems, take a significant period of time to complete and divert management's attention from other business concerns. These changes may not, however, be effective in maintaining the adequacy of our internal control.

If we are unable to conclude that we have effective internal controls over financial reporting, investors may lose confidence in our operating results, the price of the ADSs could decline and we may be subject to litigation or regulatory enforcement actions. In addition, if we are unable to meet the requirements of Section 404 of the Sarbanes-Oxley Act, the ADSs may not be able to remain listed on NASDAQ.

***ADS holders may be subject to additional risks related to holding ADSs rather than ordinary shares.***

ADS holders do not hold ordinary shares directly and, as such, are subject to, among others, the following additional risks:

- As an ADS holder, we will not treat you as one of our shareholders and you will not be able to exercise shareholder rights, except through the ADR depository as permitted by the deposit agreement.
- Distributions on the ordinary shares represented by your ADSs will be paid to the ADR depository, and before the ADR depository makes a distribution to you on behalf of your ADSs, any withholding taxes that must be paid will be deducted. Additionally, if the exchange rate fluctuates during a time when the ADR depository cannot convert the foreign currency, you may lose some or all of the value of the distribution.
- We and the ADR depository may amend or terminate the deposit agreement without the ADS holders' consent in a manner that could prejudice ADS holders.

***You must act through the ADR depositary to exercise your voting rights and, as a result, you may be unable to exercise your voting rights on a timely basis.***

As a holder of ADSs (and not the ordinary shares underlying your ADSs), we will not treat you as one of our shareholders, and you will not be able to exercise shareholder rights. The ADR depositary will be the holder of the ordinary shares underlying your ADSs, and ADS holders will be able to exercise voting rights with respect to the ordinary shares represented by the ADSs only in accordance with the deposit agreement relating to the ADSs. There are practical limitations on the ability of ADS holders to exercise their voting rights due to the additional procedural steps involved in communicating with these holders. For example, holders of our ordinary shares will receive notice of shareholders' meetings by mail and will be able to exercise their voting rights by either attending the shareholders meeting in person or voting by proxy. ADS holders, by comparison, will not receive notice directly from us. Instead, in accordance with the deposit agreement, we will provide notice to the ADR depositary of any such shareholders meeting and details concerning the matters to be voted upon at least 30 days in advance of the meeting date. If we so instruct, the ADR depositary will mail to holders of ADSs the notice of the meeting and a statement as to the manner in which voting instructions may be given by holders as soon as practicable after receiving notice from us of any such meeting. To exercise their voting rights, ADS holders must then instruct the ADR depositary as to voting the ordinary shares represented by their ADSs. Due to these procedural steps involving the ADR depositary, the process for exercising voting rights may take longer for ADS holders than for holders of ordinary shares. The ordinary shares represented by ADSs for which the ADR depositary fails to receive timely voting instructions will not be voted.

***If we are classified as a "passive foreign investment company," then our U.S. shareholders could suffer adverse tax consequences as a result.***

Generally, if, for any taxable year, at least 75% of our gross income is passive income or at least 50% of the average quarterly value of our gross assets is attributable to assets that produce passive income or are held for the production of passive income, including cash, we would be characterized as a passive foreign investment company, or PFIC, for U.S. federal income tax purposes. For purposes of these tests, passive income includes dividends, interest, and gains from the sale or exchange of investment property and rents and royalties other than rents and royalties which are received from unrelated parties in connection with the active conduct of a trade or business. If we are characterized as a PFIC, a U.S. holder of our ordinary shares or ADSs may suffer adverse tax consequences, including having gains realized on the sale of our ordinary shares or ADSs treated as ordinary income, rather than capital gain, the loss of the preferential rate applicable to dividends received on our ordinary shares or ADSs by individuals who are U.S. holders, and having interest charges added to their tax on distributions from us and on gains from the sale of our ordinary shares or ADSs. See "Taxation—U.S. Federal Income Tax Considerations—*Passive Foreign Investment Company*."

Our status as a PFIC may also depend, in part, on how quickly we utilize the cash proceeds from this offering in our business. Since PFIC status depends on the composition of our income and the composition and value of our assets, which may be determined in large part by reference to the market value of our ordinary shares or ADSs, which may be volatile, there can be no assurance that we will not be a PFIC for any taxable year. While we believe that we were not a PFIC for fiscal 2014, since the PFIC tests are applied only at the end of a taxable year no assurance of our PFIC status can be provided for fiscal 2015 or future years. Prospective U.S. investors should discuss the issue of our possible status as a PFIC with their tax advisors.

***Currency fluctuations may adversely affect the price of our ordinary shares and the ADSs.***

Our ordinary shares are quoted in Australian dollars on the ASX and the ADSs will be quoted in U.S. dollars on NASDAQ. Movements in the Australian dollar/U.S. dollar exchange rate may adversely affect the U.S. dollar price of the ADSs. In the past year the Australian dollar has generally weakened against the U.S. dollar. However, this trend may not continue and may be reversed. If the Australian dollar weakens against the U.S. dollar, the U.S. dollar price of the ADSs could decline, even if the price of our ordinary shares in Australian dollars increases or remains unchanged.

***We have never declared or paid dividends on our ordinary shares and we do not anticipate paying dividends in the foreseeable future.***

We have never declared or paid cash dividends on our ordinary shares. For the foreseeable future, we currently intend to retain all available funds and any future earnings to support our operations and to finance the growth and development of our business. Any future determination to declare cash dividends will be made at the discretion of our board of directors, subject to compliance with applicable laws and covenants under current or future credit facilities, which may restrict or limit our ability to pay dividends, and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant. We do not anticipate paying any cash dividends on our ordinary shares in the foreseeable future. As a result, a return on your investment will only occur if our ADS price appreciates.

***You may not receive distributions on our ordinary shares represented by the ADSs or any value for such distribution if it is illegal or impractical to make them available to holders of ADSs.***

While we do not anticipate paying any dividends on our ordinary shares in the foreseeable future, if such a dividend is declared, the depository for the ADSs has agreed to pay to you the cash dividends or other distributions it or the custodian receives on our ordinary shares or other deposited securities after deducting its fees and expenses. You will receive these distributions in proportion to the number of our ordinary shares your ADSs represent. However, in accordance with the limitations set forth in the deposit agreement, it may be unlawful or impractical to make a distribution available to holders of ADSs. We have no obligation to take any other action to permit the distribution of the ADSs, ordinary shares, rights or anything else to holders of the ADSs. This means that you may not receive the distributions we make on our ordinary shares or any value from them if it is unlawful or impractical to make them available to you. These restrictions may have a material adverse effect on the value of your ADSs.

***Australian takeover laws may discourage takeover offers being made for us or may discourage the acquisition of a significant position in our ordinary shares or ADSs.***

We are incorporated in Australia and are subject to the takeover laws of Australia. Among other things, we are subject to the Australian Corporations Act 2001, or the Corporations Act. Subject to a range of exceptions, the Corporations Act prohibits the acquisition of a direct or indirect interest in our issued voting shares if the acquisition of that interest will lead to a person's voting power in us increasing to more than 20%, or increasing from a starting point that is above 20% and below 90%. Australian takeover laws may discourage takeover offers being made for us or may discourage the acquisition of a significant position in our ordinary shares. This may have the ancillary effect of entrenching our board of directors and may deprive or limit our shareholders' or ADS holders' opportunity to sell their ordinary shares or ADSs and may further restrict the ability of our shareholders and ADS holders to obtain a premium from such transactions. See "Description of Share Capital—Change of Control."

***Our Constitution and Australian laws and regulations applicable to us may adversely affect our ability to take actions that could be beneficial to our shareholders.***

As an Australian company, we are subject to different corporate requirements than a corporation organized under the laws of the states of the United States. Our Constitution, as well as the Australian Corporations Act, set forth various rights and obligations that are unique to us as an Australian company. These requirements may operate differently than those of many U.S. companies. You should carefully review the summary of these matters set forth under the section entitled, "Description of Share Capital" as well as our Constitution, which is included as an exhibit to this registration statement to which this prospectus forms a part, prior to investing in the ADSs.

## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward looking statements that are subject to a number of risks and uncertainties, many of which are beyond our control. All statements, other than statements of historical fact included in this prospectus, regarding our strategy, future operations, financial position, projected costs, prospects, plans and objectives of management are forward looking statements. When used in this prospectus, the words “could,” “believe,” “anticipate,” “intend,” “estimate,” “expect,” “may,” “continue,” “predict,” “potential,” “project,” or the negative of these terms, and similar expressions are intended to identify forward looking statements, although not all forward looking statements contain such identifying words. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus, we caution you that these statements are based on a combination of facts and important factors currently known by us and our expectations of the future, about which we cannot be certain.

Forward-looking statements may include statements about:

- our plans to develop and potentially commercialize our product candidates;
- the timing of the initiation and completion of preclinical studies and clinical trials;
- the timing of patient enrollment and dosing in clinical trials;
- the timing of the availability of data from clinical trials;
- the timing of expected regulatory filings;
- the development of novel AAV vectors;
- expectations about the plans of licensees of our technology;
- the clinical utility and potential attributes and benefits of ddRNAi and our product candidates, including the potential duration of treatment effects and the potential for a “one shot” cure;
- potential future out-licenses and collaborations;
- our expectations regarding expenses, ongoing losses, future revenue, capital needs and needs for additional financing;
- our use of proceeds from this offering;
- the length of time over which we expect our cash and cash equivalents and the proceeds from this offering to be sufficient; and
- our intellectual property position and the duration of our patent portfolio.

All forward-looking statements speak only as of the date of this prospectus. You should not place undue reliance on these forward-looking statements. Although we believe that our plans, objectives, expectations and intentions reflected in or suggested by the forward-looking statements we make in this prospectus are reasonable, we can give no assurance that these plans, objectives, expectations or intentions will be achieved. We disclose important factors that could cause our actual results to differ materially from our expectations under “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this prospectus.

The forward-looking statements made in this prospectus relate only to events or information as of the date on which the statements are made in this prospectus. Except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise, after the date on which the statements are made or to reflect the occurrence of unanticipated events.

## USE OF PROCEEDS

We estimate that the net proceeds from the sale of the ADSs in this offering will be US\$        million, or US\$        million if the underwriters exercise their option to purchase additional ADSs in full, based on an assumed initial public offering price of US\$        per ADS, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us

We expect to use the net proceeds from this offering as follows:

- approximately US\$        million for clinical trials through completion of a Phase I/IIa clinical trial intended to establish clinical proof of concept of TT-034 for hepatitis C;
- approximately US\$        million for clinical trials through completion of a Phase I/IIa clinical trial intended to establish clinical proof of concept of Hepbarna for hepatitis B;
- approximately US\$        million for clinical trials through completion of a Phase I/IIa clinical trial intended to establish clinical proof of concept of the AMD program;
- approximately US\$        million for preclinical development and initial IND application for Tribetarna to support a clinical trial in drug-resistant non-small cell lung cancer;
- approximately US\$        million for development of the OPMD program, through preclinical proof of concept;
- approximately US\$        million for development of ddRNAi-modified stem cells as therapeutics, through preclinical proof of concept;
- approximately US\$        million for development of CAR T, through preclinical proof of concept;
- approximately US\$        million for the development of scalable manufacturing for preclinical and clinical purposes which we believe, when combined with the amounts assigned to specific programs above, will be sufficient to support our preclinical studies and clinical trials as well as the discovery, development and acquisition of complementary targets and technologies; and
- the remainder for working capital, other research and development and general corporate purposes.

As of the date of this prospectus, we cannot specify with certainty all of the particular uses for the net proceeds from this offering. The amounts and timing of our actual expenditures may vary significantly from our expectations depending upon numerous factors, including the progress of our research and development efforts, the progress of our clinical trials, our operating costs and factors described under “Risk Factors” in this prospectus. Accordingly, we retain the discretion to allocate the net proceeds of this offering and we reserve the right to change the allocation of the net proceeds described above.

Pending these uses, we intend to invest the net proceeds from this offering in investment grade, interest-bearing instruments, securities or certificates of deposit.

An increase or decrease in the initial public offering price of US\$1.00 per ADS would increase or decrease the net proceeds that we will receive from the offering by US\$        million, assuming the number of ADSs offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions. Similarly, each increase or decrease of one million in the number of ADSs offered by us would increase or decrease the net proceeds to us from this offering by US\$        million, assuming the assumed initial public offering price remains the same and after deducting estimated underwriting discounts and commissions.

## PRICE RANGE OF ORDINARY SHARES

The following table presents, for the periods indicated, the high and low market prices for our ordinary shares reported on the ASX, under the symbol BLT. All prices are in Australian dollars.

	High	Low
	A\$	A\$
Annual:		
<i>Fiscal year ended June 30,</i>		
2014 .....	2.38	0.29
2013 .....	0.50 <sup>(1)</sup>	0.25 <sup>(1)</sup>
2012 .....	0.75 <sup>(1)</sup>	0.25 <sup>(1)</sup>
2011 .....	1.00 <sup>(1)</sup>	0.50 <sup>(1)</sup>
2010 .....	1.75 <sup>(1)</sup>	0.50 <sup>(1)</sup>
Quarterly:		
<i>Fiscal year ending June 30, 2015</i>		
Fourth quarter (through June 22, 2015) .....	0.89	0.70
Third quarter .....	1.08	0.71
Second quarter .....	1.07	0.52
First quarter .....	1.32	0.87
<i>Fiscal year ended June 30, 2014</i>		
Fourth quarter .....	1.84	0.86
Third quarter .....	2.38	0.56
Second quarter .....	0.75	0.35
First quarter .....	0.41	0.25 <sup>(1)</sup>
<i>Fiscal year ended June 30, 2013</i>		
Fourth quarter .....	0.50 <sup>(1)</sup>	0.25 <sup>(1)</sup>
Third quarter .....	0.50 <sup>(1)</sup>	0.25 <sup>(1)</sup>
Second quarter .....	0.50 <sup>(1)</sup>	0.25 <sup>(1)</sup>
First quarter .....	0.50 <sup>(1)</sup>	0.25 <sup>(1)</sup>
Most Recent Six Months:		
May 2015 .....	0.89	0.76
April 2015 .....	0.87	0.70
March 2015 .....	0.92	0.75
February 2015 .....	0.99	0.75
January 2015 .....	1.08	0.71
December 2014 .....	0.99	0.68

(1) Takes into account a 25:1 share consolidation that became effective in July 2013.

On June 22, 2015, the closing price of our ordinary shares as traded on the ASX was A\$0.78 per ordinary share (US\$0.61 per share based on the foreign exchange rate of A\$1.00 to US\$0.78 as published by the Reserve Bank of Australia as of such date).

Based on information known to us, as of March 31, 2015, we had 115,881,763 ordinary shares outstanding, with 26,160,411 of our ordinary shares being held in the United States by 102 holders and 89,721,352 of our ordinary shares being held in Australia by 3,978 holders. A large number of our ordinary shares are held in nominee companies so we cannot be certain of the identity of those beneficial owners.



## **DIVIDEND POLICY**

We have not declared or paid any dividends on our ordinary shares, and we do not anticipate paying any dividends in the foreseeable future. Our board of directors presently intends to reinvest all earnings in the continued development and operation of our business.

Payment of dividends in the future, if any, will be at the discretion of our board of directors. If our board of directors elects to pay dividends, the form, frequency and amount will depend upon our future operations and earnings, capital requirements and surplus, general financial conditions, contractual restrictions and other factors that our board of directors may deem relevant.

## EXCHANGE RATE INFORMATION

The Australian dollar is convertible into U.S. dollars at freely floating rates. There are no legal restrictions on the flow of Australian dollars between Australia and the United States. Any remittances of dividends or other payments by us to persons in the United States are not and will not be subject to any exchange controls.

Our financial statements are prepared and presented in Australian dollars.

The table below sets forth for the periods identified the number of U.S. dollars per Australian dollar as published by the Reserve Bank of Australia. We make no representation that any Australian dollar or U.S. dollar amounts could have been, or could be, converted into U.S. dollars or Australian dollars, as the case may be, at any particular rate, the rates stated below, or at all.

	<u>At Period End</u>	<u>Average Rate</u>	<u>High</u>	<u>Low</u>
Fiscal year ended June 30,				
2015 (through June 22, 2015) . . . . .	0.7794	0.8399	0.9458	0.7590
2014 . . . . .	0.9420	0.9187	0.9672	0.8716
2013 . . . . .	0.9275	1.0271	1.0593	0.9202
Month ended:				
May 31, 2015 . . . . .	0.7663	0.7906	0.8122	0.7663
April 30, 2015 . . . . .	0.7981	0.7739	0.7993	0.7590
March 31, 2015 . . . . .	0.7634	0.7731	0.7873	0.7604
February 28, 2015 . . . . .	0.7792	0.7790	0.7886	0.7648
January 31, 2015 . . . . .	0.7781	0.8092	0.8244	0.7781
December 31, 2014 . . . . .	0.8202	0.8256	0.8504	0.8112

(1) Determined by averaging the published rate on the last day of each full month during the fiscal year.

## CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of December 31, 2014, presented both in Australian dollars and U.S. dollars:

- on an actual basis; and
- on an as adjusted basis to give effect to the sale of                    ADSs in this offering and the receipt of the net proceeds at an assumed price of US\$                    per ADS, which is the midpoint of the price range set forth on the cover of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, and assuming no exercise of the underwriters' over-allotment option and no other change to the number of ADSs offered as set forth on the cover page of this prospectus.

	As of December 31, 2014			
	Actual (A\$)	Actual (US\$) <sup>(1)</sup>	As Adjusted (A\$)	As Adjusted (US\$)
Cash and cash equivalents . . . . .	\$ 26,827,488	\$ 22,003,906	\$	\$
Equity:				
Contributed equity . . . . .	\$ 129,551,591	\$106,258,215	\$	\$
Share-based payments reserve . . . . .	2,676,629	2,195,371		
Foreign exchange translation reserve . . . . .	(1,281,588)	(1,051,158)		
Accumulated losses . . . . .	(101,329,387)	(83,110,363)		
Total equity . . . . .	29,617,245	24,292,065		
Total capitalization . . . . .	\$ 29,617,245	\$ 24,292,065	\$	\$

(1) The amounts have been translated into U.S. dollars from Australian dollars based upon the exchange rate as published by the Reserve Bank of Australia as of December 31, 2014. These translations are merely for the convenience of the reader and should not be construed as representations that the Australian dollar amounts actually represent such U.S. dollar amounts or could be converted into U.S. dollars at the rate indicated.

An increase or decrease in the initial public offering price of US\$1.00 per ADS would increase or decrease cash and cash equivalents, total equity and total capitalization on an as adjusted basis by A\$                    million and US\$                    million, assuming the number of ADSs offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions. Similarly, each increase or decrease of one million in the number of ADSs offered by us would increase or decrease cash and cash equivalents, total equity and total capitalization on an as adjusted basis by A\$                    million and US\$                    million, assuming the assumed initial public offering price remains the same and after deducting estimated underwriting discounts and commissions.

## DILUTION

If you invest in the ADSs, your interest will be diluted to the extent of the difference between the initial public offering price per ADS and our net tangible book value per ADS after this offering. Dilution results from the fact that the initial public offering price per ADS is substantially in excess of the net tangible book value per 20 ordinary shares underlying the ADSs. Our net tangible book value as at December 31, 2014 was A\$29.6 million (US\$24.3 million), or A\$0.256 (US\$0.210) per ordinary share, equivalent to A\$5.12 (US\$4.20) per ADS. Net tangible book value per ADS represents the amount of total tangible assets, minus the amount of total liabilities, divided by the total number of ordinary shares outstanding and multiplied by 20, the number of ordinary shares underlying each ADS. Dilution is determined by subtracting net tangible book value per ADS from the assumed initial public offering price per ADS.

Without taking into account any other changes in our net tangible book value after December 31, 2014, other than to give effect to our sale of ADSs offered in this offering at the assumed initial public offering price of US\$      per ADS, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our adjusted net tangible book value as at December 31, 2014 would have been US\$      million, or US\$      per ADS. This represents an immediate increase in net tangible book value of US\$      per ADS to existing shareholders and an immediate dilution in net tangible book value of US\$      per ADS to purchasers of ADSs in this offering. The following table presents this dilution to new investors purchasing ADSs in the offering:

Assumed initial public offering price .....		US\$
Net tangible book value as at December 31, 2014 .....	US\$	
Increase in net tangible book value attributable to new investors .....		
As-adjusted net tangible book value immediately after the offering .....		
Dilution to new investors .....		US\$

Each increase or decrease in the initial public offering price of US\$1.00 per ADS would increase or decrease the as-adjusted net tangible book value after this offering by US\$      per ADS, and the dilution to investors in the offering by US\$      per ADS, assuming the number of ADSs offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions. Similarly, each increase or decrease of one million in the number of ADSs offered by us would increase or decrease the as-adjusted net tangible book value after this offering by US\$      per ADS, and the dilution to investors in the offering by US\$      per ADS, assuming the assumed initial public offering price remains the same and after deducting estimated underwriting discounts and commissions.

The following table summarizes, as of December 31, 2014, on the as-adjusted basis described above, the differences between the existing shareholders as of December 31, 2014 and the new investors in this offering with respect to the number of ADSs, or equivalent number of ordinary shares, purchased from us, the total consideration paid to us and the average price per ADS, or equivalent number of ordinary shares, based on an assumed initial public offering price of US\$            per ADS, which is the midpoint of the price range set forth on the cover page of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	ADS or Equivalent Ordinary Shares Purchased <sup>(1)</sup>		Total Consideration		Average Price Per ADS or Equivalent Ordinary Shares <sup>(1)</sup>
	Number	%	Amount	%	
Existing shareholders . . . . .		%	US\$	%	US\$
New investors . . . . .					
Total . . . . .		100%	US\$	100%	

(1) Reflects            ordinary shares as equivalent to each ADS.

Each increase or decrease in the initial public offering price of US\$1.00 per ADS would increase or decrease the total consideration paid by new investors by US\$            million, or US\$            per ADS, assuming that the number of ADSs offered by us, as set forth on the cover page of this prospectus, remains the same and before deducting estimated underwriting discounts and commissions. Each increase or decrease of one million in the number of ADSs offered by us would increase or decrease the total consideration paid by new investors by US\$            million, or US\$            per ADS, assuming the assumed initial public offering price remains the same and before deducting estimated underwriting discounts and commissions.

To the extent that we grant options or other equity awards to our employees or members of our management in the future, and those options or other equity awards are exercised or become vested or other issuance of our ordinary shares are made, there will be further dilution to new investors.

The share information above:

- is based on 115,563,610 ordinary shares outstanding as of December 31, 2014; and
- excludes an aggregate of 25,684,481 ordinary shares issuable upon the exercise of options outstanding at December 31, 2014, at a weighted average exercise price of A\$1.27, of which options to purchase 21,172,996 ordinary shares were vested, at a weighted average exercise price of A\$1.29.

## SELECTED HISTORICAL CONSOLIDATED FINANCIAL DATA

The following tables set forth summary historical financial data for the periods indicated.

The consolidated statement of profit or loss and other comprehensive income data and consolidated statement of financial position data for and as of the fiscal years ended June 30, 2013 and 2014 are derived from the audited consolidated financial statements included in this prospectus. The consolidated statement of profit or loss and other comprehensive income data for the six-month periods ended December 31, 2013 and 2014 and the consolidated statement of financial position data as of December 31, 2014 are derived from the unaudited consolidated financial statements that are included in this prospectus. The consolidated statement of financial position data as of December 31, 2013 are derived from the unaudited consolidated statement of financial position as of December 31, 2013 not included in this prospectus. In our management's opinion, these financial statements include all adjustments necessary for the fair presentation of our financial condition as of such dates and our results of operations for such periods.

Our financial statements have been prepared in Australian dollars and in accordance with International Accounting Standards. Our financial statements comply with IFRS, as issued by the IASB.

You should read the selected consolidated financial data in conjunction with our consolidated financial statements and related notes beginning on page F-1 of this prospectus, and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this prospectus. Our historical results do not necessarily indicate our expected results for any future periods. Financial results for the six months ended December 31, 2014 are not necessarily indicative of the results that may be expected for the full fiscal year ending June 30, 2015.

	For the year ended June 30,		For the six months ended December 31,	
	2014	2013	2014	2013
			(unaudited)	(unaudited)
<b>Statement of Profit or Loss and Other Comprehensive Income Data:</b>				
Revenue:				
Revenue .....	A\$ 597,940	A\$ 639,849	A\$ 639,167	A\$ 223,917
Other income .....	775,833	824,333	—	—
Total revenue .....	<u>1,373,773</u>	<u>1,464,182</u>	<u>639,167</u>	<u>223,917</u>
Costs and expenses:				
Royalties and license fees .....	(192,753)	(30,000)	(40,000)	(5,596)
Research and development .....	(3,757,869)	(1,280,012)	(2,210,023)	(1,850,012)
Employment related .....	(2,444,015)	(1,832,065)	(2,343,524)	(1,243,816)
Share based expenses .....	(355,116)	(518,749)	—	—
Impairment costs .....	—	(1,503,296)	—	—
Travel related expenses .....	(585,359)	(345,826)	(516,528)	(209,772)
Consultants costs .....	(652,839)	(336,570)	(400,305)	(304,341)
Occupancy costs .....	(121,582)	(100,153)	(131,364)	(61,785)
Corporate expenses .....	(646,315)	(531,686)	(436,353)	(386,415)
Foreign exchange translation .....	(111,399)	1,526,215	391,955	14,625
Total costs and expenses .....	<u>(8,867,247)</u>	<u>(4,952,142)</u>	<u>(5,686,142)</u>	<u>(4,047,112)</u>
Loss before income tax .....	(7,493,474)	(3,487,960)	(5,046,975)	(3,823,195)
Income tax benefit .....	454,365	—	—	454,365
Loss for the period .....	<u>A\$ (7,039,109)</u>	<u>A\$ (3,487,960)</u>	<u>A\$ (5,046,975)</u>	<u>A\$ (3,368,830)</u>
Loss per share, basic and diluted .....	A\$ (0.0781)	A\$ (0.0825)	A\$ (0.044)	A\$ (0.043)
Weighted-average shares outstanding, basic and diluted .....	90,432,177	41,688,975	115,218,666	78,846,552

	As of June 30,		As of December 31,	
	2014	2013	2014	2013
			(unaudited)	(unaudited)
<b>Statement of Financial Position Data:</b>				
Cash and cash equivalents . . . . .	A\$31,359,199	A\$1,587,299	A\$26,827,488	A\$5,183,854
Total current assets . . . . .	34,447,525	1,722,590	29,917,889	8,071,440
Total assets . . . . .	34,495,202	1,750,710	30,336,095	8,095,936
Total current liabilities . . . . .	954,680	1,110,370	718,850	404,981
Total liabilities . . . . .	954,680	1,110,370	718,850	404,981
Total equity . . . . .	33,540,522	640,340	29,617,245	7,690,955

## MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

*You should read the following discussion and analysis of our financial condition and results of operations in conjunction with the section entitled "Selected Historical Consolidated Financial Data" and our consolidated financial statements and related notes included elsewhere in this prospectus. This discussion contains forward-looking statements that involve risks and uncertainties. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of various factors, including, but not limited to, those set forth under "Risk Factors" and elsewhere in this prospectus.*

*Our financial statements have been prepared in Australian dollars and in accordance with International Accounting Standards. Our financial statements comply with IFRS, as issued by the IASB. Our fiscal year end is June 30. References to a particular "fiscal year" are to our fiscal year ended June 30 of that year.*

### Overview

We are a clinical-stage biotechnology company with a pipeline of in-house and partnered therapeutic programs based on our patented gene-silencing technology, ddRNAi. We are developing treatments for chronic and life-threatening human diseases such as hepatitis C, hepatitis B, age-related macular degeneration, drug-resistant non-small cell lung cancer and oculopharyngeal muscular dystrophy based on this technology. In addition, we have licensed ddRNAi technology to other biopharmaceutical companies that are progressing their programs towards, or are in, clinical development for applications, including HIV/AIDS, retinitis pigmentosa, Huntington's disease, cancer immunotherapy and intractable neuropathic pain.

Our focus is to validate that ddRNAi is safe and efficacious in a clinical setting. With this goal in mind, we are advancing our technology into a Phase I/IIa clinical trial for TT-034 as a therapy for hepatitis C. The success of this "first in human" trial would be a key step in validating ddRNAi for therapeutic use, seeking regulatory approval of a product candidate based on ddRNAi and ultimately commercializing the product if it achieves approval. In the future, we expect to earn revenue primarily from licensing programs, strategic alliances and collaboration arrangements with pharmaceutical companies. There can be no assurance, however, as to whether we will enter into any additional such arrangement or what the terms of any such arrangement could be.

Since we were incorporated in Australia in 1995, we have devoted the majority of our resources to development efforts relating to ddRNAi. While we have established some licensing arrangements, we do not have any products approved for sale and have not generated any revenue from product sales. We have funded our operations primarily from private placements of ordinary shares, including A\$31.5 million of gross proceeds raised in February 2014. We have also been awarded research and development grants from the Australian federal government, totaling A\$0.8 million in fiscal 2014 and have earned licensing revenue from licensing our ddRNAi technology to five biopharmaceutical companies, totaling A\$0.3 million in the same period.

In October 2012, we acquired Tacere Therapeutics, Inc., an RNA interference therapeutics company based in California with a development program focused on hepatitis C. As consideration for the acquisition, we issued a total of 4,092,854 ordinary shares (taking into account a 25:1 share consolidation that became effective in July 2013), representing 9.8% of our issued capital immediately after the transaction, having an aggregate value of A\$1.5 million.

We have incurred losses from operations in each year since inception. Our net losses were A\$7.0 million and A\$3.5 million for the fiscal years ended June 30, 2014 and 2013, respectively, and A\$5.0 million for the six months ended December 31, 2014. The majority of our net losses resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our



operations. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We expect our expenses will increase substantially in connection with our ongoing activities as we:

- pursue clinical proof of concept across our programs, including treatments for hepatitis C, hepatitis B, AMD, drug-resistant non-small cell lung cancer and OPMD;
- continue preclinical development of cell therapy and immunotherapy programs through preclinical proof of concept;
- continue our research and development efforts of ddRNAi-based technology;
- seek regulatory approval for our product candidates; and
- add personnel and resources to support our product development and commercialization efforts.

As of March 31, 2015, we had cash and cash equivalents of A\$26.7 million.

We may generate revenue from licensing programs, strategic alliances or collaboration arrangement with pharmaceutical companies. These arrangements are likely to be more appealing to them when our pipeline is more advanced. We do not expect to generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for one or more of our product candidates, which we expect will take a number of years, is subject to significant uncertainty and may never occur.

We expect that the net proceeds from this offering and our existing cash and cash equivalents will be sufficient to enable us to advance planned preclinical programs and clinical trials for our current product candidates for at least the next 24 months. We will continue to pursue licensing programs, strategic alliances and collaboration arrangements with pharmaceutical companies and we regard this as our key value creation opportunity unless and until we are able to gain regulatory approval for one of our product candidates and decide to commercialize it ourselves. If we were to decide to take one or more product candidates to commercialization on our own, the process of obtaining regulatory approval for the selected programs and building the commercial infrastructure that would be necessary to commercialize them, if approved, would require substantial additional funding.

Our current operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned. These additional funds could be raised through public or private equity or debt financings, government or other third-party funding, strategic alliances and licensing arrangements or a combination of these approaches. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and compromise our ability to develop our product candidates and pursue our strategy.

We expect to incur losses for the foreseeable future, and we expect these losses to increase as we continue our development of, and seek regulatory approvals for, our product candidates. Because of the numerous risks and uncertainties associated with product development in our field, we are unable to predict the timing or amount of increased expenses, or when or if we will be able to generate product revenue or achieve or maintain profitability. Our ability to generate revenue from licensing, strategic alliances and collaboration arrangements and product sales will depend on a number of factors, including, among others, obtaining and maintaining adequate coverage and reimbursement from third-party payors for any of our product candidates that may receive regulatory approval. Even if we are able to generate revenues from licensing programs, strategic alliances or collaboration arrangements or commercial sale of our products, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and we could be forced to reduce our operations.

## **Financial operations overview**

### ***Revenue***

To date, we have derived revenues from licensing fees, the Australian federal government's Research and Development Tax Incentive program and interest income. We have not generated any revenues from the sales of products. Revenues from licensing fees and the tax incentive program are included in the revenue line item on our statements of profit or loss.

Our licensing fees have been generated through the licensing of our ddRNAi technology to biopharmaceutical companies.

Our grant revenue is generated through the Australian federal government's Research and Development Tax Incentive program, under which the government provides a cash refund for the 45% of eligible research and development expenditures, including salaries, by small Australian entities having a tax loss. For this purpose, small Australian entities are defined as those with less than A\$20 million in revenue. This grant is available for our research and development activities in Australia, as well as activities in the United States to the extent such U.S.-based expenses relate to our activities in Australia, do not exceed half the expenses for the relevant activities and are approved by the Australian government. Because the grants are determined by the Australian government following the completion of a fiscal year based upon eligible research and development expenditures, grants are recorded in the fiscal year received rather than the fiscal year to which they relate.

We also record interest and other financial income earned from bank accounts, term deposits and short-term investments as other income in our statements of profit or loss.

### ***Research and development expenses***

Research and development expenses consist primarily of costs incurred for the development of our product candidates, which include:

- expenses incurred under agreements with academic research centers, clinical research organizations and investigative sites that conduct our clinical trials; and
- the cost of acquiring, developing, and manufacturing clinical trial materials.

Research and development expenses do not include employment related expenses, which are included in our Statement of Profit or Loss and Other Comprehensive Income as a separate line item.

Research and development costs are expensed as incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

We cannot determine with certainty the duration and completion costs of the current or future product development, preclinical studies or clinical trials of our product candidates. The duration, costs, and timing of clinical trials and development of our product candidates will depend on a variety of factors, including:

- the scope, rate of progress, and expense of our ongoing as well as any additional clinical trials and other research and development activities;
- the countries in which trials are conducted;
- future clinical trial results;
- uncertainties in clinical trial enrollment rates or drop-out or discontinuation rates of patients;
- potential additional safety monitoring or other studies requested by regulatory agencies;
- significant and changing government regulation; and
- the timing and receipt of any regulatory approvals.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA, or another regulatory authority were to require us to conduct clinical trials beyond those that we anticipate will be required to complete clinical development of a product candidate or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

Our research and development expenses, categorized by product candidate or program, in fiscal 2014, fiscal 2013 and the six months ended December 31, 2014 were as follows:

Product candidate or program	For the year ended June 30,		For the six months ended December 31,
	2014	2013	2014
TT-034 for the treatment of HCV . . . . .	A\$2,475,086	A\$ 456,437	A\$ 848,269
Hepbarna for the treatment of HBV . . . . .	—	—	60,416
TT-211 and TT-231 for the treatment of AMD . . . . .	793	208,151	630,077
Tribetarna for the treatment of drug-resistant NSCLC . . . . .	752,683	41,519	382,069
Intractable neuropathic pain . . . . .	1,688	193,971	—
Pabparna for treatment of OPMD . . . . .	40,299	145,207	—
Other project related research and development costs . . . . .	487,320	234,727	289,192
Total . . . . .	<u>A\$3,757,869</u>	<u>A\$1,280,012</u>	<u>A\$2,210,023</u>

We plan to increase our research and development expenses for the foreseeable future as we continue the development of ddRNAi product candidates and explore further potential applications of our technology.

***Employment related costs***

Employment related costs include salaries for all our employees and related benefits, including the grant of share options, which are valued and included in the statements of profit or loss and other comprehensive income as share based expenses.

***Impairment***

We assess at the end of each fiscal year and half year whether there is an indication that an asset may be impaired. If any such indication exists, or when annual impairment testing is required for an asset, such as goodwill, intangible assets with indefinite useful lives and intangible assets not yet available for use, we make an estimate of the asset's recoverable amount. An asset's recoverable amount is the higher of its fair value less costs to sell and its value in use and is determined for an individual asset, unless the asset does not generate cash inflows that are largely independent of those from other assets or groups of assets and the asset's value in use cannot be estimated to be close to its fair value. In such cases, the asset is tested for impairment as part of the cash generating unit to which it belongs. When the carrying amount of an asset or cash-generating unit exceeds its recoverable amount, the asset or cash-generating unit is considered impaired and is written down to its recoverable amount.

In assessing value in use, the estimated future cash flows are discounted to their present value using a pre-tax discount rate that reflects current market assessments of the time value of money and the risks specific to the asset. Impairment losses relating to continuing operations are recognized in those expense categories consistent with the function of the impaired asset unless the asset is carried at revalued amount (in which case the impairment loss is treated as a revaluation decrease).

### ***Royalties and license fees***

We pay royalties and license fees in connection with our licensing of intellectual property from third parties. In connection with our acquisition of Tacere in 2012, we agreed to pay to the former shareholders of Tacere royalties on certain licensing revenue earned by us through the license of certain products, including TT-034, covered by a patent controlled by Tacere in October 2012. Any such royalties would be calculated as follows: 15% if the license is entered into prior to commencement of a Phase III clinical study and 2.5% if the license is entered into after commencement of a Phase III clinical study. Also, if we were to directly sell these products, then we would pay a royalty of 2.5% on net sales to the former shareholders of Tacere.

In August 2009, we entered into a collaborative agreement with Biomics Biotech Co., Ltd., or Biomics, pursuant to which we agreed to share any revenue generated from commercializing our jointly filed patents which relate to single-stranded RNA and shRNA sequences for treatment of hepatitis B. Any such revenue generated would be distributed to Biomics and us commensurate with our respective contributions to the intellectual property subject to the agreement, which contributions are expected to be equal.

### **Foreign exchange translation**

The foreign currency translation reserve represents the currency translation movements of subsidiary company balances denominated in foreign currencies at year end. Foreign currency monetary items are translated at the year-end exchange rate. Non-monetary items measured at historical cost continue to be carried at the exchange rate at the date of the transaction. Non-monetary items measured at fair value are reported at the exchange rate at the date when fair values were determined. Movements in the foreign currency translation reserve are shown in our Statement of Profit or Loss and Other Comprehensive Income.

Foreign currency transactions are translated into functional currency using the exchange rates prevailing at the date of the transactions. Exchange rate differences are recognized in the Statement of Profit or Loss and Other Comprehensive Income.

The significant movement in the foreign currency translation reserve and foreign exchange transactional gain or loss in the fiscal year ended June 30, 2013 is due to historic intercompany loan balances between Benitec and its foreign subsidiaries that are eliminated on consolidation which were deemed to be non-repayable and were accordingly transferred to equity during fiscal 2014. As a result of the transfer of historical intercompany receivable and payable balances to equity, these balances are translated at a historical rate and no further foreign exchange translational reserve or transactional gain or loss on these balances was required at June 30, 2014.

### **Critical Accounting Policies and Estimates**

The preparation of our financial statements requires us to make estimates and judgments that can affect the reported amounts of assets, liabilities, revenues and expenses, as well as the disclosure of contingent assets and liabilities at the date of our financial statements. We analyze our estimates and judgments and we base our estimates and judgments on historical experience and various other assumptions that we believe to be reasonable under the circumstances. Actual results may vary from our estimates. Our significant accounting policies are detailed in Note 1 to our consolidated financial statements for the fiscal year ended June 30, 2014 appearing elsewhere in this prospectus. We have summarized below the accounting policies of particular importance to the portrayal of our financial position and results of operations and that require the application of significant judgment or estimates by our management.

*Share-based payments transactions.* We measure the cost of equity-settled transactions with employees by reference to the fair value of the equity instruments at the date at which they are granted. The fair value is determined using a Black-Scholes model.

*Tax losses.* Given our history of recent losses, we have not recognized a deferred tax asset with regard to unused tax losses and other temporary differences, as it has not been determined whether we or our subsidiaries

will generate sufficient taxable income against which the unused tax losses and other temporary differences can be utilized. We note that the availability of tax losses is subject to Australian continuity of ownership test or, if we fail that test, the same business test. If we continue to obtain funding from new shareholders, then we may not comply with the continuity of ownership test.

### Certain Differences Between IFRS and GAAP

IFRS differs from GAAP in a few respects. While we have not assessed the materiality of differences between IFRS and GAAP, we note in particular that IFRS permits the recording of finance income and research and development grants as revenue, unlike GAAP, under which interest and other finance income would not be recorded as revenue but instead as net finance income and research and development grants would be recorded as an offsetting reduction to research and development expenses. In addition, under IFRS, all employment-related expenses are reported in their own line item in our Statement of Profit or Loss and Other Comprehensive Income, unlike GAAP, under which employment-related expenses are generally allocated to line items such as research and development expense or general and administrative expense based on the functions performed by each applicable employee.

### Results of Operation

The following discussion relates to our consolidated results of operations, financial condition and capital resources. You should read this discussion in conjunction with our consolidated financial statements and the notes thereto contained elsewhere in this prospectus.

#### *Comparison of the fiscal years ended June 30, 2014 and 2013*

We raised significant capital in fiscal 2014 that enabled us to accelerate our research and development efforts. In particular, we raised A\$39.6 million, net of transaction costs, in private placements of ordinary shares to institutional investors and a shareholder purchase plan to shareholders resident in Australia and New Zealand. With these funds available, we were able to advance the TT-034 program for hepatitis C, as well as other programs in our pipeline, including our hepatitis B, drug-resistant non-small cell lung cancer and AMD programs. We submitted an IND application for TT-034 to the FDA in December 2013 and, with the application approved in January 2014, we were able to commence clinical trials with TT-034.

#### *Revenue*

	For the fiscal year ended June 30,		Increase (Decrease)
	2014	2013	
Revenue:			
Licensing revenue and royalties . . . . .	A\$ 276,824	A\$ 521,140	A\$(244,316)
Australian government research and development grants . . . . .	775,833	824,333	(48,500)
Other income:			
Finance income—interest . . . . .	321,116	118,709	202,407
Total revenue . . . . .	<u>A\$1,373,773</u>	<u>A\$1,464,182</u>	<u>A\$ (90,409)</u>

Licensing revenue and royalties decreased by A\$0.2 million, or 47%, from A\$0.5 million in fiscal 2013 to A\$0.3 million in fiscal 2014 due to amounts earned in fiscal 2013 that were not repeated in fiscal 2014.

Grants from the Australian government decreased A\$48,500, or 6%, from fiscal 2013 to fiscal 2014 because we undertook less research and development activity on approved “eligible expenditure” in fiscal 2013, and thus received and recorded less grant revenue in fiscal 2014, compared to activities in fiscal 2012.

Finance income more than doubled in fiscal 2014 from fiscal 2013 as a result of a private placement of ordinary shares to institutional investors and a shareholder purchase plan in 2014 that raised proceeds of A\$39.6 million, thus providing for higher bank deposit and short-term investment balances in fiscal 2014 compared to fiscal 2013.

#### *Expenses*

*Royalties and licence fees.* Royalties and licence fees decreased by A\$0.2 million from fiscal 2013 to fiscal 2014 due primarily to licences being established in fiscal 2013, with upfront payments representing most of the change in revenue.

*Research and development expense.* Research and development expense more than doubled to A\$3.8 million in fiscal 2014 compared to fiscal 2013, primarily due to (i) fiscal 2014 including a full 12 months of research and development activity by Tacere compared to only eight months of research and development activity in fiscal 2013 following our acquisition of Tacere on October 30, 2012 and (ii) the acceleration of our activities in connection with the TT-034 program for the treatment of hepatitis C. In addition, the completion of a private placement of ordinary shares in February 2014 enabled us to accelerate other research and development activity in the latter half of fiscal 2014.

*Employment related expenses.* Employment-related expenses increased by A\$0.6 million, or 33%, in fiscal 2014 compared to fiscal 2013, due in large part to the strategy of building our staff capabilities to match our anticipated longer-term requirements, such as the appointment of senior scientific, executive and support staff, including staff acquired through the acquisition of Tacere.

*Share based expenses.* Share based expenses decreased by A\$0.2 million, or 32%, from fiscal 2013 to fiscal 2014. Share based expenses are calculated using a Black-Scholes model. The share based expense model uses a data set that includes share price and exercise price, exercise probability, volatility, exercise time and interest rates. Variation in these factors and a reduced level of option grants to staff were the major contributors to this expense decrease. We recognize share based expenses over the service period in which the employee earns the award, which is the vesting period of the award.

*Impairment costs.* Impairment costs of A\$1.5 million relating to identifiable intangibles on the acquisition of Tacere were recognized in fiscal 2013. The Tacere acquisition in-process research reflected the excess of the consideration we paid over the fair value of the identifiable assets we acquired, less liabilities we assumed. The write-off of the identifiable intangibles was recorded following a review for impairment, and was considered to be the most appropriate accounting treatment as the intellectual property was a preclinical asset and, hence, the future economic benefit was uncertain.

*Travel related costs.* Travel related costs increased by A\$0.2 million, or 69%, from fiscal 2013 to fiscal 2014 due to increased staff levels and participation in international conferences, in addition to meetings with pharmaceutical companies. Travel also increased as a result of the acquisition of Tacere and the progression of the HCV program to a clinical trial.

*Consultants costs.* Consultants costs increased by A\$0.3 million, or 94%, from fiscal 2013 to fiscal 2014, as we retained specialist advisers in relation to our key programs and built appropriate shareholder relations capabilities.

*Occupancy costs.* Occupancy costs increased by A\$21,429, or 21%, from fiscal 2013 to fiscal 2014 due to the increased lease costs arising from the acquisition of Tacere and increased space under lease in Australia.

*Corporate expenses.* Corporate expenses increased by A\$0.1 million, or 22%, from fiscal 2013 to fiscal 2014 due to an increase in the size of the business and increases in consequent expenses.

*Foreign exchange translation.* A foreign exchange loss of A\$0.1 million was recorded in fiscal 2014 compared to a gain of A\$1.5 million in fiscal 2013 reflecting the historic intercompany loan balances between Benitec and its foreign subsidiaries that were transferred to equity during fiscal 2014.

*Loss for the period*

As a result of the foregoing, our loss for the period after income tax benefit increased by A\$3.5 million, or 102%, from A\$3.5 million in fiscal 2013 to A\$7.0 million in fiscal 2014.

Given our and our subsidiaries' history of recent losses, we have not recognized a deferred tax asset with regard to unused tax losses and other temporary differences, as it has not been determined whether we or our subsidiaries will generate sufficient taxable income against which the unused tax losses and other temporary differences can be utilized.

***Comparison of the six months ended December 31, 2014 and 2013***

*Revenue*

	<b>Six months ended December 31,</b>		<b>Increase (Decrease)</b>
	<b>2014</b>	<b>2013</b>	
Licensing revenue and royalties .....	A\$186,564	A\$170,723	A\$ 15,841
Finance income .....	452,603	53,194	399,409
Total revenue .....	<u>A\$639,167</u>	<u>A\$223,917</u>	<u>A\$415,250</u>

Licensing revenue and royalties increased slightly in the six months ended December 31, 2014 compared to the six months ended December 31, 2013.

Finance income increased by A\$0.4 million from A\$0.1 million for the six months ended December 31, 2013 to A\$0.5 million for the six months ended December 31, 2014 as a result of a private placement of ordinary shares to institutional investors and a shareholder purchase plan in February 2014 that raised A\$39.6 million, thus providing for higher interest returns on increased bank account cash balances for the six months ended December 31, 2014.

Grant revenue is recognized when there is reasonable assurance that we will comply with the conditions attaching to the grant and the grant will be received. In the six months ended December 31, 2014 and December 31, 2013, no grant revenue met these criteria.

*Expenses*

*Royalties and licence fees.* Royalties and licence fees increased by A\$34,404 from the six months ended December 31, 2013 to the six months ended December 31, 2014 due to licensing payments made in the six months to December 31, 2014 that were not incurred in the earlier period.

*Research and development expense.* Research and development expense increased by A\$0.4 million, or 19%, due to higher research and development activity in the six months ended December 31, 2014, including the dosing of a third patient in our Phase I/IIa clinical trial for TT-034 and the execution of an agreement with 4D Molecular Therapeutics LLC, or 4DMT, to develop novel vectors with retinal tissue specificity.

*Employment related expenses.* Employment-related expenses increased by A\$1.1 million, or 88%, to A\$2.3 million in the six months ended December 31, 2014 compared to the corresponding period in 2013, primarily due to an increase in share-based expense to A\$0.8 million in the six months ended December 31, 2014 from A\$0.1 million in the six months ended December 31, 2013 and increased staff levels.

*Travel related costs.* Travel related costs increased by A\$0.3 million, or 146%, from the six months ended December 31, 2013 to the six months ended December 31, 2014 due to increased staff levels and participation in international conferences, in addition to meetings with pharmaceutical companies.

*Consultants costs.* Consultants costs increased by A\$0.1 million, or 32%, from the six months ended December 31, 2013 to the six months ended December 31, 2014, as we retained specialist advisers in relation to our key programs and built appropriate shareholder relations capabilities

*Occupancy costs.* Occupancy costs increased by A\$0.1 million, or 113%, from the six months ended December 31, 2013 to the six months ended December 31, 2014 due to the increased lease costs for the Tacere laboratory and increased space under lease in Australia.

*Corporate expenses.* Corporate expenses increased by A\$49,938, or 13%, from the six months ended December 31, 2013 to the six months ended December 31, 2014 due to an increase in the size of the business and increases in consequent expenses.

*Foreign exchange translation.* Foreign exchange translation income increased slightly in the six months ended December 31, 2013 to A\$0.4 million in the six months ended December 31, 2014 due to the benefit from retaining cash in U.S. dollars while the Australian dollar devalued against the U.S. dollar.

#### *Loss for the period*

As a result of the foregoing, our loss for the period after income tax benefit increased by A\$1.7 million, or 50%, from A\$3.4 million in the six months ended December 31, 2013 to A\$5.0 million in the six months ended December 31, 2014.

Given our and our subsidiaries' history of recent losses, we have not recognized a deferred tax asset with regard to unused tax losses and other temporary differences, as it has not been determined whether we or our subsidiaries will generate sufficient taxable income against which the unused tax losses and other temporary differences can be utilized.

#### **Liquidity and capital resources**

We have incurred cumulative losses and negative cash flows from operations since our inception in 1995, and as of December 31, 2014 we had accumulated losses of A\$101.3 million. We anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may raise through a combination of equity offerings, debt financings, other third-party funding and other collaborations, strategic alliances and licensing arrangements.

We have had no borrowings in fiscal 2013, fiscal 2014 or the first six months of fiscal 2015 and do not currently have a credit facility.

As of March 31, 2015, we had cash and cash equivalents of A\$26.7 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. Currently, our cash and cash equivalents are held in bank accounts. Our short-term investments consist of term deposits with maturity within 180 days.



## Cash flows

The following table sets forth the primary sources and uses of cash for each of the periods set forth below:

	For the year ended June 30,		For the six months ended December 31,	
	2014	2013	2014 (unaudited)	2013 (unaudited)
Net cash used in operating activities . . . . .	A\$ (9,270,339)	A\$(2,732,596)	A\$(4,786,947)	A\$(6,105,036)
Net cash provided by (used in) investing activities . . . . .	(32,365)	133,714	(394,334)	—
Net cash provided by financing activities . . . . .	39,075,618	1,086,844	257,615	9,703,483

*Operating activities.* For the six months ended December 31, 2014 and 2013, net cash used in operating activities was A\$4.8 million and A\$6.1 million, respectively. Net cash used in operating activities was A\$9.3 million for fiscal 2014 and A\$2.7 million for fiscal 2013. The use of net cash in all periods resulted from our net losses.

*Investing activities.* Net cash used in investing activities for the six months ended December 31, 2014 was A\$0.4 million, which related to purchases of equipment. There were no purchases of equipment or other investing activities in the six months ended December 31, 2013. Net cash used in investing activities in fiscal 2014 was A\$32,365, which related to purchases of equipment. Net cash provided by investing activities in fiscal 2013 was A\$0.1 million, which primarily related to costs associated with the acquisition of Tacere in October 2012.

*Financing activities.* For the six months ended December 31, 2014 and 2013, net cash provided by financing activities was A\$0.3 million and A\$9.7 million, respectively. Net cash provided by financing activities was A\$39.1 million for fiscal 2014 and A\$1.1 million for fiscal 2013. All such cash from financing activities related to the issuance of ordinary shares. In addition to issuances from the exercise of options to purchase ordinary shares, in fiscal 2014, A\$39.5 million was raised from private placements and A\$2.8 million was raised from a share purchase plan.

## Operating capital requirements

In the future, we expect our revenue stream will be generated mostly from licensing, strategic alliances and collaboration arrangements with pharmaceutical companies. While we continue to progress discussions and advance opportunities to engage with pharmaceutical companies and continue to seek licensing partners for ddRNAi in disease areas that are not our focus, there can be no assurance as to whether we will enter into such arrangements or what the terms of any such arrangement could be.

While we have established some licensing arrangements, we do not have any products approved for sale and have not generated any revenue from product sales. We do not know when, or if, we will generate any revenue from product sales. We do not expect to generate significant revenue from product sales unless and until we obtain regulatory approval of and commercialize one of our current or future product candidates.

Unless and until we establish significant revenues from licensing programs, strategic alliances or collaboration arrangements with pharmaceutical companies, or from product sales, we anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of product candidates and begin to prepare to commercialize any product that receives regulatory approval. We are subject to the risks inherent in the development of new gene therapy products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business.

We expect that the net proceeds from this offering together with our existing cash and cash equivalents will be sufficient to enable us to complete planned preclinical proof-of-concept studies and clinical trials for our lead product candidates through at least the next 24 months. In order to complete the planned preclinical proof-of-concept studies and clinical trials for our lead product candidates and to build the infrastructure that we believe will be necessary to commercialize our lead product candidates, we will require substantial additional funding.

We have based our projections of operating capital requirements on assumptions that may prove to be incorrect and we may use all of our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the timing and costs of our planned clinical trials for our product candidates;
- the timing and costs of our planned preclinical studies for our product candidate;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and costs of seeking regulatory approvals;
- revenue received from commercial sales of any of our product candidates that may receive regulatory approval;
- the terms and timing of any future collaborations, licensing, consulting or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the extent to which we need to in-license or acquire other products and technologies.

***Contractual obligations and commitments***

The following table summarizes our contractual obligations as of December 31, 2014:

	Payments due by period				
	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
Operating lease obligations . . . . .	A\$ 141,082	A\$ 95,781	A\$ 45,301	A\$ —	A\$ —
Obligations to clinical research organizations . . .	1,057,467	422,842	634,625	—	—
Total . . . . .	<u>A\$1,198,549</u>	<u>A\$518,623</u>	<u>A\$679,926</u>	<u>A\$ —</u>	<u>A\$ —</u>

We have obligations under contracts with clinical research organizations relating to their work on our clinical trials. These obligations, which are subject to termination under certain circumstances, include:

- In 2012, we appointed Synteract Inc. as a clinical research organization responsible for the progression of TT-034 into Phase I/II clinical trials in the United States.
- In 2014, we appointed European-based Clinical Trials Group as a clinical research organization responsible for the progression of our non-small cell lung cancer therapeutic Tribetarna into Phase II clinical trials.

**Off-balance sheet arrangements**

We did not have over the past three fiscal years, and we currently do not have, any off-balance sheet arrangements as defined in the rules and regulations of the Securities and Exchange Commission.

**Quantitative and qualitative disclosures about market risks**

We are exposed to market risk related to changes in interest rates and exchange rates.

As of June 30, 2014 and 2013 and December 31, 2014, we had cash and cash equivalents of A\$31.4 million, A\$1.6 million and A\$26.8 million, respectively, primarily held in bank accounts and term deposits. Our primary exposure to market risk is interest rate sensitivity, which is affected primarily by changes in the general level of Australian interest rates. Our available for sale securities are subject to interest rate risk and will fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% increase in interest rates would not have a material effect on the fair market value of our portfolio.

We are exposed to fluctuations in foreign currencies that arise from foreign currencies held in bank accounts and the translation of results from our operations outside Australia. Our foreign exchange exposure is primarily the U.S. dollar. Foreign currency risks arising from commitments in foreign currencies are managed by holding cash in that currency. Foreign currency translation risk is not hedged.

## BUSINESS

### Overview

We are a clinical-stage biotechnology company developing a novel, proprietary therapeutic technology platform that combines gene silencing and gene therapy with a goal of providing sustained, long-lasting silencing of disease-causing genes from a single administration. We believe our technology has the potential to be a “one shot” cure for a wide range of diseases that are currently addressed by strict ongoing treatment regimens or that have no effective treatment or only palliative care options. We are using our technology, called DNA-directed RNA interference, or ddRNAi, to develop our pipeline of product candidates for the treatment of numerous chronic and life-threatening human diseases, such as hepatitis C, hepatitis B, age-related macular degeneration, or AMD, drug-resistant non-small cell lung cancer, or NSCLC, and oculopharyngeal muscular dystrophy, or OPMD. These diseases have large patient populations, with the exception of OPMD which is a rare disease. In addition, we have licensed our ddRNAi technology to other biopharmaceutical companies whose pipeline programs are progressing towards, or are in, clinical development for applications including HIV/AIDS, retinitis pigmentosa, Huntington’s disease, cancer immunotherapy and intractable neuropathic pain.

Many diseases are known to be caused by the inappropriate expression of a gene or multiple genes. It has been observed since 1998 that RNA interference, or RNAi, is a mechanism that can potentially be used to specifically turn off, or silence, genes whose sequences are known. Thus, RNAi can potentially be used to treat or cure diseases with a genetic basis by targeting a specific region of the molecular sequence of the disease-causing gene. RNAi is potentially applicable to over 20,000 human genes and a large number of disease-causing microorganism-specific genes. The mechanism of action of RNAi involves the introduction of short interfering RNA, or siRNA, into a cell. The siRNA’s sequence is constructed to match a short region of the target gene. The siRNA is processed by the cell’s own enzymes to destroy the target gene’s messenger RNA, or mRNA, thus preventing the disease-causing gene from being expressed. This occurs as long as the siRNA remains prevalent in the cell.

Our approach differs from the standard RNAi approach, which is commonly referred to as siRNA and is being developed by a number of other companies, including Alnylam Pharmaceuticals, Inc., or Alnylam, Tekmira Pharmaceuticals Corporation, or Tekmira, and Dicerna Pharmaceuticals, Inc., or Dicerna. In this standard RNAi approach, double-stranded siRNA is produced synthetically and subsequently introduced into the target cell either by chemical modification of the RNA or by a range of other delivery methods. While clinical efficacy has been demonstrated for a number of indications utilizing this approach, it has a number of limitations, which include:

- Once administered, siRNA levels within cells are finite and limited to the initial amount delivered. Extended therapeutic benefit requires repeated administration for multiple cycles.
- Patient adherence challenges due to dosing frequency and treatment duration.
- Therapeutic concentrations of siRNA are not stably maintained because the levels of synthetic siRNA in the cells decrease over time.
- Delivery of siRNA into the appropriate target cells has been a considerable challenge. Unmodified siRNA is unstable in the bloodstream, can cause an adverse immune response and does not readily cross membranes to enter cells. Therefore, novel chemical modifications or the use of novel delivery materials are required to introduce the siRNA into the target cells, making it complicated to develop therapeutics.
- Because the liver acts to clear foreign contaminants from the bloodstream, current systemic delivery of siRNA molecules is limited primarily to targeting the liver. As a result, the majority of siRNA pipeline drugs have been restricted to liver diseases.
- When injected into the body, siRNA is recognized as a foreign contaminant and can cause an adverse immune response, or interferon response, potentially resulting in serious adverse effects.

- There are multiple target disease-causing genes in some diseases, including certain viral infections and certain types of cancer. siRNA-based applications typically involve multiple siRNA molecules, one for each gene desired to be silenced, and may require specialized delivery formulations to ensure distribution of each molecule in the target cells. This delivery challenge makes it more difficult to develop treatments for diseases that implicate multiple genes.
- siRNA only acts to silence genes, but cannot be used to replace defective genes with normally functioning genes.

Our ddRNAi technology is designed to utilize the specificity and gene silencing effect of RNA interference while overcoming many of the limitations associated with the ongoing administration of siRNA. Our ddRNAi approach combines RNA interference with gene therapy. Unlike siRNA, our ddRNAi technology starts with a DNA construct. Gene therapy vectors, which are carrier molecules, often viruses, that deliver genetic material into the cell, are used to deliver the DNA construct to the nucleus of the targeted cells. The DNA construct then generates double-stranded short hairpin RNAs, or shRNAs, which are processed by the cell into siRNAs, which in turn silence the disease-associated genes. Advantages of our ddRNAi approach include:

- ddRNAi is designed to produce sustained, long-lasting silencing of the disease-causing gene, following a single administration, leading to the potential for “one shot” cures for a wide range of diseases, which could eliminate the requirement for patient compliance to take regular doses of medicine for long-term management of their disease.
- ddRNAi technology can potentially use any clinically validated gene therapy vector, enabling it to target a wide range of tissues, including, but not limited to, the liver.
- Because ddRNAi uses the cell’s own transcriptional mechanisms to produce shRNA, a constant level of shRNA can potentially be produced so that intracellular levels of siRNA do not fall below threshold levels required for disease suppression.
- The level of shRNA in the cells can potentially be fine-tuned to achieve optimal concentrations.
- Off-tissue effects can be minimized by using tissue specific promoters that are designed to restrict expression of shRNA to only the target tissue.
- The DNA constructs are shielded in gene therapy vectors that are designed to avoid activating the interferon response.
- ddRNAi provides the option to both silence the defective gene and replace the defective gene with a normal version, using the same gene therapy vector. Thus silencing and replacement of the mutant gene occurs in the same cell. We believe this “silence and replace” strategy is ideally suited to developing therapeutics for a number of genetic disorders.
- ddRNAi can be designed to express multiple siRNAs in the same cell, targeting either a single gene at several different sites to minimize the risk of viral resistance, or multiple genes in distinct cellular pathways, potentially enabling treatment of complex genetic diseases such as cancer, diabetes and heart disease.
- ddRNAi can elicit long-term response by continued expression of siRNA from a single administration, potentially preventing viral reinfection.

Our strategy is to discover, develop and commercialize treatments that leverage the capabilities of ddRNAi. We intend to do so by progressing our pipeline of ddRNAi-based therapeutics designed to treat and cure a number of human diseases, thereby demonstrating the broad clinical application of ddRNAi.

Our lead product candidate, TT-034, which currently is in a Phase I/IIa first-in-human clinical trial, is being developed to treat patients chronically infected with the most common genotype, GT-1, of the hepatitis C virus, or HCV. We expect to receive efficacy data in the fourth quarter of 2015. If the results of the trial are favorable,

we anticipate commencing a phase IIb/III trial in the second quarter of 2017. The primary endpoint for the Phase I/IIa trial is safety, measured by the incidence of serious adverse events and changes in clinical parameters. The secondary endpoints are efficacy-based, measured by shRNA expression in the liver, and sustained reduction in HCV viral load in the blood. Of the five patients who have been dosed thus far, there have been no treatment-related serious adverse effects observed. Three of the five patients have been biopsied to date, and we have seen shRNA expression in all three. According to the World Health Organization, or the WHO, 130 million to 150 million individuals worldwide have chronic hepatitis C. Hepatitis C is a leading cause of cirrhosis and hepatocellular carcinoma, which often requires a liver transplant. Patients suffering from HCV have limited treatment options that require adherence to strict recurrent treatment regimens, cause debilitating side effects that can cause patients to deviate from their prescribed treatment regimen, and lack the ability to prevent reinfection. We believe TT-034 represents the first systemic administration of a ddRNAi-based therapeutic, making us the only company to date to advance into a clinical trial an RNAi therapeutic for systemic administration by gene therapy vectors.

We are also developing Hepbarna, which currently is in preclinical studies, for the treatment of the hepatitis B virus, or HBV. We plan to file an investigational new drug, or IND, application in the first quarter of 2017. HBV is a small DNA virus that, according to the WHO, infects up to 240 million people worldwide, resulting in up to 780,000 deaths per year. Infection with HBV occurs in phases ranging from a silent, acute phase that can be resolved by the immune system to a persistent chronic infection requiring life-long therapy. In the case of a chronic HBV infection, the presence of viral particles and proteins, particularly the s-antigen, causes hepatic inflammation leading to liver dysfunction, acute hepatic failure, cirrhosis or hepatocellular carcinoma. Patients suffering from HBV have limited treatment options from therapies consisting of antivirals and, less commonly, interferon therapy. These treatments require adherence to strict recurrent treatment regimens, may cause the hepatitis B virus to mutate and develop antiviral drug resistance, and may only provide viral suppression through the course of administration, and not a cure. The long-term use of interferon, particularly in high doses, may also be associated with significant side effects, including nausea, vomiting, shortness of breath, dizziness and fatigue, that can cause patients to deviate from the course of treatment. Hepbarna is designed to be a single administration ddRNAi-based monotherapy that is delivered using a gene therapy vector that targets the liver and inhibits viral replication and s-antigen production on a long-term basis. As both HBV and HCV replicate in the liver, we have designed Hepbarna to mimic the design elements of TT-034, which we believe could help expedite Hepbarna's regulatory pathway.

In addition to TT-034 for HCV and Hepbarna for HBV, we are focusing on developing product candidates to treat AMD, OPMD and drug-resistant NSCLC. For selected product candidates, at the appropriate stage, we may collaborate with large pharmaceutical companies to further develop and, if approved, commercialize them to achieve broad product distribution. For certain products we deem to be outside of our immediate focus, we will continue to out-license, where appropriate, applications of our ddRNAi technology for the development of a range of therapeutics.

## **Our Strengths**

We believe that the combination of our proprietary ddRNAi technology and our deep expertise and know-how in designing and clinical development of ddRNAi-based therapeutics will enable us to achieve and maintain a leading position in gene silencing for treatment of human disease. Our key strengths include:

- A first mover advantage for ddRNAi-based therapeutics;
- Exclusive rights to a novel, proprietary ddRNAi technology platform that is potentially the basis of single-administration therapies with sustained, long-term silencing of disease-causing genes;
- A pipeline of programs focused on life threatening or chronic diseases with either large patient populations, including hepatitis C, hepatitis B, AMD and drug-resistant NSCLC, or rare disease status potentially supporting an orphan drug classification, including OPMD;

- A product candidate, TT-034, currently in a Phase I/IIa clinical trial that we believe, based on preliminary results from three patients, has clinical proof of concept for the production of shRNA in the liver from a single administration;
- Collaborations with third parties to expand the technology platform and develop additional expertise in DNA delivery technologies, in scalable manufacturing, in DNA construct design and in developing related diagnostics to help identify the most appropriate patient populations to benefit from these novel treatments;
- Out-licensing agreements with third parties utilizing our ddRNAi technology to develop therapies outside of our core research areas, which we believe could provide further validation of our technology's potential to address numerous diseases;
- Our development team has more than 50 years of combined experience in designing and developing ddRNAi therapeutics and includes founding scientists in the ddRNAi field; and
- Rights to intellectual property that includes a patent portfolio protecting our ddRNAi technology platform in numerous jurisdictions through 2019, and a growing portfolio of patents protecting improvements to our ddRNAi technology and product candidates in numerous jurisdictions through at least 2025.

## Our Strategy

Our objective is to become the leader in discovering, developing, clinically validating and commercializing ddRNAi-based therapeutics for a range of human diseases with high unmet clinical need or large patient populations, and to thereby provide a better life for patients with these diseases. Our strategy to accomplish this goal is to:

- **Progress our pipeline of proprietary ddRNAi-based therapeutics.** Our lead product candidate, TT-034, is a single administration ddRNAi-based therapeutic currently in Phase I/IIa to treat the most common genotype of HCV. We are also pursuing early preclinical research in HBV, AMD, drug-resistant NSCLC and OPMD. We plan to submit IND applications for our drug-resistant NSCLC product candidate in the third quarter of 2016 and for our HBV and AMD product candidates in the first and second quarters of 2017, respectively. We expect to complete preclinical proof-of-concept studies for our OPMD product candidate in the third quarter of 2016.
- **Continue our leadership position in ddRNAi-based therapeutics.** We believe we are the only company to date to advance into a clinical trial an RNAi therapeutic for systemic administration by gene therapy vectors. We have developed significant experience in ddRNAi through our work on HCV, HBV, AMD, drug-resistant NSCLC and OPMD. We have strong relationships with key opinion leaders in the field and will continue to engage with the medical and scientific community to communicate the potential therapeutic value of ddRNAi.
- **Further develop and improve our ddRNAi platform technology and its associated intellectual property position.** In addition to progressing our pipeline of product candidates, we will further develop and improve our ddRNAi platform technology and its associated intellectual property through in-house development and in-licensing of complementary technologies. One such example is our relationship with 4D Molecular Therapeutics LLC, or 4DMT, a company that is developing a vector to deliver our ddRNAi constructs to the retinal cells of the eye from an intravitreal injection to treat patients with AMD.
- **Develop drugs in our core disease areas and partner selectively to commercialize and expand our pipeline.** The adaptability of our platform also presents an opportunity for us to selectively form collaborations to expand our capabilities and product offerings into a range of diseases and potentially to accelerate the development and commercialization of ddRNAi therapeutics more broadly. We will continue to expand our franchise of ddRNAi-based therapeutics by out-licensing, where appropriate, applications of ddRNAi for the development of a range of therapeutics outside of our immediate focus.

Once clinical proof of concept has been achieved for a product candidate, we plan, where appropriate, to enter into collaborations with pharmaceutical companies to develop that product candidate and ultimately commercialize it if it receives regulatory approval.

- **Pursue indications with high unmet medical need or large patient populations.** Each of our five current core indications are severe diseases with high unmet medical need or large patient populations. We believe there is a strong rationale for treating these diseases and other diseases that have well-characterized gene targets that can be silenced, thus preventing the disease-causing gene from being expressed. Given the poor prognosis and limited treatment options for most of these diseases, we believe our ddRNAi-based product candidates may offer a potential single-treatment alternative for these patients. Our ddRNAi-based product candidates, if successful, may offer a potentially superior long-term value proposition for our patients and the healthcare system more broadly, which we believe will allow us to derive premium value while delivering patients life-altering treatments. We also intend to develop ddRNAi applications in novel technologies, including cell therapy and immunotherapy, such as chimeric antigen receptor T cells, or CAR T, for a range of additional disease areas.

### **Our Technology—ddRNAi**

Our proprietary technology platform is called DNA-directed RNA interference, or ddRNAi, which is designed to produce long-term silencing of disease-causing genes, by combining RNA interference, or RNAi, with delivery agents typically associated with gene therapy.

Standard gene therapy is normally used to compensate for abnormal or malfunctioning genes or to make a beneficial protein to address a defect. If a mutated gene causes a necessary protein to be faulty or missing, gene therapy is used to introduce a wild type, or normal, copy of the gene to restore the function of the protein. This is the approach to gene therapy taken by a number of other companies to date.

With our ddRNAi approach, gene therapy vectors are used to deliver a DNA construct that produces shRNAs, which are processed by the cell into siRNAs, which then silence the disease-associated genes.

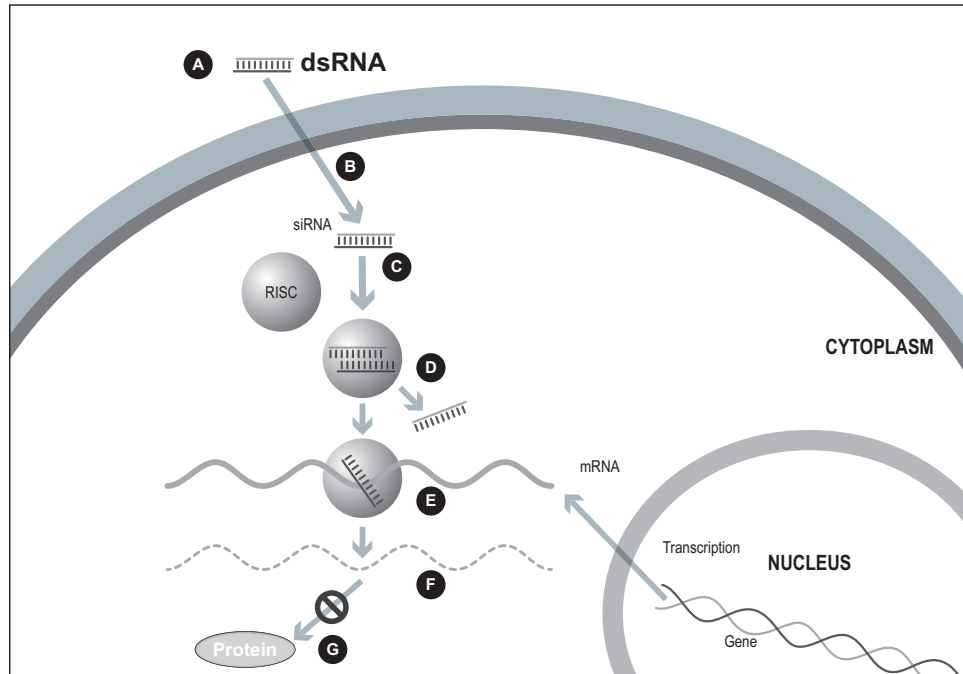
#### ***Overview of RNAi and siRNA approach***

Many diseases are known to be caused by the inappropriate expression of a gene or multiple genes. These disease-associated genes can be turned off, or silenced, by the use of RNAi, resulting in a treatment or cure of the disease. Thus, RNAi provides the ability to develop therapeutics against diseases caused by inappropriate gene expression, by targeting a specific region of the molecular sequence of the disease-causing gene. RNAi is potentially applicable to over 20,000 human genes and a large number of disease-causing microorganism-specific genes.

The mechanism of action of RNAi involves the introduction of siRNA into a cell. The siRNA's sequence is constructed to match a short region of the target gene. The siRNA is processed by the cell's own enzymes to destroy the target gene's mRNA, thus preventing the disease-causing gene from being expressed. This occurs as long as the siRNA remains prevalent in the cell. In the standard RNAi approach, siRNA is produced synthetically in the laboratory and introduced into the target cell either by chemical modification of the RNA or by a range of delivery materials. A number of other companies, including Alnylam, Tekmira, and Dicerna, utilize this approach in their RNAi product candidates.



Figure 1. The siRNA approach.



A small double stranded RNA, or dsRNA, molecule (A), comprising one strand known as the sense strand and another strand known as the antisense strand, which are complementary to each other, is synthesized in the laboratory. These small dsRNAs are called small interfering RNAs, or siRNAs. The sequence of the sense strand corresponds to a short region of the target gene mRNA. The siRNA is delivered to the target cell (B), where a group of enzymes, referred to as the RNA Interference Specificity Complex, or RISC, process the siRNA (C), where one of the strands (usually the sense strand) is released (D). RISC uses the antisense strand to find the mRNA that has a complementary sequence (E) leading to the cleavage of the target mRNA (F). As a consequence, the output of the mRNA (protein production) does not occur (G).

### *Our Approach to Gene Silencing—ddRNAi*

Our ddRNAi technology is designed to utilize the specificity and gene silencing effect of RNAi while overcoming many of the limitations of siRNA. Our ddRNAi approach combines RNA interference with gene therapy vectors to deliver a DNA compound to the target diseased tissue in order to silence the disease-associated genes.

#### *Gene therapy*

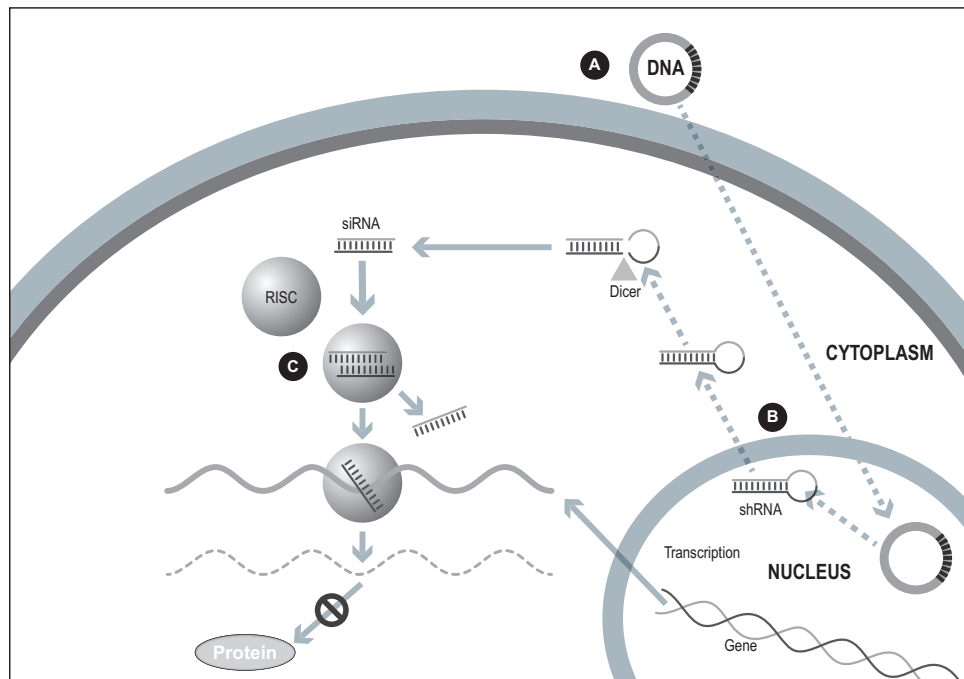
Gene therapy is designed to introduce genetic material into cells, usually to compensate for abnormal or malfunctioning genes or to make a beneficial protein to address a defect. If a mutated gene causes a necessary protein to be faulty or missing, gene therapy is used typically to introduce a normal copy of the gene to restore the function of the protein. Genetic material that is inserted directly into a cell usually does not function. Instead, a carrier called a vector is genetically engineered to deliver the gene. Certain viruses are often used as vectors because they can deliver the new gene by infecting the cell. The vector viruses are designed not to cause disease when used in people. Some types of vector viruses, such as lentivirus, integrate their genetic material, including the new gene, into a chromosome in the human cell. Other vector viruses, such as adenoviruses and adeno-associated viruses, or AAV, introduce their DNA into the nucleus of the cell, but the DNA of the vector virus is not integrated into a chromosome; only the therapeutic gene is integrated. Most of our ddRNAi programs utilize AAV as the delivery vector. A number of viral vectors can produce gene expression for months or years following a single administration, depending on the target tissue.

The vector can be given intravenously or injected directly into a specific tissue in the body, where it enters individual cells. Alternatively, a sample of the patient's cells can be removed and exposed to the vector in a laboratory setting. The cells containing the vector are then returned to the patient where they produce the expressed RNA or protein.

*ddRNAi*

Our ddRNAi technology utilizes DNA as the therapeutic molecule designed to generate shRNAs continuously in the target cell. A range of viral and non-viral gene therapy vectors can be used to deliver the DNA construct into the cell's nucleus. Once delivered, the DNA sequence codes for specific shRNAs, which are then processed by the cell's endogenous machinery into siRNA. The siRNA created by the cell then completes the RNAi cycle described above by cleaving the mRNA of the target gene thus preventing the disease-causing gene from being expressed.

**Figure 2. The ddRNAi approach.**



A DNA construct is delivered to the target cell's nucleus by a gene therapy vector (A) such as an AAV. Once in the nucleus, the DNA construct continuously produces shRNAs (B) which are processed by an enzyme called Dicer into siRNAs (C). The processed siRNA is incorporated into RISC and silences the target gene using the same mechanism shown in Figure 1.

## Our Pipeline

We are developing a portfolio of product candidates based on our proprietary ddRNAi gene silencing technology focused on chronic and life threatening conditions with disease-associated genes.

Focus	Indication	Product Candidate	Company	Discovery	Preclinical Proof of Concept (PoC)		Clinical Trials		Anticipated Milestones
					In Vitro	Studies In Vivo	Phase I/IIa	Phase IIb/III	
Infectious Disease	Hepatitis C (GT-1)	TT-034	Benitec						Efficacy data Q4 2015 Completion of Phase I/IIa trial Q4 2016 Initiation of Phase IIb/III trial Q2 2017
	Hepatitis B	Hepbarna	Benitec						Completion of <i>in vivo</i> PoC study Q2 2016 IND application filing Q1 2017 Initiation of Phase I/IIa trial Q2 2017
Ocular Disease	AMD	TT-211	Benitec						AAV vector developed Q4 2015 Completion of <i>in vivo</i> PoC studies Q2 2016 IND application filing Q2 2017 Initiation of Phase I/IIa trial Q3 2017
Cancer	Drug-Resistant Non-Small Cell Lung Cancer	Tribetarna	Benitec						Dose optimization Q4 2015 IND-enabling studies complete Q3 2016 IND application filing Q3 2016
Genetic Disease	OPMD	Pabpama	Benitec						Completion of pre-clinical PoC study Q3 2016

### TT-034 for the Treatment of Hepatitis C

#### Overview

We are developing a ddRNAi-based therapeutic, TT-034, for the treatment of the most common genotype of the human hepatitis C virus. We are currently conducting a Phase I/IIa first-in-human clinical trial of TT-034. The primary endpoint for this study is safety, measured by incidence of serious adverse events and changes in clinical parameters. The secondary endpoints are efficacy-based, measured by shRNA expression in the liver, and sustained reduction in HCV viral load in the blood. Of the five patients that have been dosed thus far, there have been no treatment-related serious adverse effects observed. Three of the five patients have been biopsied to date, and we have seen shRNA expression in all three. Assuming our TT-034 clinical trial continues to progress in accordance with its design, we expect efficacy data to become available in the fourth quarter of 2015. If the results of the trial are favorable, we anticipate commencing a Phase IIb/III trial in the second quarter of 2017.

Hepatitis C is a complex public health problem, characterized by a high prevalence of chronic infection by an RNA virus, an increasing burden of HCV-associated disease, low rates of testing and treatment, and the prospect of increasing incidence associated with injectable drug abuse. According to the WHO, over 170 million individuals worldwide have chronic hepatitis C. Chronic infection can result in cirrhosis and death in 20% of patients due to end-stage liver disease or hepatocellular carcinoma. Despite the recent addition of more effective direct acting antiviral drugs, or DAAs, the current standard of care is expensive and requires daily dosing for 12 to 24 weeks. The use of ddRNAi-based drugs offers the possibility of a “one shot” cure, where the disease is treated with a single infusion.

Publicly reported sales of the HCV therapeutics currently on the market exceeded US\$12 billion in 2014.

#### Current Hepatitis C Treatments

HCV exists as six closely related, but distinct genotypes, or GTs, with GT-1, -2, and -3 most commonly found in the United States. Currently, the most common treatment for HCV in the United States is subcutaneous interferon and ribavirin administered for 24 to 72 weeks. In addition to this, a range of antiviral drugs targeting various stages of the HCV lifecycle have recently become available. These drugs are described below with their associated treatment limitations.

- Sofosbuvir (Sofaldi)—approved by the FDA in December 2013 in combination with interferon and/or ribavirin for GT-1, -2, -3 and -4. Sofosbuvir has been reported to produce sustained virological response after 12 to 24 weeks of treatment. Some hepatitis C patients are excluded from receiving Sofosbuvir due

to severe renal impairment, and Sofosbuvir has been associated with adverse events under certain circumstances. Sofosbuvir is an inhibitor of the NS5B HCV viral protein. Common side effects can include fatigue, headache, nausea, insomnia, itching, rash, decreased appetite and diarrhea.

- Simeprevir (Olysio)—approved by the FDA in November 2013 for the treatment of individuals with GT-1 chronic hepatitis C in combination with interferon and ribavirin. The recommended length of treatment is 12 weeks. In November 2014, the FDA approved the use of simeprevir in combination with sofosbuvir for patients with GT-1 chronic hepatitis C. Simeprevir is an NS3/4A HCV viral protein inhibitor. The most common adverse effects attributable to simeprevir are skin rash, including a potentially serious photosensitivity reaction, itching, nausea, muscle pain and indigestion.
- Ledipasvir-Sofosbuvir (Harvoni)—approved by the FDA in October 2014 as fixed-dose combination therapy for GT-1 chronic hepatitis C. Some hepatitis C patients are excluded from receiving Harvoni due to severe renal impairment, and Harvoni has been associated with adverse events under certain circumstances. The recommended length of treatment currently is 12 to 24 weeks. Ledipasvir inhibits the NS5A HCV viral protein. Common side effects can include diarrhea, headache, nausea, insomnia and fatigue.
- Viekira Pak—a complex all-oral regimen consisting of four medications: ombitasvir, paritaprevir, ritonavir and dasabuvir. This regimen is also used in combination with ribavirin for some patients. It was approved by the FDA in December 2014. In the Viekira Pak, ombitasvir, paritaprevir and ritonavir are combined as a fixed-dose tablet and the dasabuvir is a separate tablet. Ombitasvir is a NS5A inhibitor, paritaprevir is an inhibitor of the NS3/4A serine protease, and dasabuvir is a non-nucleoside NS5B polymerase inhibitor. Ritonavir does not have activity against HCV. It is used as a pharmacologic booster for paritaprevir. The recommended length of treatment is 12 to 24 weeks. The most common side effects observed in clinical trials have been fatigue, nausea, insomnia, itching, skin reactions and weakness.

In addition to the treatment limitations, a factor in currently marketed anti-viral drugs to treat HCV infection is their lack of ability to prevent reinfection. Once a treatment regime is completed and the virus cleared, there is no ongoing protection provided by the drugs to prevent the patient from being reinfected if the virus is encountered again after treatment. The treatment for reinfection is another dose of one of these drugs, requiring another treatment regime of weeks or months.

Sovaldi and Harvoni reported combined sales of US\$12.4 billion in 2014. Abbvie Inc. reported approximately US\$48 million in U.S. sales for Viekira Pak during the last quarter of 2014, and it has been reported that analysts estimate Viekira Pak will generate more than US\$2.5 billion in sales in 2015. We believe these sales figures indicate that there is a market demand for effective HCV therapeutics.

#### ***Our ddRNAi-Based Hepatitis C Therapeutic—TT-034***

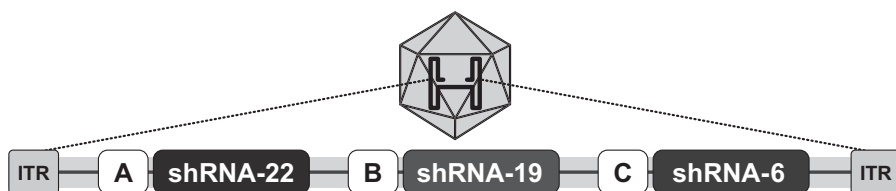
TT-034 is expected to be a single administration monotherapy delivering an AAV vector targeting the liver and expressing three shRNAs that target three separate conserved regions on the HCV genome. TT-034 is designed to clear the viral infection and provide long-term prevention of reinfection.

#### ***TT-034—Design and Mechanism of Action***

As the viral genome of HCV comprises a single strand of RNA and its replication occurs strictly within the cytoplasm, HCV is a strong candidate for therapeutics based upon RNAi. Cleaving the RNA genome by the expressed siRNAs destroys the ability of the virus to replicate. In addition, since the HCV mRNA directly serves as the template for protein synthesis, cleaving the HCV mRNA also prevents expression of key viral proteins. These include structural proteins, the building blocks for the virus, an ion channel and six non-structural proteins that are used to replicate the viral RNA, identified as NS2, NS3, NS4A, NS4B, NS5A, and NS5B. Thus, in addition to destroying the HCV mRNA, TT-034 also prevents the expression of viral proteins required to replicate the virus.

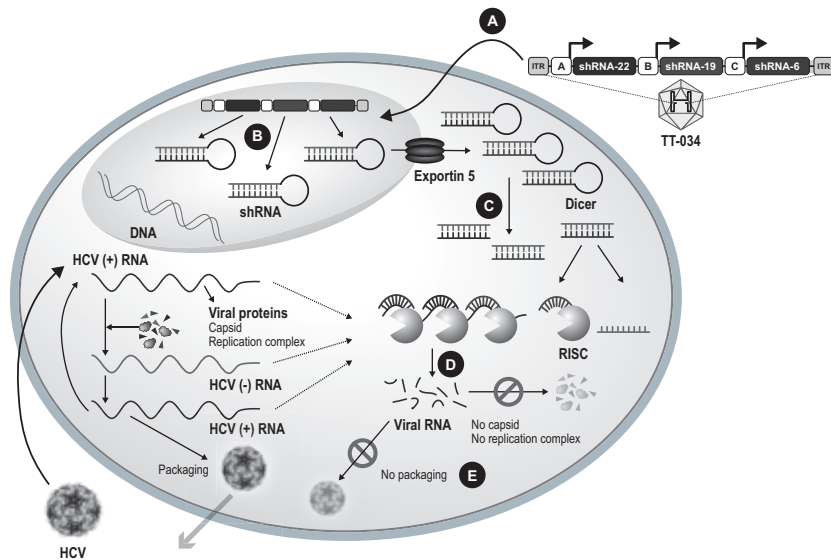
TT-034 is designed to target three distinct highly conserved regions of the HCV RNA, by generating three separate shRNAs from a single DNA construct (*Figure 3*), so that none of the viral proteins are expressed. Thus, unlike direct acting antivirals currently on the market that only target some of the viral proteins, TT-034 is designed to inhibit the expression of all of them. The DNA construct is delivered to liver cells using an AAV viral vector. The shRNAs are processed by the patient's liver cells into siRNAs which are designed to mediate sequence-specific cleavage of target regions of the hepatitis C virus (*Figure 4*). In our preclinical studies of TT-034 in mice and non-human primates, we observed persistent expression of shRNA for 180 days, the duration of each of the studies. Based on preclinical animal data, we believe that following a single-dose administration of TT-034, sustained expression of shRNAs that inhibit viral replication in liver cells known as hepatocytes, resulting in clearance of HCV, will be achievable.

**Figure 3. The design for TT-034**



TT-034 comprises a triple construct book-ended by inverted terminal repeat, or ITR, sequences. The construct targets three separate conserved regions of the HCV RNA delivered with an AAV vector which has very high attraction to hepatocytes.

**Figure 4. The mechanism of action of TT-034**



TT-034 is delivered to the nucleus of hepatocytes via an AAV vector (A). Upon reaching the nucleus the construct expresses three shRNAs (B) that are processed by the cell's endogenous machinery to produce siRNAs (C) that cleave the HCV RNA (D) and prevent the virus from replicating (E).

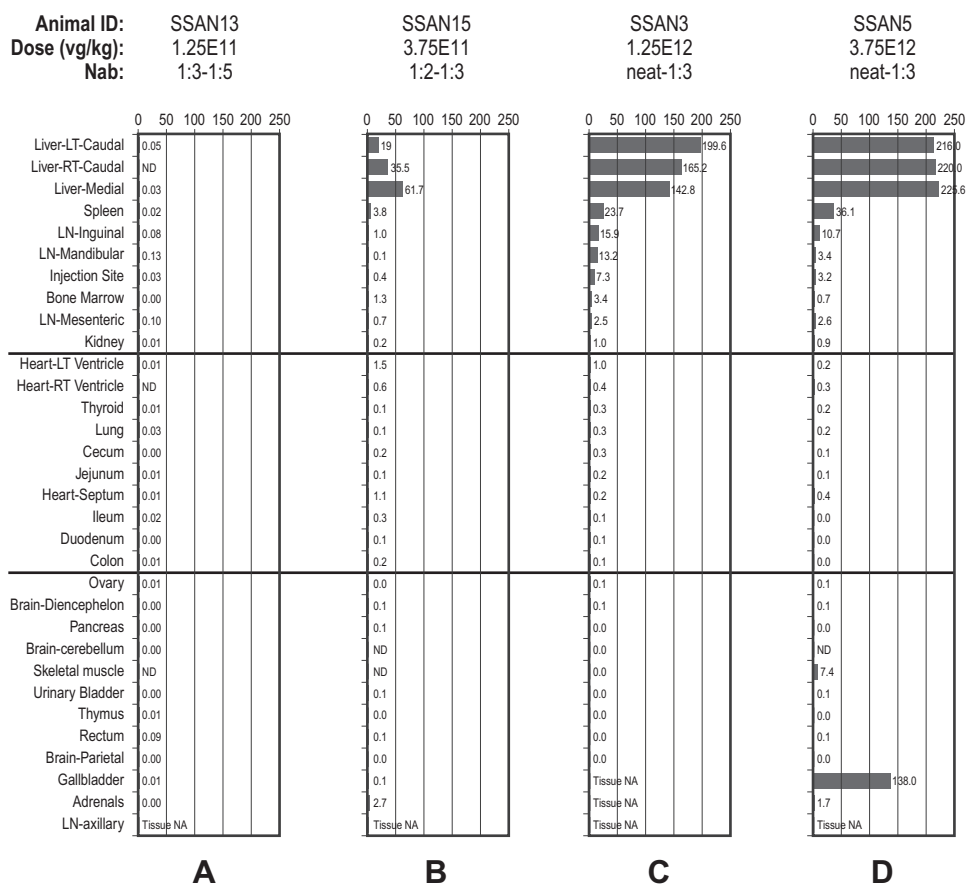
**Preclinical Highlights**

The preclinical data for the hepatitis C program was developed by Tacere Therapeutics, Inc., or Tacere, in collaboration with Pfizer, Inc., or Pfizer, until 2011, when, following its merger with Wyeth, Pfizer transferred its interest in the program to Tacere in exchange for a royalty payment. We acquired Tacere in October 2012. The first generation HCV therapeutic candidate developed by this collaboration was called TT-033.

In preclinical *in vivo* animal studies, TT-033 specifically targeted liver cells (Figure 5) with the ability to transduce nearly 100% of hepatocytes, as evidenced by shRNA6 expression (Figure 6). Because TT-033 was observed to produce excessive levels of shRNA *in vivo*, with hepatocellular toxicity in pre-clinical studies, we modified the promoter components to produce significantly less of each of the three shRNAs. The resulting second generation therapeutic candidate is TT-034, and except for its low levels of shRNA production, TT-034 is identical to TT-033. In preclinical *in vivo* animal studies of TT-034 in over 700 mice and 98 non-human primates, or NHPs, no hepatocellular toxicity was observed (as represented by data in six NHPs in Figure 7b). Furthermore, the expression of shRNA appeared to be durable, as a single treatment of clinically relevant doses of TT-034 resulted in steady-state production of therapeutic levels of shRNA in the liver of healthy non-human primates for up to 180 days (Figure 8). Some of the data from the TT-033 *in vivo* studies were included in our IND application for TT-034, which the FDA approved in January 2014, and some of that data is included in Figures 5 and 6.

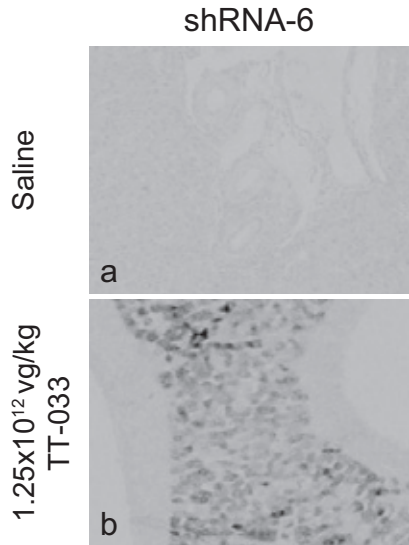
In *in vitro* models of HCV replication and infection, we observed potent inhibition of HCV replication (Figure 8), which was dose-dependent and sequence specific. We also observed that each of the three shRNAs derived from TT-034 delivered an independent antiviral effect.

**Figure 5. Liver tropism of AAV-delivered ddrRNAi anti-HCV construct**



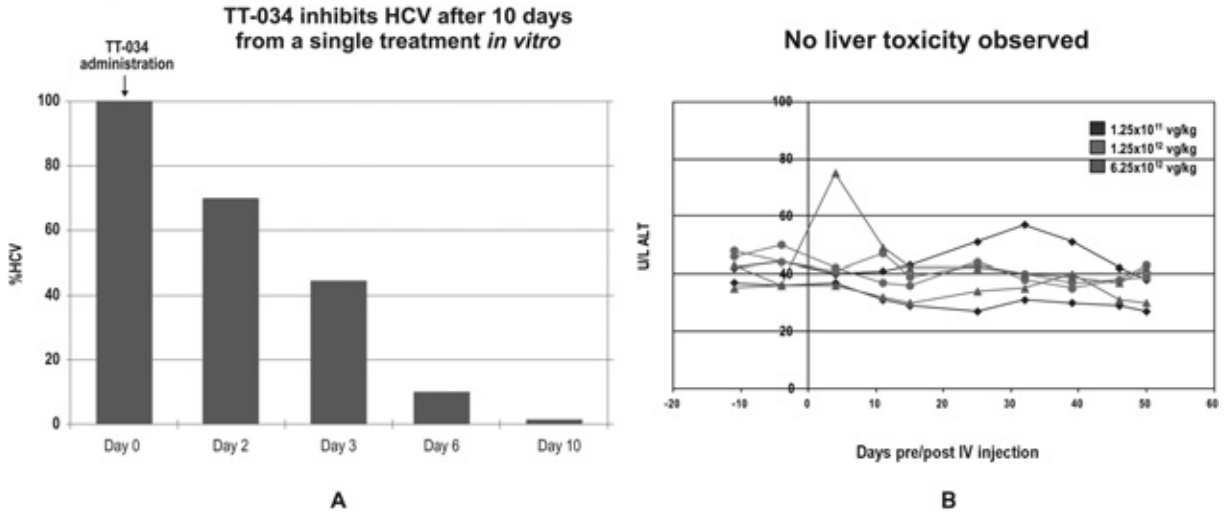
AAV delivers shRNA-expressing DNA constructs with very high specificity for liver as observed in four non-human primates, or NHPs, injected intravenously with the TT-033 therapeutic. Each NHP received a different dose of the molecule,  $1.25 \times 10^{11}$  vg/kg (A);  $3.75 \times 10^{11}$  vg/kg (B);  $1.25 \times 10^{12}$  vg/kg (C); or  $3.75 \times 10^{12}$  vg/kg (D). Following dosing, TT-033 DNA levels were measured in a wide range of each NHP's organs. As the figure below indicates, even at the highest dose (D), very little TT-033 DNA was detected in tissues other than the liver and the associated gall bladder.

**Figure 6. Transduction in hepatocytes**



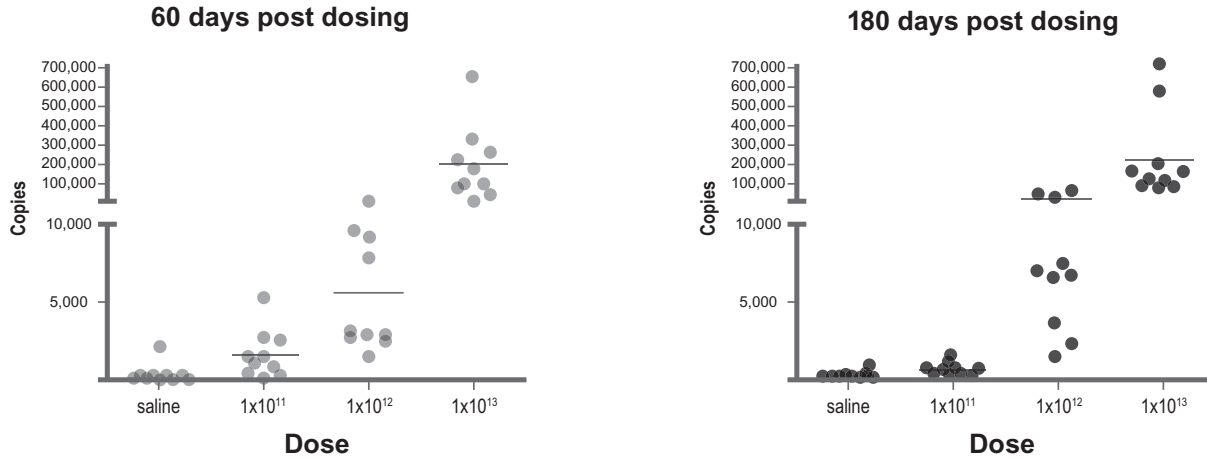
*In situ* hybridization analysis was performed using probes that were able to qualitatively detect the presence of expressed shRNA within liver cells. Sections of 30-day liver tissue were taken from animals dosed with either saline (with one example in Panel a) or with the first generation TT-033 vector (with one example in Panel b), and tested for the presence of shRNA6. Dark staining indicates those cells that produced shRNA6. This indicated cytoplasmic staining and a uniform pattern of distribution of the shRNA across nearly 100% of the hepatocytes from an animal treated with TT-033 while no staining was noted in the surrounding vascular wall and perivascular connective tissue within the hepatic parenchyma. No shRNA staining was noted in the saline-treated animal.

Figure 7. HCV inhibition and no liver toxicity



At clinically relevant doses, TT-034 produced nearly complete inhibition of HCV replication in human hepatocytes after 10 days in an *in vitro* model (A) without associated *in vivo* liver toxicity in non-human primates, or NHPs (B). (B) shows the data for six NHPs. Each of the three doses was given to two NHPs accounting for the six lines in (B) above. Toxicity was measured by evaluating levels of alanine transaminase, or ALT, an enzyme found in the liver that is commonly used clinically as a part of a diagnostic evaluation of liver damage. ALT levels below 60 international units per liter, or U/L, are considered normal for humans and levels below 53 +/- 25 U/L are considered normal for NHPs.

Figure 8. shRNA-22 expression in mouse hepatocytes



Levels of shRNA-22 expression in mouse hepatocytes persisted for at least 180 days after a single intravenous dose of TT-034.

### Clinical Highlights

In January 2014 we initiated a first-in-human Phase I/IIa clinical trial of TT-034, following the FDA's review of our IND application, which we filed in December 2013. The trial is a Phase I/IIa, first-in-human, open-label, dose escalation clinical trial designed to evaluate the safety and efficacy of a single dose of TT-034 in fourteen patients with chronic hepatitis C infection. The efficacy of delivery of TT-034 to the liver is determined by measuring shRNA expression in the liver, and efficacy of viral inhibition will be assessed by monitoring viral load. The clinical study is being conducted at three sites in the United States—Duke University, the University of



California, San Diego and the Texas Liver Institute in San Antonio. The study is expected to dose fourteen patients in five dose cohorts with doses ranging from  $4 \times 10^{10}$  vg/kg to  $4 \times 10^{12}$  vg/kg. Following administration of a single intravenous infusion of TT-034, patients are monitored for physical and clinical chemistry, including liver biopsy analysis for shRNA expression for up to 6 weeks post-treatment. A review is conducted with the data safety monitoring board, or DSMB, for the trial prior to progressing to the next cohort with escalating dose. Patients will be monitored for a total of 24 weeks of safety parameters and efficacy read-outs. We plan to follow the patients for a further 4.5 years to observe the long-term health effects of TT-034. As of April 2015, five patients have been dosed and we expect that all patients will be dosed by mid-2016. Of the five patients that have been dosed thus far, there have been no treatment-related serious adverse effects observed. Three of the five patients have been biopsied to date, and we have seen shRNA expression in all three. The biological effect observed in this trial has been observed in only the first three patients to date, is not statistically significant and might not be observed in any other patients treated with TT-034. It is also important to note that in these first two dose cohorts, the biological response was designed to be, and was observed to be, lower than the level required to achieve a therapeutic effect in those patients.

#### ***Ongoing Development Plan for TT-034***

Assuming we receive favorable results from our ongoing Phase I/IIa clinical trial, our near-term development plans for TT-034 include commencing a Phase IIb/III trial, following discussions with the FDA, at the optimal dose identified in the Phase I/IIa trial. We would aim to recruit up to 75 GT-1-infected patients for our Phase IIb/III trial.

Additional potential development pathways for TT-034 include:

- Development of TT-034 as a monotherapy for other HCV genotypes.
- Development of TT-034 as a combination therapy with oral antiviral drugs, with the aim of shortening the duration of treatment of these drugs as a result of administration with TT-034.
- Using alternative vectors for second-generation products.

#### **Hepbarna for the Treatment of Hepatitis B**

We are developing Hepbarna for the treatment of HBV. We are currently conducting preclinical studies of Hepbarna and are targeting an IND application in the first quarter of 2017. We believe that a positive outcome in our clinical trial of TT-034 for hepatitis C would validate our technology and its applicability to our hepatitis B program, thereby potentially accelerating the regulatory pathway for Hepbarna.

The human hepatitis B virus is a small DNA virus that, according to the WHO, infects up to 240 million people worldwide, resulting in up to 780,000 deaths per year. Infection with HBV occurs in phases ranging from a silent, acute phase that can be resolved by the immune system to a persistent chronic infection requiring life-long therapy. In the case of a chronic HBV infection, the presence of viral proteins, particularly the s-antigen, causes hepatic inflammation leading to liver dysfunction, acute hepatic failure, cirrhosis or hepatocellular carcinoma.

#### ***Current Hepatitis B Treatments***

HBV predominantly exists as eight genotypes, designated A through H, with distinct geographic distribution. We believe the keys to developing a successful HBV therapeutic are to stop viral replication and to prevent production of or clear specific antigens generated by the virus, in particular the HBV surface antigen, or HBsAg.

According to GlobalData, a market research firm, the global hepatitis B therapeutics market was \$3 billion in 2011, and is expected to grow to \$4.4 billion by 2019. The current therapies used as standard of care for HBV consist of antivirals composed of nucleotide and nucleoside analogues, or NUCs, and, less commonly, interferon therapy.

The most common anti-viral medications are taken as tablets each day for a year or longer and primarily act to inhibit viral replication:

- Lamivudine (Zeffix). There are almost no side effects to Lamivudine, however a significant concern is the possible development of hepatitis B virus mutations and antiviral drug resistance after long-term use.
- Adefovir (Hepsera). Adefovir is often used for people who have developed a hepatitis B virus mutation after taking Lamivudine. There are almost no side effects except for the possibility of developing hepatitis B virus mutations and antiviral drug resistance.
- Entecavir (Baraclude). Entecavir has potent activity against chronic hepatitis B. There are almost no side effects except for the possibility of developing hepatitis B virus mutations and antiviral drug resistance.
- Tenofovir (Viread). Tenofovir has potent activity against chronic hepatitis B. It is particularly useful in patients who have developed drug resistance to other medications.
- Pegylated Interferon (Pegasys). Interferon is given by injection once a week, usually for six months to a year. The drug has many potential side effects, such as flu symptoms and depression, but is reported to control the hepatitis B virus in a third of patients without need for long-term medication.

Most of these therapies can provide long-term viral load suppression but have low cure rates and have the additional risk of drug-resistant mutations. The long-term use of interferon, particularly in high doses, may also be associated with significant side effects, including nausea, vomiting, shortness of breath, dizziness and fatigue, adding to issues with patient compliance for the course of treatment. We believe that there is significant unmet medical need for HBV treatment due to the following factors:

- Inability of existing therapies to address the risk of recurrence of the infection, once an antiviral therapeutic is removed, due to the persistence of HBV covalently closed circular DNA, or cccDNA. cccDNA is a supercoiled DNA molecule that is present in the nucleus of HBV-infected cells and acts as a reservoir for further HBV infectivity. cccDNA is responsible for persistence of infection in the natural course of chronic HBV infection and during prolonged antiviral therapy.
- Mutations in the HBV genome conferring resistance to existing therapies.
- Long treatment regimens and, in some cases, significant debilitating side effects associated with current therapies, which lead to a risk of patient non-compliance.

A problem inherent to all of the current HBV antiviral treatment approaches is their inability to achieve a curative outcome. According to a study published in the *Journal of Viral Hepatitis* in 2014, HBsAg clearance occurs in only 3% of patients treated with NUCs and 7.8% of patients treated with interferon. Sustained suppression of HBV cccDNA by treatment with NUCs is only possible with continued treatment for many years, and clear-cut guidelines on when to stop treatment are not yet available. The authors concluded that there is a need for alternative therapeutic approaches such as drugs that can preferentially target stages in the life cycle of HBV, referred to as direct acting anti-virals, or DAAs, as well as new immunotherapeutic approaches. We believe that our ddRNAi-based therapeutic for HBV has characteristics of both of these approaches.

### ***Hepatitis B Treatments in Development***

#### *DAAs*

DAAs are chemicals that have been used to inhibit HBV replication by targeting one of the various stages of the viral life cycle. Use of DAAs may prove ineffective in clearing infected hepatocytes, and thus elimination of the cccDNA pool may be problematic. Accordingly, we believe combination treatments involving immunotherapeutic approaches may be necessary. Immunotherapeutic approaches that are being developed include DNA-based vaccines and molecules that are designed to activate immune responses to the hepatitis B virus. These approaches are not yet in clinical development.

### *Cytotoxics*

TetraLogic Pharmaceuticals Corporation, or TetraLogic, has conducted preclinical studies to evaluate the potential development of the chemotherapeutic drug birinapant as a hepatitis B therapeutic to stimulate apoptosis, or programmed cell death, in HBV-infected liver cells. Using a mouse model of HBV infection, TetraLogic reported that birinapant was observed to have activity in the clearance of liver cells infected with HBV. The clearance was additive when given in combination with entecavir. Birinapant caused a decline in HBsAg, whereas entecavir alone did not, implying that birinapant exerts its effect on apoptosis via a different mechanism of action.

### *siRNA*

Several therapeutics based on siRNA are in late preclinical stages or early clinical stages of development at companies such as Tekmira, Arrowhead and Alnylam. The most advanced of these therapies is Arrowhead's drug candidate, ARC-520, which consists of two siRNAs targeting HBV mRNAs. Using transient and transgenic mouse models, it was observed that a single injection of ARC-520 resulted in a 3–4 log reduction in HBV-DNA and viral antigens. In addition, 95% reduction in HBV-DNA levels and approximately 90% reduction in HBsAg levels were observed after two doses of ARC-520 in a chimpanzee chronically infected with HBV.

We believe these results highlight the potential of RNAi to have a therapeutic effect on chronic HBV infection. However, like NUCs and DAAs, siRNA-based therapeutics for HBV rely on ongoing treatment to be effective and they are subject to the other limitations of siRNA described above. Some of these limitations may have contributed to the modest efficacy of ARC-520 in their Phase I/IIa clinical trial announced by Arrowhead in 2014.

### ***Our ddRNAi-Based Hepatitis B Therapeutic—Hepbarna***

We are developing Hepbarna to address many of the limitations of therapeutics for hepatitis B currently on the market and those in development. Hepbarna is expected to be a single administration ddRNAi-based monotherapy that is delivered using an AAV vector that targets the liver and expresses three shRNAs that target highly conserved regions on the HBV genome to inhibit both viral replication and viral protein, including s-antigen, production on a long-term basis.

As both HBV and HCV replicate in the liver, we have designed Hepbarna to mimic TT-034. The same AAV vector is used in both therapeutic candidates, designed to achieve the same biodistribution and liver transduction properties. The most significant change is the replacement of the three anti-HCV shRNAs of TT-034 with three anti-HBV shRNAs in Hepbarna.

We believe the similarities between TT-034 and Hepbarna may enable, for Hepbarna's clinical development, quicker and more focused IND-enabling studies, a relatively straightforward design and regulatory approval pathway for initial clinical trials, and potentially a higher starting clinical dose based on the outcome of the TT-034 Phase I/IIa trial.

### *Hepbarna—Design and Mechanism of Action*

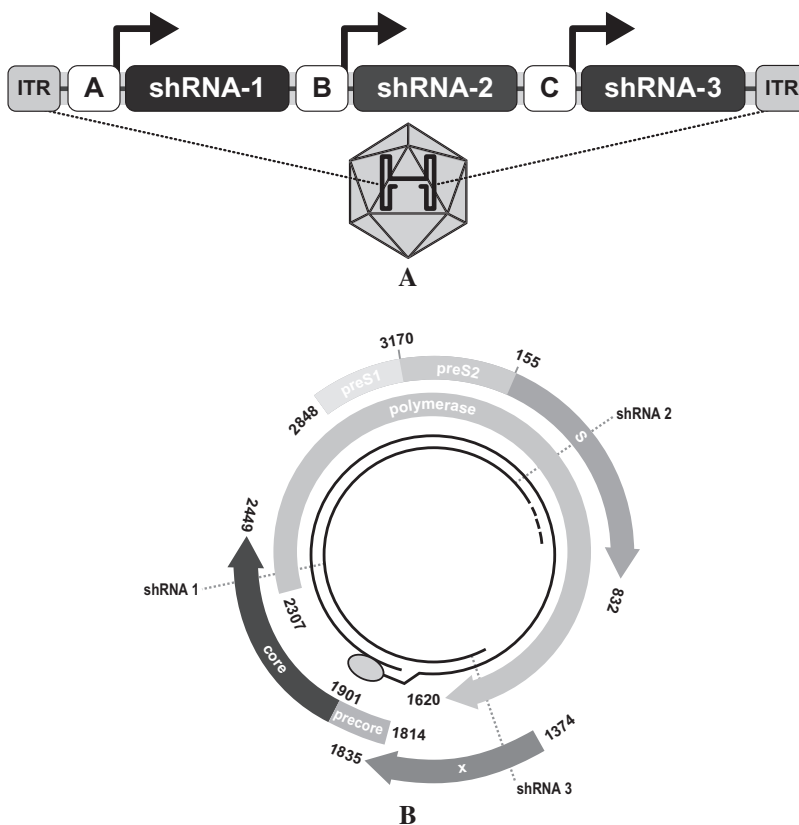
The design of the Hepbarna DNA construct takes advantage of the structure of the HBV genome. The hepatitis B virus is a small DNA virus with four overlapping open reading frames, meaning several genes are produced from the same DNA sequence by shifting the starting point of the translation process (*Figure 9*). These four genes are known as the core, surface, X and polymerase genes. The core gene encodes the core nucleocapsid protein, which is important in viral packaging and thought to help stabilize cccDNA, and hepatitis B e-antigen. The surface gene encodes proteins, including s-antigen. The X gene encodes the X protein, which has properties that may be important in liver carcinogenesis. The polymerase gene encodes a large protein with functions critical for viral packaging and replication. Although HBV is a DNA virus, it replicates through an RNA

intermediate. Hepbarna targets the viral mRNA at three overlapping regions of the genome (*Figure 9*), simultaneously silencing the surface, X, core and polymerase genes. As a result, we believe that the long-term suppression of HBV viral replication, through silencing of the polymerase gene and targeting the HBV RNA used for replication, the inhibition of HBV viral proteins production, including the s-antigen production, through silencing of the surface gene, and the inhibition of the cccDNA, through silencing of the core protein gene, could lead to eradication of HBV infection in patients by a single administration of Hepbarna.

***In vitro Development Highlights***

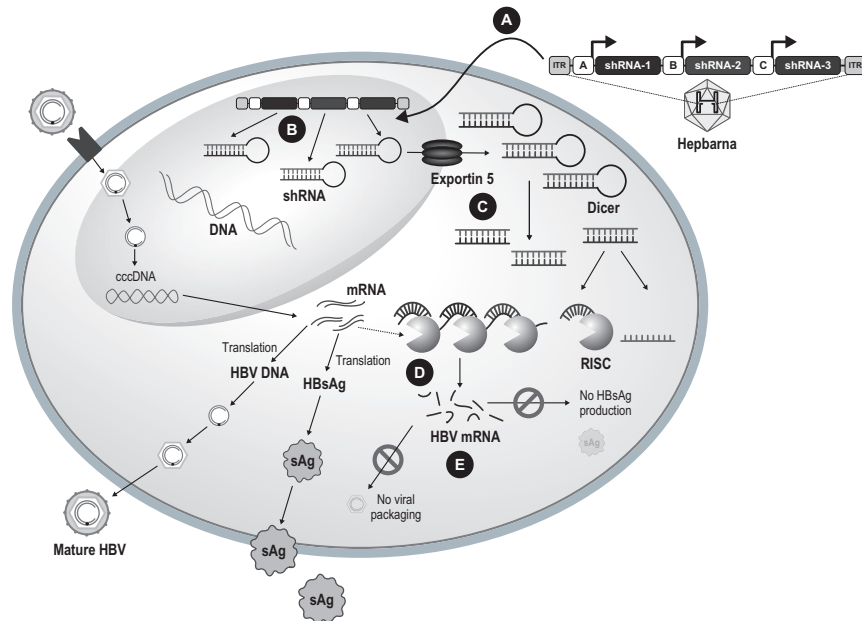
Our bioinformatics analysis of the major HBV genotypes, A through H, has identified several well-conserved regions of the genome for targeting with ddRNAi therapeutics. We have designed numerous shRNAs to target these regions, and we have identified lead candidates based on several factors, including activity, hyperfunctionality, meaning the highest activity at lowest levels, and the ability of the shRNA strand to be incorporated into the cell's natural RNA processing mechanism. The final clinical construct we have chosen is illustrated in *Figure 9*.

**Figure 9. The design for Hepbarna**



The design for Hepbarna is based on the design of TT-034, utilizing an AAV capsid and a triple construct targeting three separate conserved regions on the HBV mRNA (A); The shRNAs target regions on the overlapping reading frames of the HBV genome (B), allowing simultaneous targeting of the mRNAs that express viral proteins including DNA polymerase, s-antigen and core proteins.

**Figure 10. The mechanism of action of Hepbarna**



The DNA construct is delivered to the nucleus of hepatocytes via an AAV vector (A). Upon reaching the nucleus the construct expresses three shRNAs (B) that are processed by the cell's endogenous machinery to produce siRNAs (C) that cleave the HBV mRNA (D) and prevent the virus from replicating and producing HBsAg (E).

### ***Ongoing Development Plan for Hepbarna***

Our development plan for Hepbarna is focused on demonstrating clinical proof of concept in a Phase I/IIa clinical trial. We expect to complete *in vivo* proof-of-concept studies in the second quarter of 2016, initiating an IND application in the first quarter of 2017 and commencing a Phase I/IIa clinical trial during the second quarter of 2017. Our planned activities include:

- *In vitro* testing of Hepbarna in an HBV human hepatocyte cell culture model to assess effects on HBV and mRNA levels, suppression of viral protein production and cccDNA elimination.
- *In vivo* testing of Hepbarna in a HBV mouse model to assess parameters such as effects on HBV mRNA levels, suppression of viral protein production and cccDNA elimination.
- Manufacturing clinical grade Hepbarna for IND-enabling studies and for future clinical trials.

### **TT-211 and TT-231 for the Treatment of Age-Related Macular Degeneration**

#### ***Overview***

We are developing two ddRNAi-based therapies, one for the treatment of wet AMD, which is designated TT-211, and the other potentially for both wet and dry AMD, which is designated TT-231. The delivery vector for both TT-211 and TT-231 is being developed in collaboration with 4DMT. The aim of this program is to develop a therapeutic that provides long-term treatment of AMD from a single intravitreal injection. We believe this could replace the need for regular injections of therapeutics into the eye, which is the current standard of care.

AMD is the deterioration of the eye's macula. The macula is a small area in the retina that is responsible for central vision. AMD is the leading cause of blindness and visual impairment in older adults, often involving blood vessel overgrowth and damage to the retina resulting in the loss of vision in the central visual field. The

vascular endothelial growth factor, or VEGF-A, is responsible for stimulating the new blood vessel growth. The disease occurs in two forms, wet and dry. Dry AMD is the most common type of macular degeneration and affects 85% to 90% of the people with AMD. Dry AMD often develops into wet AMD.

In the dry form, there is a breakdown of retinal pigment epithelial cells in the macula. These cells support the light-sensitive photoreceptor cells that are critical for vision. Generally, the damage caused by the dry form is not as severe or rapid as that of the wet form. However, over time, it can cause profound vision loss. There are currently no approved treatments for dry AMD.

Wet AMD is the more advanced type of AMD. In wet AMD, which is also called exudative, or neovascular, AMD, the Bruch's membrane underlying the retina thickens, then breaks. The oxygen supply to the macula is disrupted and, as a result, new abnormal blood vessels grow through the subretinal membrane towards the macula, often raising the retina. The blood vessels are fragile, and often leak fluid that damages the macula. VEGF-A is responsible for stimulating the new blood vessel growth in wet AMD. Although it affects only 10% to 15% of those who have AMD, wet AMD accounts for 90% of the severe vision loss caused by macular degeneration.

According to a study published in *JAMA Ophthalmology*, AMD is the leading cause of irreversible vision loss in the United States, affecting an estimated 1.75 million people. It is estimated that 196 million people will be affected by AMD worldwide by 2020 according to a study published in *Lancet Global Health*.

There are a number of treatments currently available for wet AMD. According to GlobalData, the annual wet AMD treatment market across the United States, the United Kingdom, Germany, France, Spain, Italy and Japan will almost double from US\$5.1 billion in 2013 to US\$10.1 billion by 2023.

### ***Current AMD Treatments***

According to GlobalData, the global AMD treatment market is dominated by anti-VEGF drugs, including Lucentis, Avastin and Eylea, which together accounted for 98% of sales for AMD in 2013.

- Lucentis (ranibizumab) is an antibody fragment, or macromolecule, that directly inhibits VEGF-A by binding to it and thus preventing its binding to the corresponding receptor in the retina. The main challenge for Lucentis is that it requires frequent administration, typically monthly or bimonthly, via intravitreal injections.
- Avastin (bevacizumab) is a monoclonal antibody that also binds to VEGF-A. Although approved only for use in colon cancer, it is used off label for AMD. It is also injected intravitreally and requires ongoing regular injections to maintain its effect.
- Eylea (aflibercept) is a recombinant fusion protein consisting of portions of human VEGF receptors 1 and 2 extracellular domains fused to the Fc portion of human IgG1. It is recommended to be injected intravitreally every four weeks for the first three months and every eight weeks thereafter.
- Macugen (pegaptanib) is an RNA aptamer that is directed against VEGF-A. It is recommended to be injected intravitreally every six weeks.

All four treatments have similar risks and potential for adverse events, due primarily to their use of frequent intravitreal injection. Risks of intravitreal injections include increase in intra-ocular pressure, retinal detachment and endophthalmitis, or inflammation of the internal chambers of the eye. Patients and doctors dislike ocular injections and tend to prefer treatments that require these injections less frequently. The use of VEGF inhibitors can also cause blood clots.

A number of companies are developing gene therapy-based treatments for AMD. In general, these approaches involve the delivery of genes expressing proteins that are designed to inhibit new blood vessel formation, which is one of the hallmarks of the disease. The genes that are being developed include genes that express VEGF inhibitors in addition to other factors that activate new blood vessel formation. In contrast, our approach is designed to directly

silence the gene responsible for producing VEGF-A. We believe this could be more effective than other gene therapy approaches as our approach is to design ddRNAi-based therapeutics to prevent the production of VEGF-A rather than to deliver a new gene that expresses a new protein to inhibit VEGF-A after it has been produced. Furthermore, we believe that most of the other gene therapy approaches are delivered using subretinal injections. This route of administration presents challenges, including the requirement for hospitalization as a result of general anesthesia and the length of time required to complete the complicated surgical procedure.

### ***Our ddRNAi-Based AMD Therapeutics—TT-211 and TT-231***

There are several challenges in the development of AMD therapeutic market and we believe that our ddRNAi technology has the potential to address and overcome a number of these challenges, including:

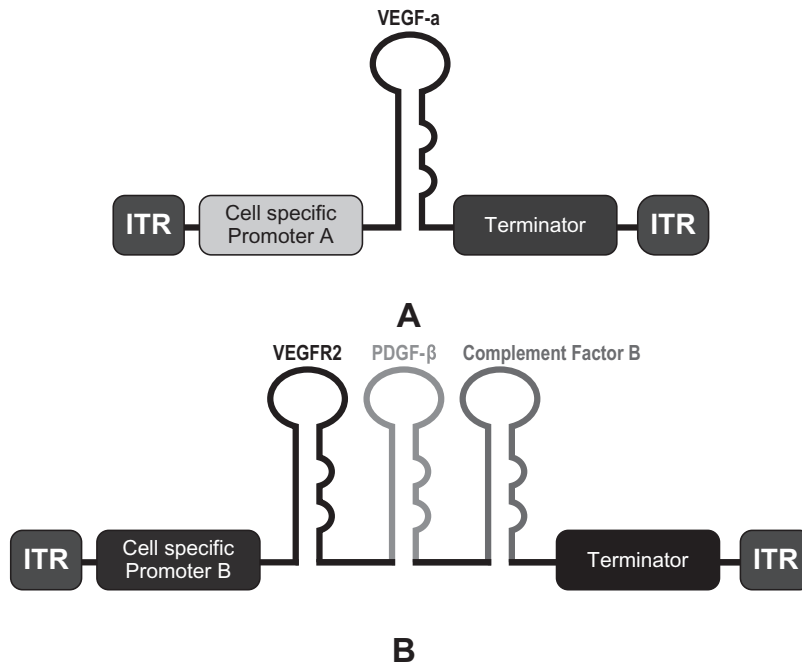
- The relatively short half-life of current standard-of-care therapies results in the need for regular administration by intravitreal injection every 4 to 8 weeks. We believe our ddRNAi-based therapies have the potential for sustained inhibition of VEGF-A, possibly for months or years, from a single intravitreal injection.
- AMD therapeutic programs under development at a number of other gene therapy companies focus on administering the product to target cells by subretinal injection. We are co-developing with 4DMT AAV vectors to target the subretinal cells following intravitreal injection, which we believe is a more commercially viable and less invasive route of administration and is the route used in most current anti-VEGF therapies.
- There are no approved treatments for dry AMD. We have designed and tested a ddRNAi construct that we believe has potential to address this unmet market need.

### ***TT-211 and TT-231- Design and Mechanism of Action***

We are developing two ddRNAi-based product candidates, one for wet AMD, called TT-211, and one for both wet and dry AMD, called TT-231, that are designed to address many of the limitations for therapeutics for AMD currently on the market or under development.

- TT-211 is a ddRNAi construct expressing a single shRNA targeting the VEGF-A gene (*Figure 11A*). VEGF-A is responsible for stimulating the new blood vessel growth in wet AMD.
- TT-231 is our second generation product candidate designed to express three shRNAs, which target three different genes, VEGF receptor 2, PDGF-beta and human complement factor B, which all play a role in the progression of AMD (*Figure 11B*). VEGFR2 is the receptor known to bind VEGF-A, so silencing that receptor should prevent it from functioning to stimulate new blood vessel growth. PDGF-beta has a known role in recruiting cells that stabilize newly formed blood vessels for long term-persistence. Human complement factor B is a known component of ocular drusen.

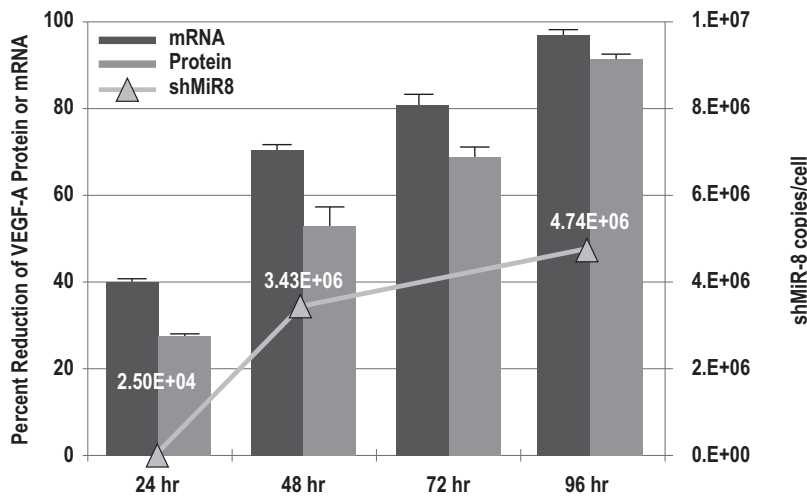
Figure 11. Our AMD ddRNAi constructs



TT-211 is a single construct targeting VEGF-A for wet AMD (A); and TT-231 is a ddRNAi construct targeting three genes shown to have a role in both wet and dry AMD (B).

We have observed in *in vitro* studies that both TT-211 (Figure 12) and TT-231 (Figure 13) are effective at silencing the target genes.

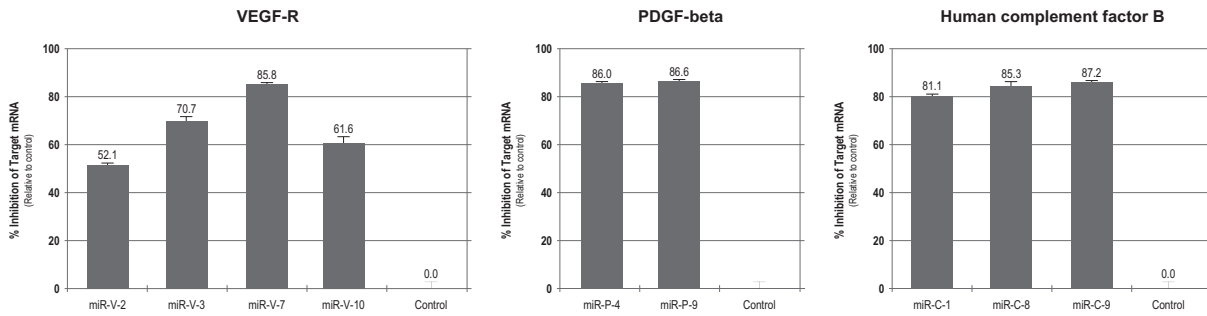
Figure 12. Effects of TT-211 on VEGF-A.



A retinal pigment epithelial cell line cultured *in vitro* was treated with the TT-211 expression construct and monitored for up to 96 hours for inhibition of VEGF-A protein (light gray bars) and mRNA (dark grey bars) expression as well as expression of the shRNA produced (triangles). The production of anti-VEGF-A shRNAs inside of the cells correlated with significant silencing of VEGF-A mRNA and protein levels. By 96 hours, greater than 90% inhibition was observed.



**Figure 13. Effects of TT-231.**

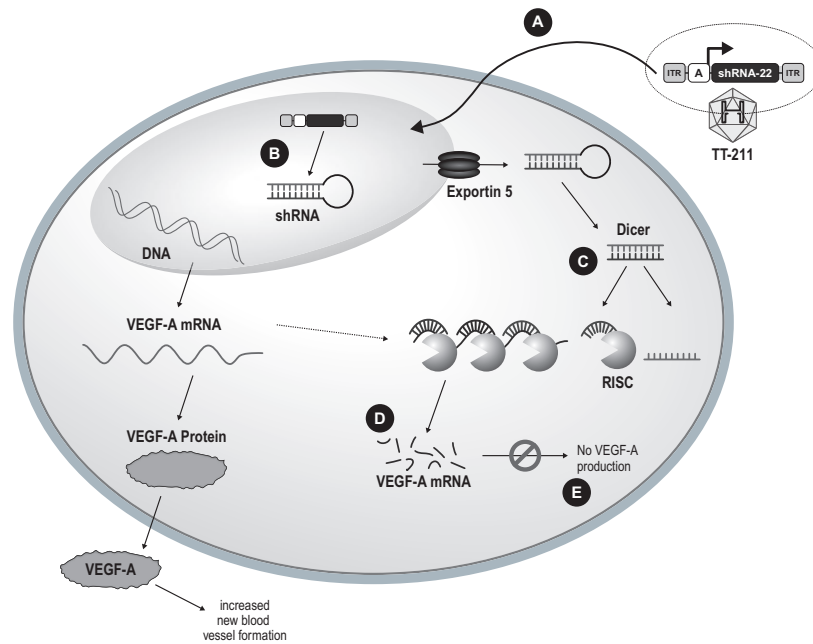


**In *in vitro* studies in retinal pigment epithelial cells, TT-231 inhibited target mRNA levels of VEGF-receptor, PDGF-beta and human complement factor B.**

#### ***Ongoing Development Plan for AMD – Development of Novel Delivery Vector***

We have engaged 4DMT to develop a vector that will deliver our ddrRNAi constructs to the retinal cells of the eye from an intravitreal injection. 4DMT has developed novel AAV vectors with desirable physical properties, such as enhanced tissue attractions, or tropisms, and reduced immunogenicity using a technique called directed evolution. This involves sequential passaging of a starting AAV library *in vivo* to isolate those variants that have the highest affinity for the target tissue. The sequential passaging for our AMD program is being conducted in non-human primates to enable identification of vectors expected to be suitable for the complex human eye structure. Preliminary results have evidenced the presence of AAV particles in the retina from intravitreal administration of the starting AAV library. We expect that 4DMT will produce a vector candidate in the fourth quarter of 2015 for use in our *in vivo* studies of TT-211 in a primate model of wet AMD. Upon production of the vector, we will initiate *in vivo* proof-of-concept studies in which the 4DMT vector will be used to deliver the TT-211 DNA construct that expresses an shRNA designed to silence VEGF-A intravitreally in a non-human primate model of AMD. We believe that the construct will silence the VEGF-A gene in the retinal cells by the mechanism shown in Figure 14.

**Figure 14. The expected mechanism of action of TT-211**



Following an intravitreal injection, the DNA construct is delivered to the nucleus of retinal cells via an AAV vector (A). Upon reaching the nucleus, the construct expresses three shRNAs (B) that are processed by the cell's endogenous machinery to produce siRNAs (C) that cleave the VEGF-A mRNA (D) and prevent the VEGF-A protein from being expressed (E) thus preventing it from stimulating the growth of new blood vessels.

We expect to complete *in vivo* proof-of-concept studies in the second quarter of 2016. We anticipate filing an IND application in the second quarter of 2017 and initiating a Phase I/IIa clinical trial in the third quarter of 2017.

### **Tribetarna for the Treatment of Drug-Resistant Non-Small Cell Lung Cancer**

We are developing Tribetarna, our ddRNAi-based therapy, for the treatment of drug-resistant non-small cell lung cancer. Tribetarna targets the silencing of beta-III tubulin, or TUBB3, a gene shown to have strong correlation with resistance to chemotherapy. We have conducted preclinical proof-of-concept studies in collaboration with the University of New South Wales, and are now in the process of conducting IND-enabling studies with a target IND application in the third quarter of 2016. In addition, we are developing a related diagnostic in order to identify those patients with NSCLC tumors that express TUBB3.

Lung cancer, including NSCLC and small cell lung carcinoma, or SCLC, is the most common form of human cancer, and about 80% of diagnosed lung cancer cases are categorized as NSCLC. According to a study published in the *Annals of Oncology*, lung cancer is the leading cause of cancer related deaths worldwide, accounting for 1.3 million deaths each year. Non-small cell lung cancers are assigned a stage from I to IV in order of severity. In stage I, the cancer is confined to the lung. In stages II and III, the cancer is confined to the lung and the lymph nodes. Stage IV cancer has spread outside of the lung and lymph nodes to other parts of the body. The prognosis of patients with NSCLC is generally poor, with patients often presenting with advanced stage disease, and less than 15% of patients diagnosed with NSCLC survive more than five years after diagnosis. Contributors to this prognosis are the resistance of NSCLC to chemotherapy in some cases and the side effects of chemotherapeutic drugs that affect patients' quality of life.

According to GBI Research, a market research firm, the NSCLC market in the leading eight developed nations was US\$5.1 billion in 2013 and is expected to grow to US\$7.9 billion by 2020.

### Current NSCLC Treatments

Current treatments for NSCLC are surgery, radiotherapy and chemotherapy, either individually or in combination. Surgery and radiotherapy have been effective in only a small percentage of patients. Chemotherapy is used for lung cancer which is later than Stage I, and is principally based on the DNA-damaging agent cisplatin in combination with one or more tubulin-binding agents, such as paclitaxel, docetaxel, vinblastine, vinorelbine or gemcitabine. In addition, etoposide, another DNA-damaging agent, or pemetrexed, a DNA and RNA synthesis inhibitor, are sometimes used.

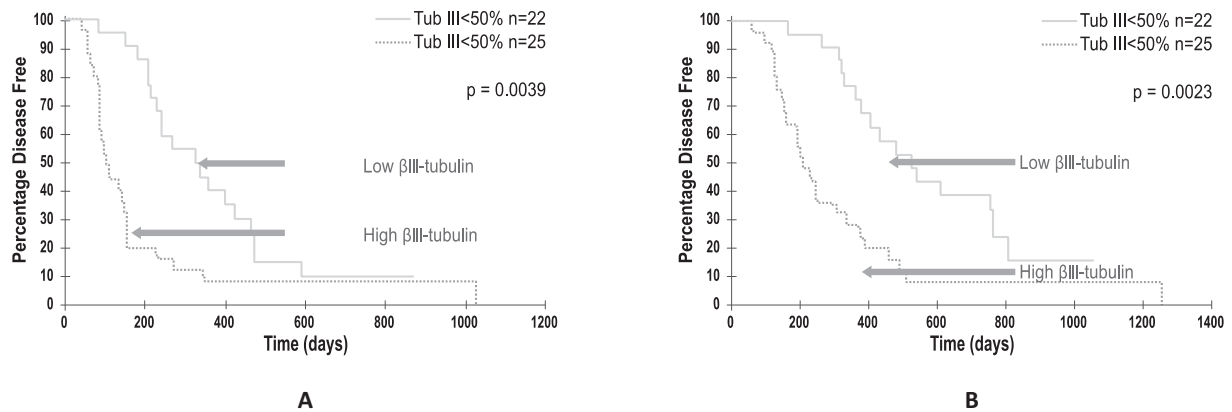
For some patients, the cancer develops resistance to chemotherapy. This limits the duration of the effectiveness of the chemotherapy approach. Resistance to therapy remains a challenge to be addressed in the NSCLC market and affects all current chemotherapeutic drugs for NSCLC.

### Our ddRNAi-Based NSCLC Therapeutic—Tribetarna

We are developing Tribetarna, our ddRNAi therapeutic, to target drug-resistant NSCLC and re-sensitize the tumors to chemotherapy by silencing the TUBB3 gene. TUBB3 expresses the protein beta-III tubulin and has been observed to be correlated with poor prognosis (*Figure 15*), tumor aggression and resistance to multiple chemotherapy agents, including DNA-damaging agents and tubulin-binding agents. It has been proposed that beta III-tubulin works to produce these effects through binding to the cell's DNA and altering the expression of key proteins involved in regulating tumorigenesis and metastasis.

Up to 70% of NSCLC patients express TUBB3. Targeting beta-III tubulin specifically, and not any of the other beta tubulin isotypes, is very challenging using current therapeutics due to the highly conserved structure of the tubulin gene family. The novelty in our ddRNAi-based approach takes advantage of the fact that the various tubulin isotypes are encoded by different genes and our ability to specifically target TUBB3. By silencing TUBB3, we believe Tribetarna may effectively re-sensitize tumors to the chemotherapy. We are developing a related diagnostic designed to identify NSCLC patients with tumors that are expressing TUBB3 for use in our planned clinical trial. We plan to discuss with the FDA and comparable foreign regulatory authorities the regulatory requirements applicable to using the diagnostic in our clinical trials.

**Figure 15. Association of beta-III tubulin and resistance to chemotherapy**



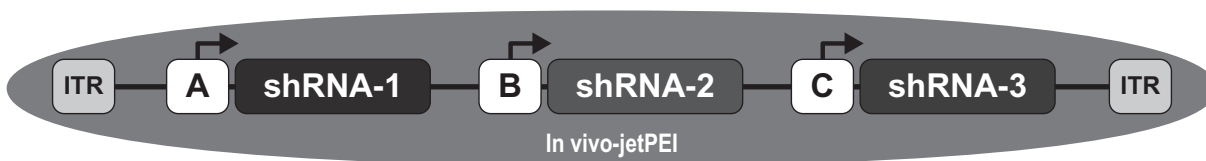
Progression free survival curves (A) and overall survival curves (B) for 47 paclitaxel-treated patients with advanced NSCLC according to the level of beta-III tubulin expression in tumors.

### Preclinical Highlights

We undertook preclinical proof-of-concept studies for Tribetarna in collaboration with researchers at UNSW who were one of the first groups to demonstrate a link between TUBB3 expression and chemoresistance in NSCLC cells. This research also established that silencing the TUBB3 gene using RNAi can restore

chemosensitivity to these cells. Tribetarna is our TUBB3 silencing construct, which simultaneously expresses three shRNAs targeting different regions of TUBB3 mRNA. The construct is delivered by a non-viral gene therapy vector, *in vivo*-jetPEI, which is a modified, low toxicity form of polyethylenimine, a cationic chemical that binds DNA and when injected intravenously has been shown to selectively target lung tissue.

**Figure 16. The structure of Tribetarna**

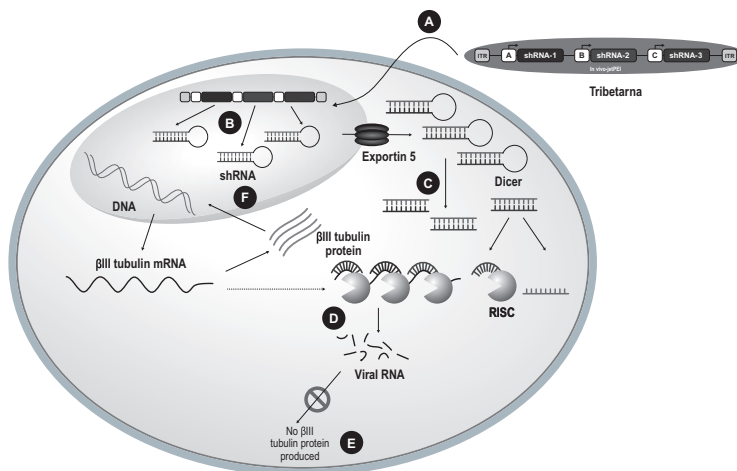


A dRNAi construct targeting three separate regions of the TUBB3 gene in *in vivo*-jetPEI, a non-viral gene therapy vector.

*Tribetarna—Design and Mechanism of Action*

Tribetarna is designed to target three distinct regions of the TUBB3 mRNA, by generating three separate shRNAs from a single DNA construct (Figure 17). We have observed over 95% reduction of the beta III tubulin in human NSCLC cells *in vitro* following administration with Tribetarna. The mechanism of action of Tribetarna is shown in Figure 17.

**Figure 17. The mechanism of action of Tribetarna**

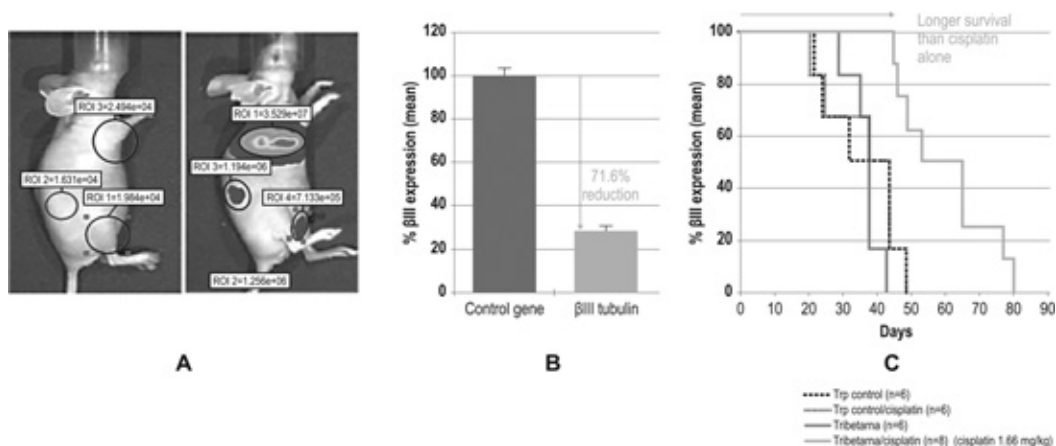


The DNA construct is delivered to the NSCLC cells via *in vivo*-jetPEI (A). Upon reaching the nucleus, the construct expresses three shRNAs (B) that are processed by the cell's endogenous machinery to produce siRNAs (C) that cleave the TUBB3 mRNA (D) and prevent the expression of beta III tubulin protein (E). Thus the protein's effects on modulating the cell's DNA to regulate cancer-associated processes (F) are eliminated.

Our collaborators at UNSW have developed a mouse model for human NSCLC. The efficacy of Tribetarna was tested in this mouse model and the following outcomes were observed:

- *in vivo*-jetPEI delivered DNA constructs with high efficiency to NSCLC tumors (Figure 18A).
- Injection of Tribetarna resulted in over 70% reduction of TUBB3 in those tumors (Figure 18B).
- The combination of Tribetarna and cisplatin administration resulted in a doubling of survival as compared with a course of cisplatin alone (Figure 18C).
- No significant toxicity was detected.

**Figure 18. JetPEI-DNA construct delivery, Tribetarna production and cisplatin treatment**



*In vivo*-jetPEI-DNA constructs localize to orthotopic NSCLC lung tumors from an intravenous injection (A); Tribetarna produces >70% knock-down in orthotopic NSCLC tumors *in vivo* (B); Animals treated with Tribetarna in combination with cisplatin were observed to survive twice as long as controls (C).

### **Ongoing Development Plan for Tribetarna**

Our development plan for Tribetarna is focused on establishing clinical proof of concept. To achieve that, within the next 12 months, we plan to conduct IND-enabling *in vivo* studies, targeting an IND application in the third quarter of 2016. These studies are planned to include toxicity and biodistribution of Tribetarna in the NSCLC mouse model, the optimal dose and timing of administration of both Tribetarna and cisplatin, and development and validation of a related diagnostic for TUBB3 expression to identify patients who may optimally benefit from this treatment. We are building a tissue and serum bank, which we intend to use, together with currently available commercial antibodies, to develop in-house either a serum-based or tissue-based diagnostic assay to facilitate the development of the related diagnostic.

TUBB3 is also expressed in a variety of other tumors, including pancreatic, ovarian, breast, renal and gastric tumors. In the future, we intend to explore whether a modified version of Tribetarna would be effective when applied to these cancer types.

### **Pabparna for Treatment of Oculopharyngeal Muscular Dystrophy**

We are developing Pabparna for the treatment of OPMD, an autosomal-dominant inherited, slow-progressing, late-onset degenerative muscle disorder that usually starts in patients during their 40s or 50s. The disease is manifested by progressive swallowing difficulties, or dysphagia, and eyelid drooping, or ptosis, due to specific effects on the pharyngeal and cricopharyngeal muscle, which is located at the top of the esophagus. The disease is caused by a specific mutation in the poly(A)-binding protein nuclear 1, or PABPN1, gene. The main pathological characteristic of OPMD is the presence of dense intranuclear inclusions of mutated PABPN1 protein.

Pabparna utilizes a “silence and replace” approach designed to silence the mutant PABPN1 gene with a ddRNAi construct and replace the mutant gene with the normal PABPN1 gene, delivered with an AAV vector. Results from *in vivo* studies in an animal model of OPMD support proof of concept of this approach in Pabparna’s individual components. In conjunction with collaborators, we are working to optimize the *in vivo* delivery of Pabparna and, assuming successful results, we plan to develop Pabparna through IND-enabling studies.

OPMD is a rare disease and has been reported in at least 33 countries. Patients suffering with OPMD are well identified and are aggregated in particular regions, which we believe should simplify clinical development

and commercialization of Pabparna, if it is approved. The largest OPMD cluster is in the French-Canadian population, with estimated prevalence of one in every one thousand people, and its highest prevalence is among Bukhara Jews living in Israel, where it affects one in six hundred people. In Europe, the estimated prevalence is one in one hundred thousand people. The relatively low abundance of patients afflicted by this disease allows this indication to be characterized as a rare disease, potentially supporting an orphan drug designation.

#### ***Current OPMD Treatments and Products in Development***

The therapies for OPMD currently available and under development consist of a symptomatic surgical intervention called cricopharyngeal myotomy, an intravenous trehalose injection, Cabaletta, and cell transplantation. Each of these therapies has treatment limitations.

Cricopharyngeal myotomy is used to address ptosis and improve swallowing in moderate-to-severely affected individuals. It is the only current treatment to improve swallowing in OPMD patients but does not correct the progressive degradation of the pharyngeal musculature, which often leads to death from swallowing difficulties and choking.

Bioblast Pharma Ltd., an Israeli biotechnology company, is developing Cabaletta. It is currently being tested in Phase II/III clinical trials in Israel and Canada. Cabaletta is a solution of trehalose administered intravenously and we believe that it will require ongoing re-administration to remain effective.

The Institut de Myologie in Paris is currently undertaking a Phase I/II trial of a cell transplantation therapy, grafting autologous myoblasts isolated from spared muscles into the pharyngeal muscle. This is a significantly invasive procedure requiring surgery in two different sites of a patient's body.

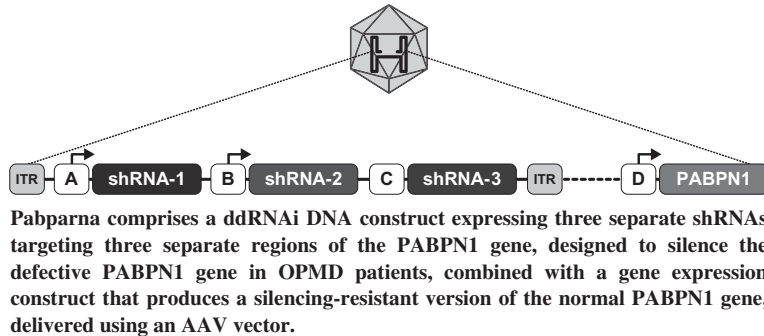
#### ***Our ddRNAi-Based OPMD Therapeutic—Pabparna***

We are developing Pabparna, a single administration ddRNAi-based gene therapy, to correct the gene defect which causes the disease and to address many of the limitations of therapeutic approaches currently available and those in development for OPMD. Pabparna is a monotherapy delivered using an AAV vector and is designed to silence the expression of the mutant PABPN1 gene in esophageal muscle cells of OPMD patients while simultaneously introducing a silencing-resistant normal form of the gene. We believe OPMD is well suited for this “silence and replace” approach since the genetic mutation is well characterized and the target tissue is relatively small. Once validated, we believe a similar approach could be applied to other inherited disorders.

*Pabparna—Design and Mechanism of Action*

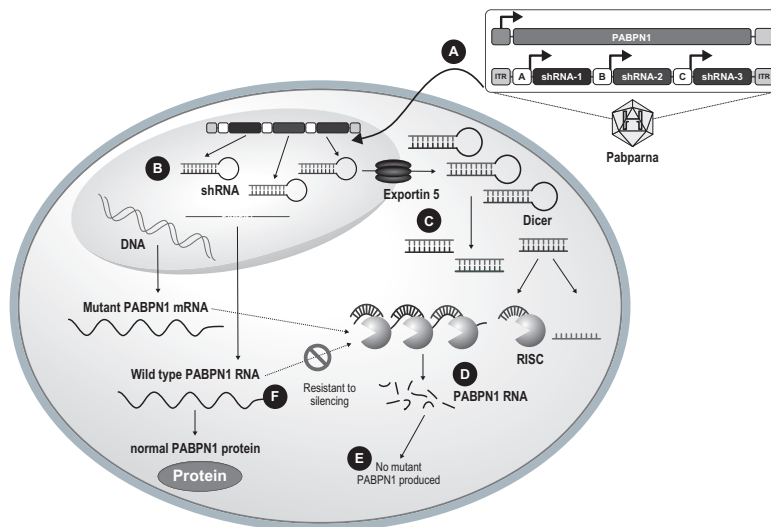
Pabparna is designed to target three distinct regions of the PABPN1 mRNA, by generating three separate shRNAs from a single DNA construct, and to express a silencing-resistant version of the normal PABPN1 gene (Figure 19).

**Figure 19. Pabparna AAV “silence and replace” combination vector**



In collaboration with researchers at the Royal Holloway University of London and the Institut de Myologie in Paris we have observed effective silencing of the PABPN1 gene *in vitro* by the ddRNAi construct. Furthermore, we have generated a gene expression construct that produces a silencing-resistant version of the normal PABPN1 gene. The mechanism of action of Pabparna is shown in Figure 20.

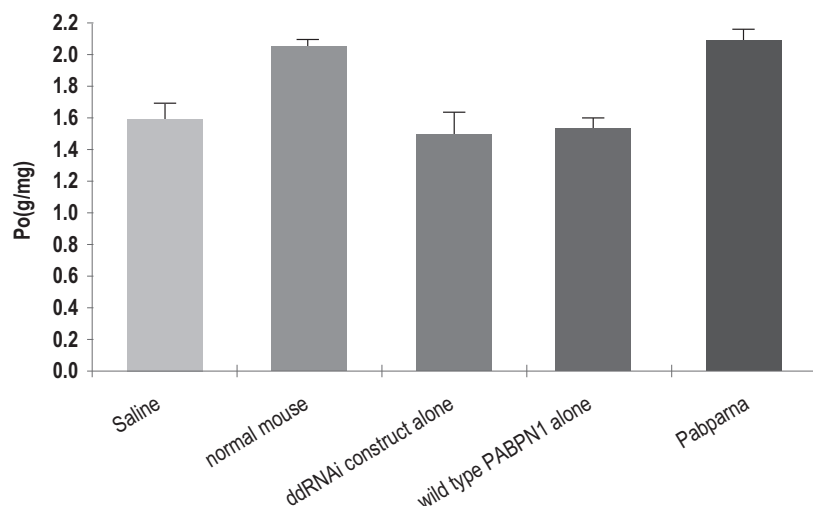
**Figure 20. The mechanism of action of Pabparna**



The DNA construct is delivered to the affected muscle cells via an AAV vector (A). Upon reaching the nucleus, the construct expresses three shRNAs (B) that are processed by the cell’s endogenous machinery to produce siRNAs (C) that cleave the mutant PABPN1 mRNA (D) and silence the expression of the mutant gene (E). In addition, the PABPN1 gene expression construct expresses a silencing-resistant version of the normal PABPN1 gene (F), which we believe may promote restoration of muscle function to the cell.

In *in vivo* studies using a transgenic mouse model of OPMD at the Royal Holloway University of London and the Institut de Myologie, we observed normalization of muscle strength following administration of the ddRNAi and gene expression constructs (*Figure 21*).

**Figure 21. Restoration of muscle function *in vivo* following gene silencing and replacement**



Restoration of muscle function *in vivo* following suppression of the mutant PABPN1 and replacement with the normal PABPN1 gene, with muscle function measured by specific tetanic force (Po). Neither the expression of a triple hairpin construct to down-regulate the mutant form of the PABPN1 protein, nor the expression of the normal protein, was sufficient by itself to restore specific force levels. The combination of the silencing of the mutant gene with the triple hairpin construct and replacement with the normal gene was observed to restore specific force capacity to healthy levels.

#### ***Ongoing Development Plans for Pabparna***

Our development plan for Pabparna is focused on investigating options for the optimal delivery of the combined constructs that comprise Pabparna. The options include combining the two constructs into a single AAV vector (*Figure 19*) and testing that combination vector *in vivo* in the OPMD mouse model, and generating and testing lentivirus-based combination vectors and testing their ability to produce gene modified autologous muscle stem cells *in vitro*.

Successful results from these studies may inform the design of later translational studies in dogs moving towards a clinical trial in OPMD patients initially via local administration of AAV vectors. We plan to have completed preclinical proof-of-concept studies using the chosen clinical construct in the third quarter of 2016.



## Our Out-Licensed Programs

We have licensed our ddRNAi technology to companies who are developing therapeutic programs in five disease areas. These licenses expand the areas and number of ddRNAi-based therapeutics being developed. Each of them provides a potential opportunity for further clinical validation of the technology and potential revenue opportunity. These licenses have been granted to small early-stage biotechnology companies with modest upfront and early development milestone payments and greater milestone payments due upon later-stage program success. Under these agreements, we have received aggregate payments of A\$521,140 and A\$276,824 for the fiscal years ended June 30, 2013 and June 30, 2014, respectively. We do not expect that any milestone payments we may receive in the future will be significant to our business.

The following table sets forth our out-licensed product candidates and their development status.

Focus	Indication	Product Candidate	Licensee	Discovery	Preclinical Proof of Concept	Clinical Trials	
						Phase I/IIa	Phase IIb/III
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				

### ***HIV/AIDS***

In March 2012, we granted a non-exclusive, royalty-bearing, worldwide license to a U.S.-based biotechnology company, Calimmune, Inc., or Calimmune. Under the agreement, Calimmune can develop, use and commercialize ddRNAi to silence up to three targets for the treatment or prevention of HIV/AIDS. Calimmune's approach was developed with core technology from the laboratory of Dr. David Baltimore, a Nobel Laureate in the area of HIV/AIDS, and involves silencing the gene that codes for a receptor protein known as CCR5. Calimmune's HIV/AIDS treatment is known as Cal-1.

The license provides for modest upfront and milestone payments and single-digit percentage royalty payments on net sales. In addition, we receive a percentage of any sub-licensing revenues received. Unless terminated at an earlier date, the license agreement continues until the expiration or termination of all patents subject to the license. We may terminate the license agreement in the event of certain breaches by Calimmune or if Calimmune commences an action or proceeding with respect to the patent rights that are the subject of the license. Calimmune may terminate the license agreement at will.

In 2014, Calimmune commenced a Phase I/IIa clinical trial of Cal-1 and the first cohort of four HIV-positive participants has been dosed. Calimmune has reported, following review of trial data by the DSMB for the trial, that none of the patients had experienced serious adverse events. The FDA has approved the next cohort dosing of three patients, who will also receive a preconditioning regimen designed to make the treatment more effective. We expect data from this study to be released by Calimmune in late 2015.

### ***Retinitis Pigmentosa***

In July 2012, we granted an exclusive, royalty-bearing, worldwide license to an Ireland-based biotechnology company, Genable Technologies Limited, or Genable, to use, develop or commercialize RNAi for treatment or prevention of retinitis pigmentosa. Genable's treatment involves suppression of the mutant and normal genes, and replacement with a normal RHO gene that has been modified to be resistant to ddRNAi gene silencing. Genable has reported that it established proof of concept in an *in vivo* model of the disease. Genable's treatment for retinitis pigmentosa, GT308, is named RhoNova.

The license provides for modest upfront and milestone payments and single-digit percentage royalty payments on net sales. In addition, we receive a percentage of any sub-licensing revenues received. Unless terminated at an earlier date, the license agreement continues until the expiration or termination of all patents subject to the license. We may terminate the license agreement in the event of certain breaches or if Genable commences an action or proceeding with respect to the patent rights that are the subject of the license. Genable may terminate the license agreement at will.

In October 2014, the European Medicines Agency, or EMA, granted RhoNova Advanced Therapy Medicinal Product classification. The classification enables Genable to procure centralized scientific advice and guidance from EMA regulators on RhoNova's ongoing development. In 2013, the FDA granted Genable orphan drug designation for RhoNova.

### ***Huntington's Disease***

In December 2012, we granted a non-exclusive, royalty-bearing, worldwide license to a Netherlands-based biotechnology company, uniQure biopharma B.V., or uniQure, to use, develop or commercialize RNAi for treatment of Huntington's disease. Our license grants to uniQure rights to develop, use and commercialize an AAV vector with a ddRNAi cassette targeting the gene associated with Huntington's disease, or the Htt gene, or an AAV-RNAi-based product for Huntington's disease directed to up to three gene targets specific to Huntington's disease.

The license provides for modest upfront and milestone payments and single-digit percentage royalty payments on net sales. In addition, we receive a percentage of any sub-licensing revenues received. Under the agreement, uniQure has an option to convert the license to an exclusive license depending upon achievement of certain preclinical milestones, and also to acquire additional licenses to our ddRNAi technology for other specific diseases. Unless terminated at an earlier date, the license agreement continues until the expiration of either all patents subject to the license or regulatory exclusivity, whichever is longer. We may terminate the license agreement in the event of certain breaches or if uniQure has not met a defined sales milestone or commences an action or proceeding with respect to the patent rights that are the subject of the license. uniQure may terminate the license agreement at will. In addition, certain rights and licenses granted to uniQure pursuant to the license agreement will automatically terminate in the event that our license of technology from Galapagos NV expires or is terminated.

In May 2013, uniQure announced that it, along with its partners in a pan-European consortium devoted to finding a gene therapy cure for Huntington's disease, were awarded a 2.5 million Euros grant for use in the development of a RNAi-based approach. uniQure has reported that it is using RNAi to non-specifically knock down all expression of the Htt gene and to specifically inhibit the mutant allele of the Htt gene. Evaluation of these two approaches is in progress.

### ***Cancer Immunotherapy***

In August 2013, we granted an exclusive, royalty-bearing, worldwide license to a U.S.-based biotechnology company, Regen Biopharma Inc., or Regen, to use ddRNAi for silencing expression of indoleamine 2,3-dioxygenase, or IDO, in dendritic cells. Regen is developing a cancer immunotherapy using the licensed technology. IDO is associated with immune-suppression and is overexpressed in some cancers. Regen has reported preclinical evidence that modification of these cells using ddRNAi targeting the silencing of IDO may significantly enhance their efficacy in cancer immunotherapy. Regen's first treatment, which is for breast cancer, is called dCellVax.

The license provides for modest upfront and milestone payments, payable in cash or stock of Regen's parent company at Regen's discretion, and single-digit percentage royalty payments on net sales. In addition, we receive a percentage of any sub-licensing revenues received. Unless terminated at an earlier date, the license agreement

continues until the expiration or termination of all patents subject to the license. We may terminate the license agreement in the event of certain breaches or if Regen has not met a defined sales milestone or commences an action or proceeding with respect to the patent rights. Regen may terminate the license agreement, in whole or in part, at will.

In November 2014, the FDA announced the issuance of an IND number for a proposed Phase I/II clinical trial assessing safety with signals of efficacy for dCellVax.

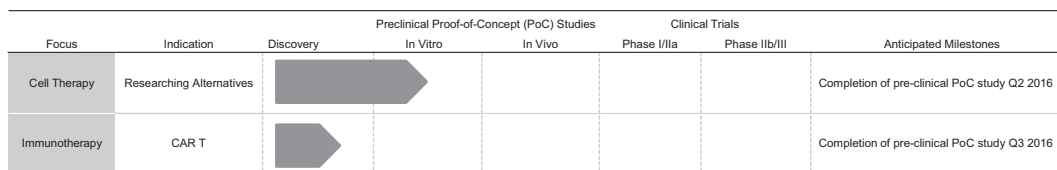
### ***Intractable Neuropathic Pain***

In November 2014, we granted an exclusive, royalty-bearing, worldwide license to a U.S.-based biotechnology company, Circuit Therapeutics, Inc., or Circuit Therapeutics, to use ddRNAi for the development of treatments for and the prevention of pain. Under the licensing agreement, Circuit Therapeutics has rights to develop, use and sell products that use RNAi to silence Nav1.7, a sodium ion channel that is exclusively expressed in certain sensory nerves and is critical for generation of pain.

The license provides for modest upfront and milestone payments and single-digit percentage royalty payments on net sales. In addition, we receive a percentage of any sub-licensing revenues received. Unless terminated at an earlier date, the license agreement continues until the expiration or termination of all patents subject to the license. We may terminate the license agreement in the event of certain breaches or if Circuit Therapeutics commences an action or proceeding with respect to the patent rights. We may also terminate the license agreement if Circuit Therapeutics has not met certain sales and development milestones. Circuit Therapeutics may terminate the license agreement at will.

### **New Areas for ddRNAi Application**

We believe the applicability of ddRNAi to disease treatment could be further expanded using a number of strategies that are in the early stages of development. These strategies include:



### ***Cell Therapies***

The use of cell therapy as a clinical tool to improve, repair or renew the function of damaged or diseased tissue has gained significant interest in the treatment of a variety of conditions, due to the unique properties of stem cell self-renewal and the ability to differentiate into a range of mature cell types. According to a 2014 report from MarketsandMarkets, a market research firm, the worldwide stem cell therapy market is expected to grow at a compound annual growth rate of 39.5% from 2015 to 2020, reaching \$330 million.

We believe ddRNAi can be used to produce modified stem cells that express shRNA for enhanced therapeutic benefit. Currently, this approach is being developed in two of our in-house programs, OPMD and drug-resistant NSCLC. In addition, one of our licensees, Calimmune, is using this strategy in their HIV/AIDS program.

- Calimmune’s HIV/AIDS program transfects a patient’s own human CD34+ hematopoietic progenitor cells *ex vivo* with a ddRNAi construct that silences the CCR5 (HIV co-receptor) gene. The modified CD34+ cells are then readministered to the patient, with the expectation that they will differentiate into mature immune cells that are resistant to being infected with HIV as they lack the expressed CCR5 protein.
- In our OPMD program, part of the collaboration with Royal Holloway University of London is to develop and test autologous muscle stem cells that express Pabparna, with the aim of transplanting them to

regenerate new esophageal muscle cells that have the mutant PABP1 gene suppressed and replaced by the normal PABPN1 gene.

- In our drug-resistant NSCLC program, we are testing the ability of proprietary stem cells and exosomes, which are lipid vesicles that bud off from the parent cell encapsulating siRNA and other cytoplasmic material, derived from the stem cells, to deliver the Tribetarna ddRNAi construct to lung tumors *in vivo*. This leverages the innate ability of stem cells to home to sites of wounding, including cancer. This could provide an alternative delivery modality for Tribetarna to target metastatic disease as well as primary tumors.

### ***Immunotherapies***

One approach to immunotherapy involves engineering patients' own immune cells to recognize and attack their tumors. This approach is called adoptive cell transfer, or ACT. ACT utilizes T cells. After isolation from a patient's blood, the T cells are genetically engineered to produce special receptors on their surface called chimeric antigen receptors, or CARs. CARs are proteins that enable T cells to recognize a specific protein, or antigen on tumor cells. These engineered CAR T cells are cultured and expanded in the laboratory and then infused into the patient. After the infusion, the technology relies on the T cells multiplying in the patient's body and, with guidance from their engineered receptor, recognize and kill cancer cells that harbor the antigen on their surfaces.

CAR T cell therapy can cause side effects, the most common being cytokine-release syndrome. The infused T cells release cytokines, chemical messengers that help the T cells function. With cytokine-release syndrome, there is a rapid and massive release of cytokines into the bloodstream, which can lead to dangerously high fevers and precipitous drops in blood pressure.

An important aim for next generation of CAR T therapies is to silence multiple genes known to be associated with cytokine release syndrome, including the T cell receptor, or TCR, and major histocompatibility complex, or MHC. We believe that ddRNAi technology could potentially be used to achieve this goal.

Most of the current CAR applications use lentivirus to deliver gene constructs expressing CARs. The packaging capacity of this vector allows the expression of several shRNA constructs along with the CAR in a single construct. Thus, the same cell population that is transduced to express the CAR can also be modified by the activity of shRNA expressed from the same vector.

In addition to silencing the TCR, we believe ddRNAi technology could potentially be used to enhance other properties of CAR T cells.

### ***Ocular diseases***

We believe a number of ocular diseases beyond AMD, such as diabetic retinopathy, could be targeted by ddRNAi therapeutics, assuming the AAV vector selection program with 4DMT is successful. This program aims to produce an AAV vector that can target a broad range of ocular cells from an intravitreal injection. We have exclusive access to modified AAV vectors 4DMT for all ocular indications using ddRNAi.

### **Intellectual Property**

We actively seek to protect the intellectual property and proprietary technology that we believe are important to our business, which includes seeking and maintaining patents claiming our ddRNAi technology, and other inventions relating to our products in development, or otherwise commercially and/or strategically important to the development of our business. We also rely on know-how and trade secrets that may be important to the development of our business and actively seek to protect the confidentiality of such know-how and trade secrets.

Our success will depend on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce our patents, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. For more information, please see “Risk Factors—Risks Related to Our Intellectual Property.”

As of April 2015, we own (8) or co-own (1) a total of nine patent families, of which one is currently in its international phase and the others have progressed to national prosecution. These families include several granted patents in the United States (8), Europe (1), Australia (3), Canada (1) and New Zealand (3). We have 19 pending national/regional applications in a total of 10 jurisdictions (excluding the member states of the European Patent Convention in which our European patents were validated). This intellectual property portfolio for our ddRNAi technology, improvements to the technology and product-specific patents can be commercialized collectively or in individual product candidate programs.

We also have a portfolio of in-licensed patents relating to the ddRNAi platform technology. The license from Commonwealth Scientific & Industrial Research Organization, or CSIRO, includes irrevocable, exclusive rights in the field of human therapeutics to CSIRO’s patents claiming ddRNAi. The license includes two patent families with granted patents in the United States (8), Europe (3), the United Kingdom (1), Australia (4) and Canada (1). The license also includes nine pending national/regional applications in a total of four jurisdictions.

The CSIRO patents subject to our license agreement include three patents in European patent office opposition proceedings and one patent application in USPTO interference proceedings.

The patent portfolios for the ddRNAi platform and our product candidate pipeline are summarized below. The expected expiration dates included in the summary below do not give effect to patent term extensions that may be available due to delays in the patent office or due to steps taken to obtain regulatory approvals.

### *ddRNAi Platform Technology*

The two patent families exclusively licensed from CSIRO include different aspects of the ddRNAi technology. The first of these patent families relates to DNA constructs and methods for using DNA to deliver RNA molecules, particularly shRNA, directed to the target gene. The granted U.S. patents in this family include claims to the structure and design of the DNA constructs, as well as human, animal and plant cells containing such DNA constructs and methods of using these constructs to reduce expression of a target gene. As of April 2015, this patent family included patents granted in the United States and granted (under opposition) in Europe. We expect any patents granted in this patent family to expire in March 2019.

The second patent family is an extension of the first patent family, and relates to chimeric DNA and methods for using DNA to deliver RNA molecules, particularly shRNA. The granted U.S. patent in this family claims DNA constructs and methods for reducing expression of a target gene in a plant as well as plant cells, subject matter that is not within our current field of use. As of April 2015, this patent family included one patent granted in the United States and one patent granted (under opposition) in Europe. We expect any patents granted in this patent family to expire in April 2019.

In December 2009, we entered into a commercial license arrangement with CSIRO for these two patent families relating to ddRNAi technology. This worldwide license in the field of human therapeutics is exclusive and irrevocable. In exchange for the license, we issued ordinary shares to CSIRO, and we are required to pay CSIRO approximately \$300,000 in the event of corporate transactions such as a merger, sale, change of control, capital reconstruction or insolvency event relating to Benitec. Under the license agreement, following notice to us and receipt of our comments, if any, CSIRO has control over prosecution of patent applications and litigation, if any.

### ***Technology Improvements***

We own two patent families that relate to improvements to ddRNAi technology. The first patent family relates to compositions of matter and methods for delivering shRNA molecules to animal cells for a variety of target genes. As of April 2015, this patent family included patents granted in the United Kingdom, Singapore and South Africa. We expect any patents granted in this patent family to expire in March 2021.

The second patent family relates to nucleic acid constructs and methods for using DNA to produce hairpin RNA molecules that can target multiple genes within one molecule. As of April 2015, this patent family included patents granted in Australia, New Zealand, Singapore and South Africa. We expect any patents granted in this patent family to expire in June 2024.

### ***Targeting the Hepatitis Virus***

We own two patents in the United States that relate to liver-specific promoters or enhancers. The first claims an expression cassette with a synthetic enhancer and a particular liver-specific promoter that may be used to express a variety of genes in liver. The second claims ddRNAi expression constructs that include a liver-specific promoter and one or more RNAi constructs that provide RNAi agents that target hepatitis virus genes. These granted U.S. patents provide options for promoter and construct design based on the target regions in the hepatitis gene of interest. The first of these two patents is expected to expire in February 2026, and the second is expected to expire in March 2027.

### ***TT-034—ddRNAi-based treatment for hepatitis C***

Our patent portfolio related to TT-034 includes two patent families relating primarily to the shRNA sequences of TT-034 and the expression cassette design of the therapeutic. The first patent family has claims for methods and genetic constructs that use the shRNA sequences of TT-034 in the treatment of hepatitis C. The patent family relates to a range of different shRNA sequences, and includes the three candidate shRNA sequences incorporated in TT-034, as well as using ddRNAi to deliver the shRNA. The design of the expression cassette in this patent family is for three shRNA sequences with independent promoters driving the expression of each shRNA. As of April 2015, this patent family included patents granted in the United States (3), Europe, Australia, Canada, China, Israel, Japan and Korea. We expect any patents granted in this patent family to expire in March 2025.

The second patent family also includes claims for methods and genetic constructs using the shRNA sequences of TT-034 in the treatment of hepatitis C. The design of the expression in this patent family is for a single promoter to drive the expression of multiple shRNA sequences. As of April 2015, this patent family included patents granted in the United States (3), Australia, China, New Zealand and Hong Kong. We expect any patents granted in this patent family to expire in February 2026.

### ***Hepbarna—our ddRNAi-based treatment for hepatitis B***

Our patent portfolio related to Hepbarna includes one patent family relating to single-stranded RNA and shRNA sequences to a range of target regions of the hepatitis B viral genome. This patent family was jointly filed with Biomics Biotech Co., Ltd., or Biomics, and Biomics subsequently assigned its ownership interests in the patent to us. As of April 2015, this patent family included pending applications in the United States, Europe, Australia, Brazil, Canada, China, India, Korea and Russia. We expect any patents granted in this patent family to have expired by October 2031.

This patent family is the outcome of a collaborative research agreement between us and Biomics Biotech Co., Ltd, which was commenced in August 2009. The ongoing arrangement provides for both parties to receive a share of any revenue generated from commercializing this patent family commensurate with our respective contributions to the intellectual property subject to the agreement, which contributions are expected to be equal.

A priority document has been filed to claim composition of matter and methods of using a range of RNA molecules in the treatment of hepatitis B. This new patent filing claims the shRNA sequences that are under development as the lead candidates for Hepbarna, and also include other target and RNA sequences to different regions of the HBV genome. This new patent application names Benitec as the sole applicant.

#### ***Our ddRNAi-based therapeutic candidates for AMD***

Our patent portfolio for AMD includes one patent family relating to the target genes for AMD. This patent family relates to the target gene sequences for our two ddRNAi-based therapeutic candidates for AMD. As of April 2015, this patent family was in the international phase, expecting national/regional patent applications to be filed in July 2015. We expect any patents to grant in this patent family to expire in January 2034.

#### ***Tribetarna—our ddRNAi-based treatment for lung cancer***

Our patent portfolio for lung cancer includes one patent family relating to methods of increasing the sensitivity of a tumor cell to DNA damaging agents (cisplatin) or tubulin-binding agents (paclitaxel) using nucleic acid constructs encoding a shRNA or siRNA directed to regions of the TUBB2A, TUBB2C, or TUBB3 tubulin genes and conjugated to polyethylenimine. This patent family is licensed exclusively from the University of New South Wales. As of April 2015, this patent family included patents granted in Australia, China, Hong Kong and Singapore. We expect any patents granted in this patent family to expire in March 2028.

In August 2013, we entered into a commercial license arrangement with NewSouth Innovations Pty Limited, or NSi, of University of New South Wales for this patent portfolio. The license provides for modest up-front and ongoing license fees, and also milestone and single digit percentage royalty payments on net sales. A percentage of sub-licensing revenue is also payable to NSi. We may terminate the license at will, and in the event of certain breaches by NSi. NSi may terminate the license in the event of certain breaches by us.

#### ***Know-How***

In addition to patent protection of ddRNAi technology and our product candidates, we also rely on proprietary know-how that is not patentable or that we elect not to patent, as valuable intellectual property for our business. This know-how is related to the areas of, among others, identifying nucleic acid targets for ddRNAi technology and designing ddRNAi constructs for targeting preferred genes. We have implemented a number of security measures to safeguard our know-how including limiting access to our research facilities, databases and networks. We also protect know-how by way of confidentiality agreements when engaging with external providers for progressing our pipeline of therapeutic candidates.

#### ***Laws and Regulations Regarding Patent Terms***

The term of individual patents depends upon the legal terms of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent term may be shortened if a patent is terminally disclaimed over another patent or as a result of delays in patent prosecution by the patentee. A patent's term may be lengthened by a patent term adjustment, which compensates a patentee for administrative delays by the USPTO in granting a patent. The patent term of a European patent is 20 years from its filing date, which, unlike in the United States, is not subject to patent term adjustments.

The term of a patent that covers an FDA-approved biologic may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the biologic is under clinical testing regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product

approval and only one patent applicable to an approved biologic may be extended. Similar provisions are available in Europe and other jurisdictions to extend the term of a patent that covers an approved biologic although the eligibility requirements for any duration of such extension vary. In the future, if and when our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products.

### **Trademarks**

Our trademarks include registrations for company branding and product names for our pipeline in development.

<u>Trade Mark (program)</u>	<u>Trade Mark Number</u>	<u>Filing date</u>	<u>Jurisdiction</u>	<u>Status</u>
<b>BENITEC BIOPHARMA®</b> . . . . .	1448046	13 Sep 2011	Australia	Registered
<b>BENITEC BIOPHARMA®</b> . . . . .	4636053	11 Feb 2014	United States	Registered
<b>SILENCING GENES FOR LIFE®</b> . . . . .	1448041	13 Sep 2011	Australia	Registered
<b>SILENCING GENES FOR LIFE™</b> . . . . .	NA (Appln: 86488147)	22 Dec 2014	United States	Pending
<b>Tribetarna® (Lung cancer)</b> . . . . .	1526479	19 Nov 2012	Australia	Registered
<b>Hepbarna® (Hepatitis B)</b> . . . . .	1526483	19 Nov 2012	Australia	Registered
<b>Nervarna® (Pain)</b> . . . . .	1526478	19 Nov 2012	Australia	Registered
<b>Pabparna™ (OPMD)</b> . . . . .	Not yet filed	N/A	N/A	Unregistered

### **Manufacturing**

The manufacture of the complex biological products required for gene therapy is complex and difficult. We do not currently own or operate manufacturing facilities for the production of preclinical, clinical or commercial quantities of any of our product candidates. We have contracted with Omnia Biologics, Inc., or Omnia, for the production of TT-034. We are also exploring long-term manufacturing alliances with a number of potential partners to investigate manufacturing processes in order to produce materials at reasonable scale and cost of goods to support future commercialization efforts. We do not have a long-term agreement with any third-party manufacturer, but we plan to establish such a relationship with an appropriate manufacturer to serve our long-term needs.

Manufacturing is subject to extensive regulations that impose various procedural and documentation requirements, which govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others. Our contract manufacturing organizations manufacture our product candidates under cGMP, conditions. cGMP is a regulatory standard for the production of pharmaceuticals that will be used in humans.

### **Sales and Marketing**

We have not yet established sales, marketing or product distribution operations because our product candidates are in preclinical or clinical development. If we receive marketing and commercialization approval for any of our product candidates, we intend to market the product through strategic alliances and distribution agreements with third parties. In certain cases we may market an approved product directly worldwide or in selected geographical segments. The ultimate implementation of our strategy for realizing the financial value of our product candidates is dependent on the results of clinical trials for our product candidates, the availability of funds and the ability to negotiate acceptable commercial terms with third parties.

### **Competition**

The biopharmaceutical industry is characterized by intense and dynamic competition to develop new technologies and proprietary therapies. Any product candidates that we successfully develop and commercialize will have to compete with existing therapies and new therapies that may become available in the future. While we believe that our proprietary technology estate and scientific expertise in gene silencing using ddRNAi provide us with competitive advantages, we face potential competition from many different sources, including larger and better-funded pharmaceutical, specialty pharmaceutical and biotechnology companies, as well as from academic



institutions and governmental agencies and public and private research institutions that may develop potentially competitive products or technologies. We are aware of several companies focused on developing gene therapy or gene silencing product candidates, including:

- Alnylam, Tekmira and Arrowhead—developing siRNA-based therapeutics for hepatitis B;
- Avalanche Biotechnologies, Inc., Applied Genetic Technologies Corporation and Oxford Biomedica—developing gene therapies for wet AMD

We are not aware of any companies developing a gene therapy or gene silencing approach for HCV, NSCLC, or OPMD. There are other therapies either being marketed or currently in development for all of these diseases, some of which already have significant market share.

Our product candidates, if approved, would also compete with treatments that have already been approved and accepted by the medical community, patients and third-party payors. For example, with respect to hepatitis C, our product candidate would compete with small molecule treatments such as Sovaldi and Harvoni, each of which was developed by Gilead Sciences, Inc., and Viekira Pak, a regimen consisting of four medications developed by Abbvie Inc.

Many of our competitors and potential competitors, alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and the commercialization of those treatments. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical study sites and subject registration for clinical studies, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

We anticipate that we will face intense and increasing competition as new products enter the market and advanced technologies become available. We expect any treatments that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price, the level of competition and the availability of reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, we expect that our therapeutic products, if approved, will be priced at a significant premium over competitive products and our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of competitive products including biosimilar or generic products.

## **Government Regulation**

As a pharmaceutical and biological product company that wishes to conduct clinical trials and ultimately obtain marketing approval in the United States, we are subject to extensive regulation by the FDA, and other federal, state, and local regulatory agencies. The Federal Food, Drug, and Cosmetic Act, or the FDC Act, the Public Health Service Act, or PHS Act, and their implementing regulations set forth, among other things, requirements for the research, testing, development, manufacture, quality control, safety, effectiveness, approval, labeling, storage, record keeping, reporting, distribution, import, export, advertising and promotion of our products. A failure to comply explicitly with any requirements during the product development, approval, or post-approval periods, may lead to administrative or judicial sanctions. These sanctions could include the imposition by the FDA or an IRB, of a suspension on clinical trials, refusal to approve pending marketing applications or supplements, withdrawal of approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution.

Although the discussion below focuses on regulation in the United States, we anticipate seeking approval for the testing and marketing of our products in other countries. Generally, our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Additionally, some significant aspects of regulation in the European Union are addressed in a centralized way through the EMA, but country-specific regulation remains essential in many respects.

Government regulation may delay or prevent testing or marketing of our products and impose costly procedures upon our activities. The testing and approval process, and the subsequent compliance with appropriate statutes and regulations, requires substantial time, effort, and financial resources, and we cannot be certain that the FDA or any other regulatory agency will grant approvals for our products or any future products on a timely basis, if at all. The FDA's or any other regulatory agency's policies may change and additional governmental regulations may be enacted that could prevent or delay regulatory approval of our products or any future products or approval of new indications or label changes. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative, judicial, or administrative action, either in the United States or abroad.

### ***Recent Developments in Regulation of Gene Therapy***

Although the FDA has not yet approved any human gene therapy product for sale, it has provided guidance for the development of gene therapy products. For example, the FDA has established the Office of Cellular, Tissue and Gene Therapies within CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews. In addition, the FDA has issued a growing body of clinical guidelines, chemical, manufacturing and control, or CMC, guidelines and other guidelines, all of which are intended to facilitate industry's development of gene therapy products.

In 2012, the EMA approved a gene therapy product called Glybera, which is the first gene therapy product approved by regulatory authorities in the United States or the European Union.

### ***Marketing Approval***

In the United States, for premarket approval purposes, the FDA regulates gene products as biologics under the FDC Act, the PHS Act and related regulations.

The steps required before a new biologic may be marketed in the United States generally include:

- nonclinical pharmacology and toxicology laboratory and animal tests according to good laboratory practices, or GLPs, and applicable requirements for the humane use of laboratory animals or other applicable regulations;

- submission of an IND application which must become effective before human clinical trials may begin;
- adequate and well-controlled human clinical trials according to GCPs and any additional requirements for the protection of human research subjects and their health information to establish the safety and efficacy of the investigational product for each targeted indication;
- submission of a biologics license application, or BLA, to the FDA;
- FDA's pre-approval inspection of manufacturing facilities to assess compliance with cGMPs and, if applicable, the FDA's good tissue practices, or GTPs, for the use of human cellular and tissue products to prevent the introduction, transmission, or spread of communicable diseases;
- FDA's audit of clinical trial sites that generated data in support of the BLA; and
- FDA approval of a BLA, which must occur before a product can be marketed or sold.

### ***Product Development Process***

Before testing any biologic in humans, the product enters the nonclinical, or preclinical, testing stage. Nonclinical tests include laboratory evaluations of product chemistry, toxicity, and formulation, as well as animal studies to assess the potential safety and activity of the product. The conduct of nonclinical tests must comply with federal regulations and requirements including GLPs.

Where a gene therapy trial is conducted at, or sponsored by, institutions receiving NIH funding for recombinant DNA research, prior to the submission of an IND to the FDA, a protocol and related documentation is submitted to and the trial is registered with the NIH Office of Biotechnology Activities, or OBA, pursuant to the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. Compliance with the NIH Guidelines is mandatory for investigators at institutions receiving NIH funds for research involving recombinant DNA, however many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. The NIH is responsible for convening the RAC, a federal advisory committee, which discusses protocols that raise novel or particularly important scientific, safety or ethical considerations at one of its quarterly public meetings. The OBA will notify the FDA of the RAC's decision regarding the necessity for full public review of a gene therapy protocol. RAC proceedings and reports are posted to the OBA web site and may be accessed by the public.

The product sponsor then submits the results of the nonclinical testing, together with manufacturing information, analytical data, any available clinical data or literature, and a proposed clinical protocol, to the FDA in an IND, which is a request for authorization from the FDA to administer an investigational product to humans. Some nonclinical testing may continue even after the IND application is submitted. IND authorization is required before interstate shipping and administration of any new product to humans that is not the subject of an approved BLA. The IND automatically becomes effective 30 days after receipt by the FDA unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial and places the clinical trial on a clinical hold. In such case, the IND sponsor must resolve any outstanding concerns with the FDA before the clinical trial may begin. Further, an IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial before it commences at that site. If the site has an IBC, it may also have to review and approve the proposed clinical trial. Clinical trials involve the administration of the investigational product to patients under the supervision of qualified investigators following GCPs, requirements meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, investigators, and monitors. Clinical trials are conducted under protocols that detail, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, the parameters to be used in monitoring safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur, and the efficacy criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND. The informed written consent of each participating subject is required and the form and content of the informed consent must be approved by each IRB.

The clinical investigation of an investigational product is generally divided into three phases. Although the phases are usually conducted sequentially, they may overlap or be combined. The three phases of an investigation are as follows:

- Phase I includes the initial introduction of an investigational product into humans. Phase I clinical trials may be conducted in patients with the target disease or condition or on healthy volunteers. These studies are designed to evaluate the safety, metabolism, pharmacokinetics and pharmacologic actions of the investigational product in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness. During Phase I clinical trials, sufficient information about the investigational product's pharmacokinetics and pharmacological effects may be obtained to permit the design of Phase II clinical trials. The total number of participants included in Phase I clinical trials varies, but is generally in the range of 20 to 80.
- Phase II includes the controlled clinical trials conducted to evaluate the effectiveness of the investigational product for a particular indication(s) in patients with the disease or condition under study, to determine dosage tolerance and optimal dosage, and to identify possible adverse side effects and safety risks associated with the product. Phase II clinical trials are typically well-controlled, closely monitored, and conducted in a limited patient population, usually involving no more than several hundred participants. Phase IIa trials provide information on the impact of dose ranging on safety, biomarkers and proof of concept, while Phase IIb trials are patient dose-ranging efficacy trials.
- Phase III clinical trials are controlled clinical trials conducted in an expanded patient population at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the investigational product has been obtained, and are intended to further evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the product, and to provide an adequate basis for product approval. Phase III clinical trials usually involve several hundred to several thousand participants. In most cases, the FDA requires two adequate and well controlled Phase III clinical trials to demonstrate the efficacy of the product. FDA may accept a single Phase III trial with other confirmatory evidence in rare instances where the trial is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible.

Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected adverse events; any findings from other studies, tests in laboratory animals or *in vitro* testing that suggest a significant risk for human subjects; or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. The FDA typically recommends that sponsors observe subjects for potential gene therapy-related delayed adverse events for a 15-year period, including a minimum of five years of annual examinations followed by 10 years of annual queries, either in person or by questionnaire, of trial subjects.

The decision to terminate a clinical trial of an investigational biologic may be made by the FDA or other regulatory authority, an IRB, an IBC, or institutional ethics committee, or by a company for various reasons. The FDA may place a clinical hold and order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. If the FDA imposes a clinical hold, trials may not recommence without FDA and IRB authorization and then only under terms authorized by the FDA and IRB. In some cases, clinical trials are overseen by an independent group of qualified experts organized by the trial sponsor, or the clinical monitoring board or DSMB. This group provides authorization for whether or not a trial may move forward at designated check points. These decisions are based

on the limited access to data from the ongoing trial. The suspension or termination of a clinical trial can occur during any phase of clinical trials if it is determined that the participants or patients are being exposed to an unacceptable health risk. In addition, there are requirements for the registration of ongoing clinical trials of drugs and biologics on public registries and the disclosure of certain information pertaining to the trials as well as clinical trial results after completion.

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed investigational product information is submitted to the FDA in the form of a BLA for a biologic to request marketing approval for the product in specified indications.

Human gene therapy products are a new category of therapeutics. Because this is a relatively new and expanding area of novel therapeutic interventions, there can be no assurance as to the length of the trial period, the number of patients the FDA will require to be enrolled in the trials in order to establish the safety, efficacy, purity and potency of human gene therapy products, or that the data generated in these trials will be acceptable to the FDA to support marketing approval. The NIH and the FDA have a publicly accessible database, the Genetic Modification Clinical Research Information System, which includes information on gene transfer trials and serves as an electronic tool to facilitate the reporting and analysis of adverse events on these trials. Over the last several years the FDA has issued helpful guidance on development of gene therapy products and shown a willingness to work closely with developers, especially with those working in orphan disease areas.

#### ***Biologics License Application Approval Process***

In order to obtain approval to market a biologic in the United States, a BLA must be submitted to the FDA that provides data from nonclinical studies and clinical trials and manufacturing information establishing to the FDA's satisfaction the safety, purity, and potency or efficacy of the investigational product for the proposed indication. The BLA must be accompanied by a substantial user fee payment unless a waiver or exemption applies.

The FDA will initially review the BLA for completeness before it accepts it for filing. Under the FDA's procedures, the agency has 60 days from its receipt of a BLA to determine whether the application will be accepted for filing based on the agency's threshold determination that the application is sufficiently complete to permit substantive review. After the BLA submission is accepted for filing, the FDA reviews the BLA to determine, among other things, whether the proposed product is safe, pure and potent, which includes determining whether it is effective for its intended use, and whether the product is being manufactured in accordance with cGMP, to assure and preserve the product's identity, safety, strength, quality, potency and purity, and in accordance with biological product standards. The FDA will inspect the facilities at which the product is manufactured to ensure the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications. For a human cellular or tissue product, the FDA also will not approve the product if the manufacturer is not in compliance with the GTPs. These are FDA regulations that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues, and cellular and tissue based products, which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the GTP requirements is to ensure that cell and tissue based products are manufactured in a manner designed to prevent the introduction, transmission, and spread of communicable disease. Additionally, before approving a BLA, the FDA may inspect one or more clinical sites to assure compliance with GCP.

If the FDA determines the application, manufacturing process or manufacturing facilities are not acceptable, it typically will outline the deficiencies and often will request additional testing or information, or corrective action for a manufacturing facility. This may significantly delay further review of the application. If the FDA finds that a clinical site did not conduct the clinical trial in accordance with GCP, the FDA may determine the data generated by the clinical site should be excluded from the primary efficacy analyses provided in the BLA. Additionally, notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

The FDA may refer applications for novel products or products that present difficult questions of safety or efficacy to an advisory committee. The FDA also may determine a REMS is necessary to assure the safe use of the biologic, in which case the BLA sponsor must submit a proposed REMS. The REMS may include, but is not limited to, a Medication Guide, a communications plan, and other elements to assure safe use, such as restrictions on distribution, prescribing, and dispensing.

After the FDA completes its initial review of a BLA, it will either license, or approve, the product, or issue a complete response letter to communicate that it will not approve the BLA in its current form and to inform the sponsor of changes that the sponsor must make or additional clinical, nonclinical or manufacturing data that must be received before the FDA can approve the application, with no implication regarding the ultimate approvability of the application. If a complete response letter is issued, the sponsor may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application.

The testing and approval process for both a drug and biologic requires substantial time, effort and financial resources and this process may take several years to complete. Data obtained from clinical trials are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals, which could delay or preclude us from marketing our products.

### ***Orphan Drug Designation***

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product candidate intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug or biological product available in the United States for this type of disease or condition will be recovered from sales of the product candidate. Orphan product designation must be requested before submitting a BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product candidate that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same biological product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. Orphan drug status in the European Union has similar, but not identical, benefits.

### ***Expedited Development and Review Programs***

The FDA has a fast track program that is intended to expedite or facilitate the process for reviewing new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for fast track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new

biologic or drug may request the FDA to designate the biologic or drug as a fast track product at any time during the clinical development of the product. Unique to a fast track product, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product submitted to the FDA for marketing, including under a fast track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new biological or drug product designated for priority review in an effort to facilitate the review. Additionally, a product may be eligible for accelerated approval. Biological or drug products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a biological or drug product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Lastly, under the provisions of the new Food and Drug Administration Safety and Innovation Act, enacted in 2012, a sponsor can request designation of a product candidate as a “breakthrough therapy.” A breakthrough therapy is defined as a drug or biological that is intended, alone or in combination with one or more other drugs or biological, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug or biological may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs and biologicals designated as breakthrough therapies are also eligible for accelerated approval and receive the same benefits as drugs and biologicals with Fast Track designation. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Fast Track designation, and priority review may expedite the product approval process, but do not change the standards for approval. Accelerated approval and breakthrough therapy designation do change the standards for product approval and thus may expedite the development and/or approval process.

### ***FDA Additional Requirements***

The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase 4 clinical trials may be made a condition to be satisfied for continuing drug and biologic approval. The results of Phase 4 clinical trials can confirm the efficacy of a product candidate and can provide important safety information. In addition, the FDA has express statutory authority to require sponsors to conduct post-market studies to specifically address safety issues identified by the agency.

Even if a product candidate receives regulatory approval, the approval may be limited to specific disease states, patient populations and dosages, or might contain significant limitations on use in the form of warnings, precautions or contraindications, or in the form of an onerous REMS, restrictions on distribution, or post-marketing study requirements. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. In addition, we cannot predict what adverse governmental regulations may arise from future U.S. or foreign governmental action.

### ***Medical device requirements***

Our contemplated diagnostics, for use with certain of our therapeutic products, are regulated by FDA as *in vitro* diagnostic, or IVD, medical devices. Such IVD devices must comply with applicable FDA IVD-specific regulations as well as FDA regulations applicable more broadly to medical devices. These FDA regulations include requirements for registering establishments with FDA; listing IVD devices with FDA; reporting certain adverse events related to IVD devices to FDA; complying with the Quality System Regulation (current good manufacturing practices for devices); labeling IVD devices; and obtaining premarket approval or clearance prior to marketing IVD devices (unless exempt). There are also regulations covering the requirements for investigational devices and the conduct of clinical investigations of devices. Like drugs and biologics, failure to comply with applicable device/IVD requirements can result in legal or administrative enforcement actions against an IVD device firm, its officers or employees, and/or its products.

### ***FDA Post-Approval Requirements***

Any products manufactured or distributed by us or on our behalf pursuant to FDA approvals are subject to continuing regulation by the FDA, including requirements for record-keeping, reporting of adverse experiences with the biologic or drug, and submitting biological product deviation reports to notify the FDA of unanticipated changes in distributed products. Manufacturers are required to register their facilities with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements, which impose certain quality processes, manufacturing controls and documentation requirements upon us and our third-party manufacturers in order to ensure that the product is safe, has the identity and strength, and meets the quality, purity and potency characteristics that it purports to have. In November 2013, the Drug Quality and Security Act, or DQSA, became law and establishes requirements to facilitate the tracing of prescription drug and biological products through the pharmaceutical supply distribution chain. This law includes a number of new requirements that will be implemented over time and will require us to devote additional resources to satisfy these requirements, including serializing the product and using new technology and data storage to electronically trace the product from manufacturer to dispenser. If our products are not covered by the serialization and tracing requirements of the DQSA, they may be subject to state pedigree and traceability requirements. We cannot be certain that we or our present or future suppliers will be able to comply with the cGMP and other FDA regulatory requirements. If our present or future suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, refuse to approve any BLA, force us to recall a product from distribution, shut down manufacturing operations or withdraw approval of the applicable BLA. Noncompliance with cGMP or other requirements can result in issuance of warning or untitled letters, civil and criminal penalties, seizures, and injunctive action.

The FDA and other federal and state agencies closely regulate the labeling, marketing and promotion of drugs and biologics. Government regulators, including the Department of Justice and the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities, recently have increased their scrutiny of the promotion and marketing of drugs and biologics. While doctors are free to prescribe any product approved by the FDA for any use, a company can only make claims relating to safety and efficacy of a product that are consistent with FDA approval, and the company is allowed to market a product only for the particular use and treatment approved by the FDA. In addition, any claims we make for our products in advertising or promotion must, among other things, be appropriately balanced with important safety information and otherwise be adequately substantiated. Failure to comply with these requirements can result in adverse publicity, warning or untitled letters, corrective advertising, injunctions, potential civil and criminal penalties, criminal prosecution, and agreements with governmental agencies that materially restrict the manner in which a company promotes or distributes products.

### ***Pediatric Research Equity Act***

Under the Pediatric Research Equity Act, or PREA, as amended, a BLA or supplement must contain data to assess the safety and efficacy of the product for the claimed indications in all relevant pediatric subpopulations



and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Manufacturers must submit a pediatric study plan to the IND not later than 60 days after the end-of-phase 2 meeting with the FDA; if there is no such meeting, before the initiation of any phase 3 studies or a combined phase 2 and phase 3 study; or if no such study will be conducted, no later than 210 days before a marketing application or supplement is submitted. The intent of PREA is to compel sponsors whose products have pediatric applicability to study those products in pediatric populations, rather than ignoring pediatric indications for adult indications that could be more economically desirable. The FDA may grant deferrals for submission of data or full or partial waivers. By its terms, PREA does not apply to any product for an indication for which orphan designation has been granted, unless the FDA issues regulations stating otherwise. Because the FDA has not issued any such regulations, submission of a pediatric assessment is not required for an application to market a product for an orphan-designated indication.

### ***Patent Term Restoration and Marketing Exclusivity***

Depending on the timing, duration and specifics of FDA marketing approval of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application. Only one patent applicable to an approved biological is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent and within sixty days of approval of the biological. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

The Biologics Price Competition and Innovation Act of 2009, which was included within the Patient Protection and Affordable Care Act, created an abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product, and grants a reference biologic twelve years of exclusivity from the time of first licensure. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structure of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation that are still being worked out by the FDA.

Pediatric exclusivity is another type of exclusivity in the United States. Pediatric exclusivity, if granted, provides an additional six months of exclusivity to be attached to any existing exclusivity, e.g., twelve year exclusivity, or patent protection for a drug. This six month exclusivity, which runs from the end of other exclusivity protection or patent delay, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

### ***Government Regulation Outside the United States***

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a request for a clinical trial authorization, or CTA, must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and the IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed.

The requirements and process governing the conduct of clinical trials, product approval or licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of a biological product under European Union regulatory systems, we must submit a marketing authorization application. The application required in the European Union is similar to a BLA in the United States, with the exception of, among other things, country-specific document requirements. The European Union also provides opportunities for market exclusivity. For example, in the European Union, upon receiving marketing authorization, a new biological generally receives eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a biosimilar application. During the additional two-year period of market exclusivity, a biosimilar marketing authorization can be submitted, and the innovator's data may be referenced, but no biosimilar product can be marketed until the expiration of the market exclusivity. The innovator may obtain an additional one year of market exclusivity if the innovator obtains an additional authorization during the initial eight year period for one or more new indications that demonstrate significant clinical benefit over existing therapies. This data and market exclusivity regime in the European Union of a total of 10 or 11 years protects against generic competition, but does not protect against the launch of a competing product if the competitor, rather than referencing the clinical data of the originator, has conducted its own clinical trials to support its marketing authorization application.

Orphan drugs in the European Union are eligible for 10-year market exclusivity. This 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- the applicant consents to a second orphan medicinal product application; or
- the applicant cannot supply enough orphan medicinal product.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

### ***Pharmaceutical Coverage, Pricing and Reimbursement***

Sales of our products, when and if approved for marketing, will depend, in part, on the extent to which our products will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly reducing reimbursements for medical products, biologicals, drugs and services. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost containment

programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of interchangeable products. Adoption of price controls and cost containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our product candidates or a decision by a third-party payor not to cover our product candidates could reduce physician usage of our products once approved and have a material adverse effect on our sales, results of operations and financial condition.

The containment of healthcare costs has become a priority of federal, state and foreign governments. Third-party payors are increasingly challenging the prices charged for drug products and medical services, examining the medical necessity and reviewing the cost effectiveness of drug products and medical services, in addition to questioning safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after FDA approval or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit.

In the United States and some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the ACA, was enacted. The ACA includes measures that have significantly changed, and are expected to continue to significantly change, the way healthcare is financed by both governmental and private insurers. Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

### ***Other Healthcare Laws***

Although we currently do not have any products on the market, we may be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and other countries in which we conduct our business. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine and open payment laws and regulations, many of which may become more applicable to us if our product candidates are approved and we begin commercialization. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

### **Facilities**

Our corporate headquarters are located in Sydney, Australia and consist of approximately 1,700 square feet of leased office space under a lease that expires in August 2015. Our research and development facility is located in Hayward, California, and consists of approximately 4,750 square feet of leased office space under a lease that expires in May 2018.

We believe that our existing facilities are adequate for our current needs.

**Employees**

As of March 31, 2015, we had 21 full-time employees, 11 of whom have a PhD or other post-graduate degrees. Of these full-time employees, 13 are engaged in research and development activities and 8 are engaged in finance, legal, human resources, facilities and general management. Our employees are located in Sydney, Australia and at our research and development facility located in Hayward, California.

**Legal Proceedings**

We are not currently a party to any material legal proceedings. From time to time, we may be subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, any such future litigation could have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

## MANAGEMENT

### Directors and Executive Officers

The following table sets forth information covering our current directors and executive officers.

<u>Name</u>	<u>Position</u>
Peter French . . . . .	Chief Executive Officer and Managing Director
Peter Francis . . . . .	Chairman of the Board of Directors
Greg West . . . . .	Chief Financial Officer and Company Secretary
Carl Stubbings . . . . .	Chief Business Officer
David Suhy . . . . .	Chief Scientific Officer
Georgina Kilfoil . . . . .	Chief Clinical Officer
John Chiplin . . . . .	Director
Iain Ross . . . . .	Director
J. Kevin Buchi . . . . .	Director

**Dr. Peter French** joined Benitec in July 2009 as our Chief Scientific Officer and has been our Chief Executive Officer since June 2010 and Managing Director of our board of directors since August 2013. He has an MBA in Technology Management from Deakin University and a PhD in cell biology from Deakin University. Dr. French is a Past President of the Australia and New Zealand Society for Cell and Developmental Biology, and represented Australia’s biological scientists on the Board of FASTS, an Australian government lobbying organization for science and technology. Dr. French obtained his PhD in 1987 for work performed at CSIRO, an Australian government research organization. He carried out postdoctoral research at the Children’s Medical Research Foundation, Sydney. In 1989, he became Principal Scientific Officer and Manager of the Centre for Immunology, St Vincent’s Hospital, Sydney.

**Peter Francis** has been Chairman of our Board since February 2006. Since 1993, Mr. Francis has been a partner at Francis Abourizk Lightowlers, a firm of commercial and technology lawyers with offices in Melbourne, Australia. He is a legal specialist in the areas of intellectual property and licensing and provides legal advice to corporations and research bodies. Mr. Francis completed his studies in law and jurisprudence at Monash University.

**Greg West** has been our Chief Financial Officer and Company Secretary since May 2011. From May 2010 to January 2011, he was Chief Financial Officer at Immune Systems Therapeutics, Ltd., a medical diagnostic company. Mr. West is a Chartered Accountant. He is a Director and Audit Committee Chairman of each of UOWE Limited (a business arm of Wollongong University) and IDP Education Pty Ltd and Education Australia Limited. He worked at PricewaterhouseCoopers and has held finance executive roles with financial institutions, including BT Financial Group, Deutsche Bank AG and IAG New Zealand Limited.

**Carl Stubbings** has been our Chief Business Officer since July 2012. Prior to joining our company, Mr. Stubbings was Vice President of Sales & Marketing for Focus Diagnostics, Inc., a subsidiary of Quest Diagnostics Inc. from February 2008 to June 2012.

**Dr. David Suhy** was appointed as our Chief Scientific Officer in April 2015, prior to which he served as our Senior Vice President, Research & Development since October 2012. In April 2008, he joined Tacere Therapeutics, Inc. as Director of Research & Development and continued in that role until our acquisition of Tacere in October 2012. Previous roles include Associate Director of R&D at Clontech Laboratories, Inc. and Principal Scientist at Antara Biosciences Inc. He also led the Target Validation Group at PPD Discovery, a company with proprietary technology surrounding the use of genetic suppressor elements to identify “druggable” genomic targets for large pharmaceutical companies.

**Georgina Kilfoil** was appointed as our Chief Clinical Officer in April 2015 prior to which she served as Vice President, Clinical Operations since February 2015. Ms. Kilfoil initially provided services to Benitec in October 2014 in the role of Senior Drug Development Consultant. Prior to joining Benitec, Ms. Kilfoil was a business consultant from March 2013 to September 2014 and prior to that was Senior Vice President, Management and Development at Anthera Pharmaceuticals, Inc. from March 2010 to February 2013. Previous to this, Ms. Kilfoil served as Project Management Consultant at InClin, Inc. and Vice President of Project Management at Peninsula Pharmaceuticals, Inc. Ms. Kilfoil is a certified Project Management Professional, has a Bachelor of Science Degree in Pharmacology from the University of Bristol, United Kingdom, and a Masters of Business Administration from the Australian Graduate School of Management, Sydney, Australia.

**Dr. John Chiplin** has been a Director since February 2010. Dr. Chiplin is a founder of and has served as a Managing Director of investment company, Newstar Ventures Ltd., since 1998. More recently, he has served as a director of Medistem, Inc. through its acquisition by Intrexon Corporation in 2014, as founding Chief Executive Officer of Arana Therapeutics Limited from 2006 through its acquisition by Cephalon, Inc. in 2009, as director of Domantis Ltd through its acquisition by GlaxoSmithKline plc in 2006, and as Managing Director of ITI Life Sciences Fund from 2003 to 2005. Dr. Chiplin currently serves on the board of directors of Adalta Pty Ltd, ScienceMedia Inc., Prophecy Inc., Batu Biologics Inc., The Coma Research Institute and Cynata Therapeutics Limited which is traded on the ASX. Dr. Chiplin's Pharmacy and PhD degrees are from the University of Nottingham, Nottingham, United Kingdom.

**Iain Ross** has been a Director since June 2010. Following a career with Sandoz, Fisons, Hoffman La Roche and Celltech, Mr. Ross is a Qualified Chartered Director in the United Kingdom and currently he is Chairman of the Board of Premier Veterinary Group plc, formerly Ark Therapeutics Group plc which is traded on the London Stock Exchange, and Biomer Technology Limited; and a non-executive director of Amarantus Bioscience Inc which is traded on the OTCQB, and Tissue Therapies Limited and Anantara Lifesciences Limited, which are both traded on the ASX. Mr. Ross served as the Executive Chairman for Ark Therapeutics Group plc from September 2010 to March 2013. He is also Vice Chairman of the Council of Royal Holloway, University of London.

**J. Kevin Buchi** has been a Director since April 2013. Since August 2013, he has served as Chief Executive Officer of TetraLogic Pharmaceuticals Corporation. Mr. Buchi served as Chief Executive Officer of Cephalon, Inc., or Cephalon, from December 2010 through its acquisition by Teva Pharmaceutical Industries Ltd., or Teva Pharmaceuticals, in October 2011. After the acquisition Mr. Buchi served as Corporate Vice President, Global Branded Products of Teva Pharmaceuticals. Mr. Buchi joined Cephalon in 1991 and held various positions, including Chief Operating Officer, from January 2010 to December 2010, Chief Financial Officer and Head of Business Development prior to being appointed Chief Executive Officer. Mr. Buchi currently serves as President and Chief Executive Officer and a member of the Board of Directors of TetraLogic Pharmaceuticals Corp. Mr. Buchi is also on the Board of Directors of Stemline Therapeutics, Inc., Forward Pharma A/S, Alexza Pharmaceuticals, Inc. and Epirus Biopharmaceuticals Inc. Mr. Buchi has a B.A. in chemistry from Cornell University and a Masters in Management from Kellogg Graduate School of Management at Northwestern University. He is also a Certified Public Accountant.

There are no family relationships among any of our directors or executive officers. The business addresses for each of our directors and executive officers is Benitec Biopharma Limited, F6A/1-15 Barr Street, Balmain, New South Wales, Australia.

### **Board of Directors**

Our board of directors currently consists of five members, including our Chief Executive Officer. Our directors are elected at each annual general meeting of our shareholders and serve until their successors are elected or appointed, unless their office is earlier vacated. We believe that each of our directors has relevant industry experience. The membership of our board of directors is directed by the following requirements:

- our Constitution specifies that there must be a minimum of three directors and a maximum of 10, and our board of directors may determine the number of directors within those limits;
- as set forth in our Board Charter, the membership of the board of directors should consist of a majority of independent directors who satisfy the criteria recommended by the ASX Corporate Governance Principles and Recommendations;

- the Chairman of our Board should be an independent director who satisfies the criteria for independence recommended by the ASX Corporate Governance Principles and Recommendations; and
- our board of directors should, collectively, have the appropriate level of personal qualities, skills, experience, and time commitment to properly fulfill its responsibilities or have ready access to such skills where they are not available.

Our board of directors has delegated responsibility for the conduct of our businesses to the Chief Executive Officer, but remains responsible for overseeing the performance of management. Our board of directors has established delegated limits of authority, which define the matters that are delegated to management and those that require board of directors approval. Under the Corporations Act, at least two of our directors must be resident Australians. None of our directors have any service contracts with Benitec that provide for benefits upon termination of employment.

### ***Committees***

To assist our board of directors with the effective discharge of its duties, it has established a Remuneration and Nomination Committee and an Audit and Risk Committee, which committees operate under a specific charter approved by our board of directors.

***Remuneration and Nomination Committee.*** The members of our Remuneration and Nomination Committee are Peter Francis, Kevin Buchi, John Chiplin and Iain Ross, each of whom our board of directors has determined meets the criteria for independence under Nasdaq Listing Rule 5605(a)(2). Dr. John Chiplin acts as chairman of the committee. The committee's role involves:

- identifying, evaluating and recommending qualified nominees to serve on our board of directors;
- developing and overseeing our internal corporate governance processes;
- maintaining a management succession plan;
- evaluating, adopting and administering our compensation plans and similar programs advisable for us, as well as modifying or terminating existing plans and programs;
- establishing policies with respect to equity compensation arrangements; and
- overseeing, reviewing and reporting on various remuneration matters to our board of directors.

***Audit and Risk Committee.*** The members of our Audit and Risk Committee are Peter Francis, John Chiplin, and Iain Ross, each of whom our board of directors has determined meets the criteria for independence of audit committee members set forth in Rule 10A-3(b)(1) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and the applicable rules of the NASDAQ Global Market. Each member of our audit committee meets the financial literacy requirements of the listing standards of the NASDAQ Global Market. Iain Ross acts as the chairman of the audit committee and our board of directors has determined that Iain Ross is an audit committee "financial expert," as defined by Item 407(d) of Regulation S-K under the Securities Act. The principal duties and responsibilities of our audit committee include, among other things:

- overseeing and reporting on various auditing and accounting matters to our board of directors, including the selection of our independent accountants, the scope of our annual audits, fees to be paid to the independent accountants, the performance of our independent accountants and our accounting practices;
- overseeing and reporting on various risk management matters to our board of directors.
- considering and approving or disapproving all related-party transactions;
- reviewing our annual and semi-annual financial statements and reports and discussing the statements and reports with our independent registered public accounting firm and management;
- reviewing and pre-approving the engagement of our independent registered public accounting firm to perform audit services and any permissible non-audit services;

- evaluating the performance of our independent registered public accounting firm and deciding whether to retain their services; and
- establishing procedures for the receipt, retention and treatment of complaints received by us regarding financial controls, accounting or auditing matters.

### **Code of Conduct**

We have established a code of conduct, which sets out the standards of behavior that apply to every aspect of our dealings and relationships, both within and outside Benitec. The following standards of behavior apply to all directors, executive officers and employees of Benitec:

- comply with all laws that govern us and our operations;
- act honestly and with integrity and fairness in all dealings with others and each other;
- avoid or manage conflicts of interest;
- use our assets responsibly and in the best interests of Benitec; and
- be responsible and accountable for our actions.

The Code of Conduct is available on our website at [www.benitec.com](http://www.benitec.com).

### **Remuneration**

The remuneration policy of Benitec is to align director and executive objectives with shareholder and business objectives by providing a fixed remuneration component and typically offering long-term incentives based on key performance areas. Our board of directors believes the remuneration policy to be appropriate and effective in its ability to attract and retain the best executives and directors to run and manage the consolidated entity, as well as create goal congruence between directors, executives, and shareholders.

Our board of directors is responsible for determining the appropriate remuneration package for our Chief Executive Officer, and our Chief Executive Officer is in turn responsible for determining the appropriate remuneration packages for senior management.

Executives typically receive a base salary based on factors such as experience and comparable industry information, options and performance incentives. Our board of directors reviews our Chief Executive Officer's remuneration package, and our Chief Executive Officer reviews the other senior executives' remuneration packages, annually by reference to the consolidated entity's performance, executive performance, and comparable information within the industry.

The performance of executives is measured against criteria agreed annually with each executive and is based predominantly on the overall success of Benitec in achieving its broader corporate goals. Bonuses and incentives are linked to predetermined performance criteria. Our board of directors may, however, exercise its discretion in relation to approving incentives, bonuses, and options, and can recommend changes to our Chief Executive Officer's recommendations. The policy is designed to attract the highest caliber of executives and reward them for performance that results in long-term growth in shareholder wealth.

Executives may be invited to participate in the employee share option plan.

Australian executives or directors receive a superannuation guarantee contribution required by the government and do not receive any other retirement benefits.

All remuneration paid to directors and executives is valued at the cost to us and expensed. Options are valued using the Black-Scholes methodology. The board of directors' policy is to remunerate non-executive



directors at market rates for comparable companies for time, commitment, and responsibilities. Our board of directors as a whole determines payments to the non-executive directors and reviews their remuneration annually, based on market practice, duties and accountability. The maximum aggregate amount of fees that can be paid to non-executive directors is subject to approval by shareholders at our annual general meeting. Fees for non-executive directors are not linked to the performance of the consolidated entity. However, to align directors' interests with shareholder interests, the directors are encouraged to hold our shares.

### ***Performance Based Remuneration***

Each executive's remuneration package typically has a performance-based component. The intention of this approach is to facilitate goal congruence between executives with the business and shareholders. Generally, the executive's performance based remuneration is tied to Benitec's successful achievement of certain key milestones relating to its operating activities, as well as Benitec's overall financial position.

The remuneration policy has been tailored to align the goals of shareholders, directors, and executives. Two methods are applied in achieving this aim, the first being a performance-based bonus linked to achievement of key corporate milestones, and the second being the issuance of options to the majority of directors and executives to encourage the alignment of personal and shareholder interests.

### ***Details of Remuneration for fiscal 2014***

	Short term			Post employment		Equity awards		% of remuneration	
	Salary and Fees	Cash bonus	Non-monetary Benefits	Superannuation	Termination benefits	Options	Total	consisting of options	performance based
Directors:									
Peter Francis	A\$ 113,328	—	—	—	—	A\$ 27,556	A\$ 140,884	19.6%	n/a
John Chiplin	53,000	—	—	—	—	6,890	59,890	11.5%	n/a
Iain Ross	58,000	—	—	—	—	6,890	64,890	10.6%	n/a
Mel Bridges	58,000	—	—	—	—	6,890	64,890	10.6%	n/a
Kevin Buchi	53,000	—	—	—	—	103,098	156,098	66.0%	n/a
	<u>A\$ 335,328</u>	—	—	—	—	<u>A\$151,324</u>	<u>A\$ 486,652</u>		n/a
Executive Officers:									
Peter French	A\$ 300,000	A\$150,000	—	A\$17,775	—	A\$126,061	A\$ 593,836	21.2%	46.5%
Carl Stubbings	252,000	50,000	—	17,775	—	19,391	339,166	5.7%	20.4%
Michael Graham	195,000	30,000	—	17,775	—	10,417	253,192	4.1%	16.0%
David Suhy	217,902	87,160	—	—	—	25,360	330,422	7.7%	34.1%
Greg West	217,391	50,000	—	17,775	—	15,461	300,627	5.1%	21.8%
	<u>1,182,293</u>	<u>367,160</u>	—	<u>71,100</u>	—	<u>196,690</u>	<u>1,817,243</u>		
Total	<u>A\$1,517,621</u>	<u>A\$367,160</u>	—	<u>A\$71,100</u>	—	<u>A\$348,014</u>	<u>A\$2,303,895</u>		

### Employment Agreements with Executive Officers

The key provisions of the employment agreements (other than remuneration) are set out below for each of our executive officers. None of these employment agreements have termination dates.

<u>Name of executive officer</u>	<u>Title of executive officer</u>	<u>Date of employment agreement</u>	<u>Notice period required to terminate without cause by either party</u>
Peter French . . . . .	Chief Executive Officer and Managing Director	June 9, 2010	Six months (if by Benitec) Two months (if by employee)
Greg West . . . . .	Chief Financial Officer and Company Secretary	August 23, 2011	Three months
Carl Stubbings . . . . .	Chief Business Officer	May 28, 2012	Three months
David Suhy . . . . .	Chief Scientific Officer	August 28, 2012	At will
Georgina Kilfoil . . . . .	Chief Clinical Officer	September 29, 2014	Three months

### Employee Share Option Plan

We had an employee share option plan that was approved by our shareholders in November 2009 and was in effect until November 2014. We intend to present an updated plan for consideration and approval by our shareholders at a general meeting of shareholders late in 2015.

## PRINCIPAL SHAREHOLDERS

The following table and accompanying footnotes present certain information regarding the beneficial ownership of our ordinary shares based on 115,881,763 ordinary shares outstanding as of March 31, 2015 by:

- each person known by us to be the beneficial owner of more than 5% of our ordinary shares;
- each of our directors and executive officers individually; and
- all of our directors and executive officers as a group.

Beneficial ownership is determined according to the rules of the SEC and generally means that a person has beneficial ownership of a security if he, she or it possesses sole or shared voting or investment power of that security, including options that are exercisable within 60 days of March 31, 2015. Information with respect to beneficial ownership has been furnished to us by each director, executive officer, or 5% or more shareholder, as the case may be. Ordinary shares subject to options currently exercisable or exercisable within 60 days of March 31, 2015 are deemed to be outstanding for computing the percentage ownership of the person holding these options and the percentage ownership of any group of which the holder is a member, but are not deemed outstanding for computing the percentage of any other person.

Based on information known to us, as of March 31, 2015, we had 102 shareholders in the United States. These shareholders held an aggregate of 26,160,411 of our outstanding ordinary shares, or approximately 22.58% of our outstanding ordinary shares. A large number of our ordinary shares are held by nominee companies so we cannot be certain of the identity of those beneficial owners.

Unless otherwise indicated, to our knowledge each shareholder possesses sole voting and investment power over the ordinary shares listed subject to community property laws, where applicable. None of our shareholders has different voting rights from other shareholders. Unless otherwise indicated, the address for each of the persons listed in the table below is Benitec Biopharma Limited, F6A/1-15 Barr Street, Balmain, New South Wales, Australia.

<u>Shareholder</u>	<b>Ordinary Shares Beneficially Owned Prior to Offering</b>		<b>Ordinary Shares Beneficially Owned After the Offering<sup>(1)</sup></b>	
	Number	Percent	Number	Percent
<b>5% Shareholders</b>				
RA Capital Management, LLC . . . . .	11,629,031	10.05%		%
Dr. Christopher Bremner . . . . .	8,133,547	7.02		
<b>Officers and Directors</b>				
Peter Francis . . . . .	2,024,174 <sup>(2)</sup>	1.47		*
Peter French . . . . .	2,258,452 <sup>(3)</sup>	1.64		*
Greg West . . . . .	413,333 <sup>(4)</sup>	*		*
Carl Stubbings . . . . .	632,012 <sup>(5)</sup>	*		*
David Suhy . . . . .	533,333 <sup>(6)</sup>	*		*
Georgina Kilfoil . . . . .	100,000 <sup>(7)</sup>	*		*
John Chiplin . . . . .	600,000 <sup>(8)</sup>	*		*
Iain Ross . . . . .	466,364 <sup>(9)</sup>	*		*
J. Kevin Buchi . . . . .	1,128,205 <sup>(10)</sup>	*		*
Officers and directors as a group (9 persons) . . . . .	8,155,873	5.93		

\* Represents beneficial ownership of less than 1% of the outstanding ordinary shares of Benitec.

(1) Assumes that the underwriters will not exercise their option to purchase additional ADSs.

(2) Includes (i) 424,174 shares and (ii) 1,600,000 shares that Mr. Francis has the right to acquire pursuant to options that are exercisable as of March 31, 2015 or will become exercisable within 60 days of such date.

- (3) Includes (i) 591,785 shares and (ii) 1,666,667 shares that Dr. French has the right to acquire pursuant to options that are exercisable as of March 31, 2015 or will become exercisable within 60 days of such date.
- (4) Includes 413,333 shares that Mr. West has the right to acquire pursuant to options that are exercisable as of March 31, 2015 or will become exercisable within 60 days of such date.
- (5) Includes (i) 165,346 shares and (ii) 466,666 shares that Mr. Stubbings has the right to acquire pursuant to options that are exercisable as of March 31, 2015 or will become exercisable within 60 days of such date.
- (6) Includes 533,333 shares that Dr. Suhy has the right to acquire pursuant to options that are exercisable as of March 31, 2015 or will become exercisable within 60 days of such date.
- (7) Includes 100,000 shares that Ms. Kilfoil has the right to acquire pursuant to options that are exercisable as of March 31, 2015 or will become exercisable within 60 days of such date.
- (8) Includes (i) 200,000 shares and (ii) 400,000 shares that Dr. Chiplin has the right to acquire pursuant to options that are exercisable as of March 31, 2015 or will become exercisable within 60 days of such date.
- (9) Includes (i) 66,364 shares and (ii) 400,000 shares that Mr. Ross has the right to acquire pursuant to options that are exercisable as of March 31, 2015 or will become exercisable within 60 days of such date.
- (10) Includes (i) 861,539 shares and (ii) 266,666 shares that Mr. Buchi has the right to acquire pursuant to options that are exercisable as of March 31, 2015 or will become exercisable within 60 days of such date.

To our knowledge, there have not been any significant changes in the ownership of our ordinary shares by major shareholders over the past three years, except as follows (which is based upon substantial shareholder notices filed with the ASX):

- RA Capital Management, LLC, or RA Capital, and its associates became a substantial shareholder on February 28, 2014, when it reported that it held 7,009,345 ordinary shares, or 7.0%, of the total voting power as of that date. Between April 2014 and February 2015, RA Capital acquired an aggregate of 7,009,346 ordinary shares for A\$7,500,000 and sold an aggregate of 2,389,660 ordinary shares for A\$2,608,304. On February 19, 2015, RA Capital reported that it held 11,629,031 ordinary shares, or 10.05% of the total voting power, as of that date.
- Dalit Pty Ltd, or Dalit, became a substantial shareholder on July 23, 2013, when it reported that it held 4,545,455 ordinary shares, or 6.17%, of the total voting power as of that date. As a result of a capital raising in February 2014, it ceased to be a substantial shareholder.
- Irwin Biotech Nominees Pty Ltd atf BIOA Trust became a substantial shareholder on July 23, 2013 when it reported that it held 4,769,091 ordinary shares, or 6.47%, of the total voting power as of that date. On February 28, 2014, Irwin reported that it ceased to be a substantial shareholder (as a result of share dilution due to a capital raising).
- MJGD Nominees Pty Ltd atf BSMI Trust became a substantial shareholder on July 23, 2013 when it reported that it held 4,769,091 ordinary shares, or 6.47%, of the total voting power as of that date. On February 28, 2014, MJGD reported that it ceased to be a substantial shareholder (as a result of share dilution due to a capital raising).
- Commonwealth Scientific & Industrial Research Organisation, or CSIRO, became a substantial shareholder on January 11, 2010, when it reported that it held 40,097,026 ordinary shares, or 10%, of the total voting power as of that date. On February 28, 2014, CSIRO reported that it ceased to be a substantial shareholder (as a result of share dilution due to a capital raising).

## RELATED PARTY TRANSACTIONS

Other than as disclosed below, from July 1, 2011 to December 31, 2014 we did not enter into any transactions or loans with any: (i) enterprises that directly or indirectly, through one or more intermediaries, control, are controlled by or are under common control with us; (ii) associates; (iii) individuals owning, directly or indirectly, an interest in our voting power that gives them significant influence over us, and close members of any such individual's family; (iv) key management personnel and close members of such individuals' families; or (v) enterprises in which a substantial interest in our voting power is owned, directly or indirectly, by any person described in (iii) or (iv) or over which such person is able to exercise significant influence.

- Legal services at normal commercial rates totaling A\$119,804 for fiscal 2014, A\$103,492 for fiscal 2013 and A\$166,912 for fiscal 2012 were provided by Francis Abourizk Lightowlers, a law firm in which Mr. Peter Francis is a partner and has a beneficial interest.
- Consultancy fees were paid for executive duties totaling A\$98,285 for the period to March 31, 2015, A\$40,000 for fiscal 2014, A\$40,000 for fiscal 2013 and A\$40,000 for fiscal 2012 provided by NewStar Ventures Ltd, a corporation in which Dr. John Chiplin is a director and has a beneficial interest.
- Consultancy fees were paid for executive duties totaling A\$18,999 for fiscal 2012 provided by Gladstone Partnership, an entity in which Mr. Iain Ross is a principal and has a beneficial interest.
- Annabel West, the wife of Greg West, our Chief Financial Officer, was employed by us as a part-time clerical and administrative assistant from July 2014 until March 2015 and was paid wages of A\$36,859.
- Hannah Stubbings, daughter of our Chief Business Officer, Carl Stubbings, was employed by us as a part-time intern from September 2013 until April 2014 and was paid wages of A\$19,864.

Transactions between related parties are on normal commercial terms and the conditions no more favorable than those available to other non-related parties.

## DESCRIPTION OF SHARE CAPITAL

### General

The following description of our ordinary shares is only a summary. We encourage you to read our Constitution, which is included as an exhibit to this registration statement, of which this prospectus forms a part.

We are a public company limited by shares registered under the Corporations Act by the Australian Securities and Investments Commission, or ASIC. Our corporate affairs are principally governed by our Constitution, the Corporations Act and the ASX Listing Rules. Our ordinary shares trade on the ASX, and we are applying to list the ADSs on NASDAQ.

The Australian law applicable to our Constitution is not significantly different than a U.S. company's charter documents except we do not have a limit on our authorized share capital, the concept of par value is not recognized under Australian law and as further discussed under "—Our Constitution."

Subject to restrictions on the issue of securities in our Constitution, the Corporations Act and the ASX Listing Rules and any other applicable law, we may at any time issue shares and grant options or warrants on any terms, with the rights and restrictions and for the consideration that our board of directors determine.

The rights and restrictions attaching to ordinary shares are derived through a combination of our Constitution, the common law applicable to Australia, the ASX Listing Rules, the Corporations Act and other applicable law. A general summary of some of the rights and restrictions attaching to our ordinary shares are summarized below. Each ordinary shareholder is entitled to receive notice of, and to be present, vote and speak at, general meetings.

### Changes to Our Share Capital

As of March 31, 2015, we had (i) 115,881,763 ordinary shares outstanding and (ii) 25,684,481 outstanding options to purchase an aggregate of 25,684,481 ordinary shares at a weighted average exercise price of A\$1.27.

During the last three years, the following changes have been made to our ordinary share capital:

1. On October 30, 2012, we issued 78,446,306 ordinary shares to the vendors of Tacere Therapeutics Inc. as part of the consideration under an acquisition agreement, at an issue price of A\$0.01496 per share.
2. On March 11, 2013, we issued 43,846,155 ordinary shares as part of a private placement at A\$0.013 per share to institutional and professional investors outside the United States. Participants in the placement received two free unlisted options for every five shares subscribed for in the placement and we therefore also issued 17,538,462 unlisted options with an exercise price of A\$0.013 per share.
3. On March 28, 2013, we issued 13,846,154 ordinary shares as part of a private placement at A\$0.013 per share to institutional and professional investors outside the United States. Participants in the placement received two free unlisted options for every five shares subscribed for in the placement and we therefore also issued 5,538,462 unlisted options with an exercise price of A\$0.013 per share.
4. On May 28, 2013, we issued 7,692,308 ordinary shares as part of a private placement at A\$0.013 per share to institutional and professional investors outside the United States. Participants in the placement received two free unlisted options for every five shares subscribed for in the placement and we therefore also issued 3,076,923 unlisted options with an exercise price of A\$0.013 per share.
5. On June 14, 2013, we issued 37,454,591 ordinary shares as part of a private placement at A\$0.011 per share to institutional and professional investors outside the United States.
6. On July 23, 2013, we issued 27,229,089 ordinary shares as part of a private placement at A\$0.275 per share to institutional and professional investors outside the United States.

7. On July 23, 2013, we issued 400,000 ordinary shares at A\$0.325 per share to directors resident outside the United States. Participants in the placement received two free unlisted options for every five shares subscribed for in the placement and we therefore also issued 160,000 unlisted options with an exercise price of A\$0.013 per share.
8. On August 6, 2013, we issued 10,254,696 ordinary shares at A\$0.275 per share to shareholders resident in Australia or New Zealand under a share purchase plan.
9. On October 30, 2013, we issued 955,002 ordinary shares to the vendors of Tacere Therapeutics Inc. as part of the consideration under an acquisition agreement. The consideration was A\$350,000.
10. On February 28, 2014, we issued 14,717,995 ordinary shares and 6,623,098 unlisted options, as the first tranche of a private placement transacted over two tranches to institutional investors in Australia and the United States. Consideration received from the issue of the ordinary shares was A\$15,748,255.
11. On April 15, 2014, we issued 14,717,999 ordinary shares and 6,623,105 unlisted options, as the second tranche of a private placement transacted over two tranches to institutional investors in Australia and the United States. Consideration received from the issue of the ordinary shares was A\$15,748,259.

In addition, we issued the following ordinary shares upon exercise of options over the past three fiscal years:

- 766,156 ordinary shares in fiscal 2015 (through March 31, 2015);
- 547,088 ordinary shares in fiscal 2014; and
- no ordinary shares in fiscal 2013.

## **Our Constitution**

Our Constitution is similar in nature to the bylaws of a U.S. corporation. It does not provide for or prescribe any specific objectives or purposes of Benitec. Our Constitution is subject to the terms of the ASX Listing Rules and the Corporations Act. It may be amended or repealed and replaced by special resolution of shareholders, which is a resolution passed by at least 75% of the votes cast by shareholders entitled to vote on the resolution.

Under Australian law, a company has the legal capacity and powers of an individual both within and outside Australia. The material provisions of our Constitution are summarized below. This summary is not intended to be complete nor to constitute a definitive statement of the rights and liabilities of our shareholders. Our Constitution is filed as an exhibit to the registration statement, of which this prospectus forms a part.

### ***Interested Directors***

A director may not vote in respect of any contract or arrangement in which the director has, directly or indirectly, any material interest according to our Constitution. Such director must not be counted in a quorum, must not vote on the matter and must not be present at the meeting while the matter is being considered. However, that director may execute or otherwise act in respect of that contract or arrangement notwithstanding any material personal interest.

Unless a relevant exception applies, the Corporations Act requires our directors to provide disclosure of certain interests or conflicts of interests and prohibits directors from voting on matters in which they have a material personal interest and from being present at the meeting while the matter is being considered. In addition, the Corporations Act and the ASX Listing Rules require shareholder approval of any provision of related party benefits to our directors.

### ***Directors' Compensation***

Our directors are paid remuneration for their services as directors (but excluding any remuneration payable to a director under any executive services contract with us or one of our related bodies corporate) which is

determined in a general meeting of shareholders. The aggregate, fixed sum for directors' remuneration is to be divided among the directors in such proportion as the directors themselves agree and in accordance with our Constitution. The fixed sum remuneration for directors may not be increased except at a general meeting of shareholders and the particulars of the proposed increase are required to have been provided to shareholders in the notice convening the meeting. In addition, executive directors may be paid remuneration as employees of Benitec.

Fees payable to our non-executive directors must be by way of a fixed sum and not by way of a commission on or a percentage of profits or operating revenue. Remuneration paid to our executive directors must also not include a commission or percentage of operating revenue.

Pursuant to our Constitution, any director who performs services that in the opinion of our board of directors, are outside the scope of the ordinary duties of a director may be paid extra remuneration, which is determined by our board of directors.

In addition to other remuneration provided in our Constitution, all of our directors are entitled to be paid by us for reasonable travel accommodation and other expenses incurred by the directors in attending general meetings, board meetings, committee meetings or otherwise in connection with our business.

In addition, in accordance with our Constitution, a director may be paid a retirement benefit as determined by our board of directors subject to the limits set out in the Corporations Act and the ASX Listing Rules which broadly restrict our ability to pay our officers a termination benefit in the event of a change of control of the Company or our subsidiaries as well as impose requirements for shareholder approval to be obtained to pay certain retirement benefits to our officers.

#### ***Borrowing Powers Exercisable by Directors***

Pursuant to our Constitution, the management and control of our business affairs are vested in our board of directors. Our board of directors has the power to raise or borrow money, and charge any of our property or business or any uncalled capital, and may issue debentures or give any other security for any of our debts, liabilities or obligations or of any other person, in each case, in the manner and on terms it deems fit.

#### ***Retirement of Directors***

Pursuant to our Constitution and the ASX Listing Rules, one-third of our directors, other than the managing director, must retire from office at every annual general meeting. If the number of directors is not a multiple of three, then the number nearest, to but not exceeding, one-third must retire from office. The directors who retire in this manner are required to be the directors or director longest in office since last being elected. A director, other than the director who is the Chief Executive Officer, must retire from office at the conclusion of the third annual general meeting after which the director was elected. Retired directors are eligible for a re-election to the board of directors unless disqualified from acting as a director under the Corporations Act or our Constitution.

#### ***Rights and Restrictions on Classes of Shares***

The rights attaching to our ordinary shares are detailed in our Constitution. Our Constitution provides that our directors may issue shares with preferred, deferred or other special rights, whether in relation to dividends, voting, return of share capital, or otherwise as our board of directors may determine. Subject to any approval which is required from our shareholders under the Corporations Act and the ASX Listing Rules (see “—Exemptions from Certain NASDAQ Corporate Governance Rules” and “—Change of Control”), any rights and restrictions attached to a class of shares, we may issue further shares on such terms and conditions as our board of directors resolve. Currently, our outstanding share capital consists of only one class of ordinary shares.



### ***Dividend Rights***

Our board of directors may from time to time determine to pay dividends to shareholders. All dividends unclaimed for one year after having been declared may be invested or otherwise made use of by our board of directors for our benefit until claimed or otherwise disposed of in accordance with our Constitution.

### ***Voting Rights***

Under our Constitution, and subject to any voting exclusions imposed under the ASX Listing Rules (which typically exclude parties from voting on resolutions in which they have an interest), the rights and restrictions attaching to a class of shares, each shareholder has one vote on a show of hands at a meeting of the shareholders unless a poll is demanded under the Constitution or the Corporations Act. On a poll vote, each shareholder shall have one vote for each fully paid share and a fractional vote for each share held by that shareholder that is not fully paid, such fraction being equivalent to the proportion of the amount that has been paid to such date on that share. Shareholders may vote in person or by proxy, attorney or representative. Under Australian law, shareholders of a public company are not permitted to approve corporate matters by written consent. Our Constitution does not provide for cumulative voting.

Note that ADS holders may not directly vote at a meeting of the shareholders but may instruct the depositary to vote the number of deposited ordinary shares their ADSs represent.

### ***Right To Share in Our Profits***

Pursuant to our Constitution, our shareholders are entitled to participate in our profits only by payment of dividends. Our board of directors may from time to time determine to pay dividends to the shareholders; however, no dividend is payable except in accordance with the thresholds set out in the Corporations Act.

### ***Rights to Share in the Surplus in the Event of Liquidation***

Our Constitution provides for the right of shareholders to participate in a surplus in the event of our liquidation, subject to the rights attaching to a class of shares.

### ***No Redemption Provision for Ordinary Shares***

There are no redemption provisions in our Constitution in relation to ordinary shares. Under our Constitution, any preference shares may be issued on the terms that they are, or may at our option be, liable to be redeemed.

### ***Variation or Cancellation of Share Rights***

Subject to the terms of issue of shares of that class, the rights attached to shares in a class of shares may only be varied or cancelled by a special resolution of Benitec, together with either:

- a special resolution passed by members holding shares in the class; or
- the written consent of members with at least 75% of the shares in the class.

### ***Directors May Make Calls***

Our Constitution provides that subject to the terms on which the shares have been issued directors may make calls on a shareholder for amounts unpaid on shares held by that shareholder, other than monies payable at fixed times under the conditions of allotment. Shares represented by the ADSs issued in this offering will be fully paid and will not be subject to calls by directors.

## **General Meetings of Shareholders**

General meetings of shareholders may be called by our board of directors. Except as permitted under the Corporations Act, shareholders may not convene a meeting. The Corporations Act requires the directors to call and arrange to hold a general meeting on the request of shareholders with at least 5% of the votes that may be cast at a general meeting or at least 100 shareholders who are entitled to vote at the general meeting. Notice of the proposed meeting of our shareholders is required at least 28 days prior to such meeting under the Corporations Act.

## **Foreign Ownership Regulation**

There are no limitations on the rights to own securities imposed by our Constitution. However, acquisitions and proposed acquisitions of securities in Australian companies may be subject to review and approval by the Australian Federal Treasurer under the Foreign Acquisitions and Takeovers Act 1975, or the FATA, which generally applies to acquisitions or proposed acquisitions:

- by a foreign person (as defined in the FATA) or associated foreign persons that would result in such persons having an interest in 15% or more of the issued shares of, or control of 15% or more of the voting power in, an Australian company; and
- by non-associated foreign persons that would result in such foreign person having an interest in 40% or more of the issued shares of, or control of 40% or more of the voting power in, an Australian company, where the Australian company is valued above the monetary threshold prescribed by FATA.

However, no such review or approval under the FATA is required if the foreign acquirer is a U.S. entity and the value of the target is less than A\$1,094 million.

The Australian Federal Treasurer may prevent a proposed acquisition in the above categories or impose conditions on such acquisition if the Treasurer is satisfied that the acquisition would be contrary to the national interest. If a foreign person acquires shares or an interest in shares in an Australian company in contravention of the FATA, the Australian Federal Treasurer may order the divestiture of such person's shares or interest in shares in that Australian company.

## **Ownership Threshold**

There are no provisions in our Constitution that require a shareholder to disclose ownership above a certain threshold. The Corporations Act, however, requires a shareholder to notify us and the ASX once it, together with its associates, acquires a 5% interest in our ordinary shares, at which point the shareholder will be considered to be a "substantial" shareholder. Further, once a shareholder owns a 5% interest in us, such shareholder must notify us and the ASX of any increase or decrease of 1% or more in its holding of our ordinary shares, and must also notify us and the ASX on its ceasing to be a "substantial" shareholder. Upon becoming a U.S. public company, our shareholders will also be subject to disclosure requirements under U.S. securities laws.

## **Issues of Shares and Change in Capital**

Subject to our Constitution, the Corporations Act, the ASX Listing Rules and any other applicable law, we may at any time issue shares and grant options or warrants on any terms, with preferred, deferred or other special rights and restrictions and for the consideration and other terms that the directors determine.

Subject to the requirements of our Constitution, the Corporations Act, the ASX Listing Rules and any other applicable law, including relevant shareholder approvals, we may consolidate or divide our share capital into a larger or smaller number by resolution, reduce our share capital (provided that the reduction is fair and reasonable to our shareholders as a whole and does not materially prejudice our ability to pay creditors) or buy back our ordinary shares whether under an equal access buy-back or on a selective basis.

## Change of Control

Takeovers of listed Australian public companies, such as Benitec, are regulated by the Corporations Act, which prohibits the acquisition of a “relevant interest” in issued voting shares in a listed company if the acquisition will lead to that person’s or someone else’s voting power in Benitec increasing from 20% or below to more than 20% or increasing from a starting point that is above 20% and below 90%, subject to a range of exceptions.

Generally, a person will have a relevant interest in securities if the person:

- is the holder of the securities;
- has power to exercise, or control the exercise of, a right to vote attached to the securities; or
- has the power to dispose of, or control the exercise of a power to dispose of, the securities, including any indirect or direct power or control.

If, at a particular time, a person has a relevant interest in issued securities and the person:

- has entered or enters into an agreement with another person with respect to the securities;
- has given or gives another person an enforceable right, or has been or is given an enforceable right by another person, in relation to the securities (whether the right is enforceable presently or in the future and whether or not on the fulfillment of a condition);
- has granted or grants an option to, or has been or is granted an option by, another person with respect to the securities; or
- the other person would have a relevant interest in the securities if the agreement were performed, the right enforced or the option exercised;

the other person is taken to already have a relevant interest in the securities.

There are a number of exceptions to the above prohibition on acquiring a relevant interest in issued voting shares above 20%. In general terms, some of the more significant exceptions include:

- when the acquisition results from the acceptance of an offer under a formal takeover bid;
- when the acquisition is conducted on market by or on behalf of the bidder under a takeover bid, the acquisition occurs during the bid period, the bid is for all the voting shares in a bid class and the bid is unconditional or only conditioned on prescribed matters set out in the Corporations Act;
- when shareholders of Benitec approve the takeover by resolution passed at general meeting;
- an acquisition by a person if, throughout the six months before the acquisition, that person or any other person has had voting power in Benitec of at least 19% and, as a result of the acquisition, none of the relevant persons would have voting power in Benitec more than three percentage points higher than they had six months before the acquisition;
- when the acquisition results from the issue of securities under a rights issue;
- when the acquisition results from the issue of securities under dividend reinvestment schemes;
- when the acquisition results from the issue of securities under underwriting arrangements;
- when the acquisition results from the issue of securities through operation of law;
- an acquisition that arises through the acquisition of a relevant interest in another listed company which is listed on a prescribed financial market or a financial market approved by ASIC;
- an acquisition arising from an auction of forfeited shares conducted on-market; or
- an acquisition arising through a compromise, arrangement, liquidation or buy-back.

Breaches of the takeovers provisions of the Corporations Act are criminal offenses. ASIC and the Australian Takeover Panel have a wide range of powers relating to breaches of takeover provisions, including the ability to make orders canceling contracts, freezing transfers of, and rights attached to, securities, and forcing a party to dispose of securities. There are certain defenses to breaches of the takeover provisions provided in the Corporations Act.

### **Access to and Inspection of Documents**

Inspection of our records is governed by the Corporations Act. Any member of the public has the right to inspect or obtain copies of our registers on the payment of a prescribed fee. Shareholders are not required to pay a fee for inspection of our registers or minute books of the meetings of shareholders. Other corporate records, including minutes of directors' meetings, financial records and other documents, are not open for inspection by shareholders. Where a shareholder is acting in good faith and an inspection is deemed to be made for a proper purpose, a shareholder may apply to the court to make an order for inspection of our books.

### **Exemptions from Certain NASDAQ Corporate Governance Rules**

The NASDAQ listing rules allow for a foreign private issuer, such as Benitec, to follow its home country practices in lieu of certain of the NASDAQ's corporate governance standards. In connection with our NASDAQ Listing Application, we expect to rely on exemptions from certain corporate governance standards that are contrary to the laws, rules, regulations or generally accepted business practices in Australia. These exemptions being sought are described below:

- We expect to rely on an exemption from the independence requirements for a majority of our board of directors as prescribed by NASDAQ Listing Rules. The ASX Listing Rules do not require us to have a majority of independent directors although ASX Corporate Governance Principles and Recommendations do recommend a majority of independent directors. During fiscal 2014, we did, however, have a majority of directors who were "independent" as defined in the ASX Corporate Governance Principles and Recommendations, which definition differs from NASDAQ's definition. Accordingly, because Australian law and generally accepted business practices in Australia regarding director independence differ to the independence requirements under NASDAQ Listing Rules, we seek to claim this exemption.
- We expect to rely on an exemption from the requirement that our independent directors meet regularly in executive sessions under NASDAQ Listing Rules. The ASX Listing Rules and the Corporations Act do not require the independent directors of an Australian company to have such executive sessions and, accordingly, we seek to claim this exemption.
- We expect to rely on an exemption from the quorum requirements applicable to meetings of shareholders under NASDAQ Listing Rules. In compliance with Australian law, our Constitution provides that three shareholders present, in person or by proxy, attorney or a representative, shall constitute a quorum for a general meeting. NASDAQ Listing Rules require that an issuer provide for a quorum as specified in its by-laws for any meeting of the holders of ordinary shares, which quorum may not be less than 33 1/3% of the outstanding shares of an issuer's voting ordinary shares. Accordingly, because applicable Australian law and rules governing quorums at shareholder meetings differ from NASDAQ's quorum requirements, we seek to claim this exemption.
- We expect to rely on an exemption from the requirement prescribed by NASDAQ Listing Rules that issuers obtain shareholder approval prior to the issuance of securities in connection with certain acquisitions, private placements of securities, or the establishment or amendment of certain stock option, purchase or other compensation plans. Applicable Australian law and the ASX Listing Rules differ from NASDAQ requirements, with the ASX Listing Rules providing generally for prior shareholder approval in numerous circumstances, including (i) issuance of equity securities exceeding 15% of our issued share capital in any 12-month period (but, in determining the 15% limit, securities issued under an exception to the rule or with shareholder approval are not counted), (ii) issuance of equity securities to related parties

(as defined in the ASX Listing Rules) and (iii) issuances of securities to directors or their associates under an employee incentive plan. Due to differences between Australian law and rules and the NASDAQ shareholder approval requirements, we seek to claim this exemption.

## DESCRIPTION OF AMERICAN DEPOSITARY SHARES

### American Depositary Shares

The Bank of New York Mellon, as depositary, will register and deliver American Depositary Shares, also referred to as ADSs. Each ADS will represent 20 ordinary shares (or a right to receive 20 ordinary shares) deposited with National Australia Bank Limited, as custodian for the depositary. Each ADS will also represent any other securities, cash or other property which may be held by the depositary. The depositary's office at which the ADSs will be administered is located at 101 Barclay Street, New York, New York 10286. The Bank of New York Mellon's principal executive office is located at One Wall Street, New York, New York 10286.

You may hold ADSs either (A) directly (i) by having an American Depositary Receipt, also referred to as an ADR, which is a certificate evidencing a specific number of ADSs, registered in your name, or (ii) by having ADSs registered in your name in the Direct Registration System, or (B) indirectly by holding a security entitlement in ADSs through your broker or other financial institution. If you hold ADSs directly, you are a registered ADS holder, or ADS holder. This description assumes you are an ADS holder. If you hold the ADSs indirectly, you must rely on the procedures of your broker or other financial institution to assert the rights of ADS holders described in this section. You should consult with your broker or financial institution to find out what those procedures are.

The Direct Registration System, or DRS, is a system administered by The Depository Trust Company, also referred to as DTC, pursuant to which the depositary may register the ownership of uncertificated ADSs, which ownership is confirmed by periodic statements sent by the depositary to the registered holders of uncertificated ADSs.

As an ADS holder, we will not treat you as one of our shareholders and you will not have shareholder rights. Australian law governs shareholder rights. The depositary will be the holder of the shares underlying your ADSs. As a registered holder of ADSs, you will have ADS holder rights. A deposit agreement among us, the depositary and you, as an ADS holder, and all other persons directly or indirectly holding ADSs sets out ADS holder rights as well as the rights and obligations of the depositary. New York law governs the deposit agreement and the ADSs.

The following is a summary of the material provisions of the deposit agreement. Because it is a summary, it does not contain all the information that may be important to you. For more complete information, you should read the entire deposit agreement and the form of ADR which summarizes certain terms of your ADSs. A copy of the deposit agreement is filed as an exhibit to the registration statement of which this prospectus forms a part. You may also obtain a copy of the deposit agreement at the SEC's Public Reference Room which is located at 100 F Street, NE, Washington, DC 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-732-0330. You may also find the registration statement and the deposit agreement on the SEC's website at <http://www.sec.gov>.

### Dividends and Other Distributions

#### *How will you receive dividends and other distributions on the shares?*

The depositary has agreed to pay to you the cash dividends or other distributions it or the custodian receives on shares or other deposited securities, after deducting its fees and expenses. You will receive these distributions in proportion to the number of ordinary shares your ADSs represent.

- **Cash.** The depositary will convert any cash dividend or other cash distribution we pay on the shares into U.S. dollars, if it can do so on a reasonable basis and can transfer the U.S. dollars to the United States. If that is not possible or if any government approval is needed and can not be obtained, the deposit agreement allows the depositary to distribute the foreign currency only to those ADS holders to whom it is possible to do so. It will hold the foreign currency it cannot convert for the account of the ADS holders who have not been paid. It will not invest the foreign currency and it will not be liable for any interest.

Before making a distribution, any withholding taxes, or other governmental charges that must be paid will be deducted. See “Taxation.” It will distribute only whole U.S. dollars and cents and will round fractional cents to the nearest whole cent. If the exchange rates fluctuate during a time when the depositary cannot convert the foreign currency, you may lose some or all of the value of the distribution.

- **Shares.** The depositary may distribute additional ADSs representing any shares we distribute as a dividend or free distribution to the extent reasonably practicable and permitted under law. The depositary will only distribute whole ADSs. It will try to sell shares which would require it to deliver a fractional ADS and distribute the net proceeds in the same way as it does with cash. If the depositary does not distribute additional ADSs, the outstanding ADSs will also represent the new shares. The depositary may sell a portion of the distributed shares sufficient to pay its fees and expenses in connection with that distribution.
- **Rights to purchase additional shares.** If we offer holders of our securities any rights to subscribe for additional shares or any other rights, the depositary may make these rights available to you. If the depositary decides it is not legal and practical to make the rights available but that it is practical to sell the rights, the depositary will use reasonable efforts to sell the rights and distribute the proceeds in the same way as it does with cash. The depositary will allow rights that are not distributed or sold to lapse. In that case, you will receive no value for such rights.

If the depositary makes rights available to ADS holders, it will exercise the rights and purchase the shares on your behalf all in accordance with your instructions. The depositary will then deposit the shares and deliver ADSs to you. It will only exercise rights if you pay the exercise price and any other charges the rights require you to pay and comply with other applicable instructions.

U.S. securities laws may restrict transfers and cancellation of the ADSs representing shares purchased upon exercise of rights. For example, you may not be able to trade such ADSs freely in the United States. In this case, the depositary may deliver restricted depositary shares that have the same terms as the ADSs described in this section except for changes needed to put the necessary restrictions in place.

- **Other Distributions.** The depositary will send to you anything else we distribute on deposited securities by any means it determines is legal, fair and practical. If it cannot make the distribution in that way, the depositary may adopt another legal, fair and practical method. It may decide to sell what we distributed and distribute the net proceeds in the same way as it does with cash. Or, it may decide to hold what we distributed, in which case ADSs will also represent the newly distributed property. However, the depositary is not required to distribute any securities (other than ADSs) to ADS holders unless it receives reasonably satisfactory evidence from us that it is legal to make that distribution. The depositary may sell a portion of the distributed securities or property sufficient to pay its fees and expenses in connection with that distribution.

The depositary is not responsible if it decides that it is unlawful or impractical to make a distribution available to any ADS holders. We have no obligation to register ADSs, shares, rights or other securities under the Securities Act. We also have no obligation to take any other action to permit the distribution of ADSs, shares, rights or any other property to ADS holders. This means that you may not receive the distributions we make on our ordinary shares or any value for them if it is illegal or impractical for us to make them available to you.

## **Deposit, Withdrawal and Cancellation**

### ***How are ADSs issued?***

The depositary will deliver ADSs if you or your broker deposit shares or evidence of rights to receive shares with the custodian. Upon payment of its fees and expenses and of any taxes or charges, such as stamp taxes or share transfer taxes or fees, the depositary will register the appropriate number of ADSs in the names you request and will deliver the ADSs to or upon the order of the person or persons that made the deposit.

***How can ADS holders withdraw the deposited securities?***

You may surrender your ADSs at the depositary's office. Upon payment of its fees and expenses and of any taxes or charges, such as stamp taxes or share transfer taxes or fees, the depositary will deliver the shares and any other deposited securities underlying the ADSs to the ADS holder or a person designated by you at the office of the custodian. In the alternative, at your request, risk and expense, the depositary will deliver the deposited securities at its office, if feasible.

***How do ADS holders interchange between certificated ADSs and uncertificated ADSs?***

You may surrender your ADR to the depositary for the purpose of exchanging your ADR for uncertificated ADSs. The depositary will cancel that ADR and will send to you a statement confirming that you are the registered holder of uncertificated ADSs. Alternatively, upon receipt by the depositary of a proper instruction from a registered holder of uncertificated ADSs requesting the exchange of uncertificated ADSs for certificated ADSs, the depositary will execute and deliver to you an ADR evidencing those ADSs.

**Voting Rights**

***How do you vote?***

You may instruct the depositary to vote the number of deposited ordinary shares your ADSs represent. The depositary will notify you of shareholders' meetings and arrange to deliver our voting materials to you upon our request. Those materials will describe the matters to be voted on and explain how ADS holders may instruct the depositary how to vote. For instructions to be valid, they must reach the depositary by a date established by the depositary.

***Otherwise, you won't be able to exercise your right to vote unless you withdraw the shares underlying the ADSs. However, you may not know about the meeting with a sufficient amount of advance notice to withdraw the shares.***

The depositary will attempt, as far as practical, subject to the laws of Australia and of our Constitution or similar documents, to vote or to have its agents vote the shares or other deposited securities represented by your ADSs as instructed by ADS holders. The depositary will only vote or attempt to vote as instructed.

We cannot assure you that you will receive the voting materials in time to ensure that you can instruct the depositary to vote your ordinary shares. In addition, the depositary and its agents are not responsible for failing to carry out voting instructions or for the manner of carrying out voting instructions. This means that you may not be able to exercise your right to vote and there may be nothing you can do if your ordinary shares are not voted as you requested.

In order to give you a reasonable opportunity to instruct the depositary as to the exercise of voting rights relating to deposited securities, if we request the depositary to act, we agree to give the depositary notice of any such meeting and details concerning the matters to be voted upon at least 30 days in advance of the meeting date.



## Fees and Expenses

### Persons depositing or withdrawing ordinary shares or ADS holders must pay the depositary:

\$5.00 (or less) per 100 ADSs (or portion of 100 ADSs)

\$.05 (or less) per ADS

A fee equivalent to the fee that would be payable if securities distributed to you had been shares and the shares had been deposited for issuance of ADSs

\$.05 (or less) per ADS per calendar year

Registration or transfer fees

Expenses of the depositary

Taxes and other governmental charges the depositary or the custodian have to pay on any ADS or share underlying an ADS, for example, stock transfer taxes, stamp duty or withholding taxes

Any charges incurred by the depositary or its agents for servicing the deposited securities

### For:

- Issuance of ADSs, including issuances resulting from a distribution of shares or rights or other property
- Cancellation of ADSs for the purpose of withdrawal, including if the deposit agreement terminates
- Any cash distribution to you
- Distribution of securities distributed to holders of deposited securities which are distributed by the depositary to you
- Depositary services
- Transfer and registration of shares on our share register to or from the name of the depositary or its agent when you deposit or withdraw shares
- Cable, telex and facsimile transmissions (when expressly provided in the deposit agreement)
- Converting foreign currency to U.S. dollars
- As necessary
- As necessary

The depositary collects its fees for delivery and surrender of ADSs directly from investors depositing shares or surrendering ADSs for the purpose of withdrawal or from intermediaries acting for them. The depositary collects fees for making distributions to investors by deducting those fees from the amounts distributed or by selling a portion of distributable property to pay the fees. The depositary may collect its annual fee for depositary services by deduction from cash distributions or by directly billing investors or by charging the book-entry system accounts of participants acting for them. The depositary may generally refuse to provide fee-attracting services until its fees for those services are paid. The depositary may collect any of its fees by deduction from any cash distribution payable to you that are obligated to pay those fees.

From time to time, the depositary may make payments to us to reimburse or share revenue from the fees collected from you, or waive fees and expenses for services provided, generally relating to costs and expenses arising out of establishment and maintenance of the ADS program. In performing its duties under the deposit agreement, the depositary may use brokers, dealers or other service providers that are affiliates of the depositary and that may earn or share fees or commissions.

## Payment of Taxes

You will be responsible for any taxes or other governmental charges payable on your ADSs or on the deposited securities represented by any of your ADSs. The depositary may refuse to register any transfer of your

ADSs or allow you to withdraw the deposited securities represented by your ADSs until such taxes or other charges are paid. It may apply payments owed to you or sell deposited securities represented by your ADSs to pay any taxes owed and you will remain liable for any deficiency. If the depositary sells deposited securities, it will, if appropriate, reduce the number of ADSs to reflect the sale and pay to you any proceeds, or send to ADS holders any property, remaining after it has paid the taxes.

### **Reclassifications, Recapitalizations and Mergers**

**If we:**

- Reclassify, split up or consolidate any of the deposited securities
- Distribute securities in respect of deposited shares that are not distributed to you
- Recapitalize, reorganize, merge, liquidate, sell all or substantially all of our assets, or take any similar action

**Then:**

The cash, shares or other securities received by the depositary will become deposited securities. Each ADS will automatically represent its equal share of the new deposited securities.

The depositary may distribute some or all of the cash, shares or other securities it received. It may also ask you to surrender your outstanding ADRs in exchange for new ADRs identifying the new deposited securities.

### **Amendment and Termination**

***How may the deposit agreement be amended?***

We may agree with the depositary to amend the deposit agreement and the ADRs without your consent for any reason. If an amendment adds or increases fees or charges, except for taxes and other governmental charges or expenses of the depositary for registration fees, facsimile costs, delivery charges or similar items, or prejudices a substantial right of ADS holders, it will not become effective for outstanding ADSs until 30 days after the depositary notifies ADS holders of the amendment. At the time an amendment becomes effective, you are considered, by continuing to hold your ADSs, to agree to the amendment and to be bound by the ADRs and the deposit agreement as amended.

***How may the deposit agreement be terminated?***

The depositary will terminate the deposit agreement at our direction by mailing notice of termination to the ADS holders then outstanding at least 30 days prior to the date fixed in such notice for such termination. The depositary may also terminate the deposit agreement by mailing notice of termination to us and the ADS holders if 60 days have passed since the depositary told us it wants to resign but a successor depositary has not been appointed and accepted its appointment.

After termination, the depositary and its agents will do the following under the deposit agreement (but nothing else):

- collect distributions on the deposited securities;
- sell rights and other property; and
- deliver shares and other deposited securities upon cancellation of ADSs.

Four months after termination, the depositary may sell any remaining deposited securities by public or private sale. After that, the depositary will hold the money it received on the sale, as well as any other cash it is holding under the deposit agreement for the pro rata benefit of the ADS holders that have not surrendered their ADSs. It will not invest the money and has no liability for interest. The depositary's only obligations will be to account for the money and other cash. After termination our only obligations will be to indemnify the depositary and to pay fees and expenses of the depositary that we agreed to pay.

## **Limitations on Obligations and Liability**

### *Limits on our Obligations and the Obligations of the Depositary; Limits on Liability to Holders of ADSs*

The deposit agreement expressly limits our obligations and the obligations of the depositary. It also limits our liability and the liability of the depositary. We and the depositary:

- are only obligated to take the actions specifically set forth in the deposit agreement;
- are not liable if we are or it is prevented or delayed by law or circumstances beyond our control from performing our or its obligations under the deposit agreement;
- are not liable if we or it exercises discretion permitted under the deposit agreement;
- are not liable for the inability of any holder of ADSs to benefit from any distribution on deposited securities that is not made available to holders of ADSs under the terms of the deposit agreement, or for any special, consequential or punitive damages for any breach of the terms of the deposit agreement;
- have no obligation to become involved in a lawsuit or other proceeding related to the ADSs or the deposit agreement on your behalf or on behalf of any other person;
- may rely upon any documents we believe or it believes in good faith to be genuine and to have been signed or presented by the proper person.

In the deposit agreement, we and the depositary agree to indemnify each other under certain circumstances.

## **Requirements for Depositary Actions**

Before the depositary will deliver or register a transfer of an ADS, make a distribution on an ADS, or permit withdrawal of shares, the depositary may require:

- payment of stock transfer or other taxes or other governmental charges and transfer or registration fees charged by third parties for the transfer of any shares or other deposited securities;
- satisfactory proof of the identity and genuineness of any signature or other information it deems necessary; and
- compliance with regulations it may establish, from time to time, consistent with the deposit agreement, including presentation of transfer documents.

The depositary may refuse to deliver ADSs or register transfers of ADSs generally when the transfer books of the depositary or our transfer books are closed or at any time if the depositary or we think it advisable to do so.

## **Your Right to Receive the Shares Underlying your ADSs**

You have the right to cancel their ADSs and withdraw the underlying shares at any time except:

- when temporary delays arise because: (i) the depositary has closed its transfer books or we have closed our transfer books; (ii) the transfer of shares is blocked to permit voting at a shareholders' meeting; or (iii) we are paying a dividend on our ordinary shares;
- when you owe money to pay fees, taxes and similar charges; and
- when it is necessary to prohibit withdrawals in order to comply with any laws or governmental regulations that apply to ADSs or to the withdrawal of ordinary shares or other deposited securities.

This right of withdrawal may not be limited by any other provision of the deposit agreement.

### **Pre-Release of ADSs**

The deposit agreement permits the depositary to deliver ADSs before deposit of the underlying ordinary shares. This is called a pre-release of the ADSs. The depositary may also deliver shares upon cancellation of pre-released ADSs (even if the ADSs are canceled before the pre-release transaction has been closed out). A pre-release is closed out as soon as the underlying shares are delivered to the depositary. The depositary may receive ADSs instead of shares to close out a pre-release. The depositary may pre-release ADSs only under the following conditions:

- before or at the time of the pre-release, the person to whom the pre-release is being made represents to the depositary in writing that it or its customer owns the shares or ADSs to be deposited;
- the pre-release is fully collateralized with cash, U.S. government securities or other collateral that the depositary considers appropriate; and
- the depositary must be able to close out the pre-release on not more than five business days' notice.

In addition, the depositary has agreed to limit the number of ADSs that may be outstanding at any time as a result of pre-release to 30% of the shares deposited under the deposit agreement, although the depositary may disregard the limit from time to time, if it thinks it is reasonably appropriate to do so.

### **Direct Registration System**

In the deposit agreement, all parties to the deposit agreement acknowledge that the DRS and Profile Modification System, or Profile, will apply to uncertificated ADSs upon acceptance thereof to DRS by DTC. DRS is the system administered by DTC under which the depositary may register the ownership of uncertificated ADSs, which ownership will be evidenced by periodic statements sent by the depositary to the registered holders of uncertificated ADSs. Profile is a required feature of DRS that allows a DTC participant, claiming to act on behalf of a registered holder of ADSs, to direct the depositary to register a transfer of those ADSs to DTC or its nominee and to deliver those ADSs to the DTC account of that DTC participant without receipt by the depositary of prior authorization from the ADS holder to register that transfer.

In connection with and in accordance with the arrangements and procedures relating to DRS/Profile, the parties to the deposit agreement understand that the depositary will not determine whether the DTC participant that is claiming to be acting on behalf of an ADS holder in requesting registration of transfer and delivery described in the paragraph above has the actual authority to act on behalf of the ADS holder (notwithstanding any requirements under the Uniform Commercial Code). In the deposit agreement, the parties agree that the depositary's reliance on and compliance with instructions received by the depositary through the DRS/Profile System and in accordance with the deposit agreement will not constitute negligence or bad faith on the part of the depositary.

### **Shareholder Communications; Inspection of Register of Holders of ADSs**

The depositary will make available for your inspection at its office all communications that it receives from us as a holder of deposited securities that we make generally available to holders of deposited securities. The depositary will send you copies of those communications if we ask it to. You have a right to inspect the register of holders of ADSs, but not for the purpose of contacting those holders about a matter unrelated to our business or the ADSs.

### **Disclosure of Interests**

We may from time to time request ADS holders to provide information as to the capacity in they own or owned ADSs and regarding the identity of any other persons then or previously interested in such ADSs and the nature of such interest. Each ADS holder agrees to provide any information of that kind that is requested by us or the depositary. To the extent that provisions of or governing the deposited securities or the rules or regulations of any governmental authority or securities exchange or automated quotation system may require the disclosure of beneficial or other ownership of deposited securities, other shares and other securities to us or other persons and may provide for blocking transfer and voting or other rights to enforce such disclosure or limit such ownership, the depositary has agreed to use its reasonable efforts to comply with our written instructions in respect of any such enforcement or limitation.

## SHARES ELIGIBLE FOR FUTURE SALE

Upon completion of this offering, there will be outstanding \_\_\_\_\_ ordinary shares, including shares underlying the ADSs, and \_\_\_\_\_ ADSs, representing approximately \_\_\_\_\_ % of our outstanding ordinary shares.

Future sales of substantial amounts of our ordinary shares or ADSs in the public market in the United States or in Australia, including ordinary shares issued upon exercise of outstanding options, or the possibility of such sales, could negatively affect the market price in the United States of the ADSs and our ability to raise equity capital in the future.

All of the ADSs sold in the offering will be freely transferable in the United States by persons other than our “affiliates,” as that term is defined in Rule 144 under the Securities Act. As defined in Rule 144, an “affiliate” of an issuer is a person that directly, or indirectly through one or more intermediaries, controls, or is controlled by, or is under common control with, the issuer. ADSs purchased by one of our affiliates may not be resold, except pursuant to an effective registration statement or an exemption from registration, including Rule 144 under the Securities Act (as described below).

### Lock-up Agreements

We and our executive officers and directors have generally agreed not to sell or transfer any ordinary shares, ADSs or other capital stock of Benitec or securities convertible into or exchangeable or exercisable for ordinary shares, ADSs or other capital stock of Benitec, for 180 days after the date of the underwriting agreement without first obtaining the written consent of BMO Capital Markets Corp. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer to sell, sell, pledge, contract to sell, purchase any option to sell, grant any option for the purchase of, lend, or otherwise dispose of directly or indirectly, including the filing or participation in a filing with the SEC of a registration statement under the Securities Act to register, any of our ordinary shares or ADSs or any securities convertible into, or exercisable or exchangeable for our ordinary shares, ADSs, options or warrants or other rights to acquire ordinary shares or ADSs; or
- enter into any swap or other agreement, arrangement, hedge or transaction that transfers, in whole or in part, directly or indirectly, the economic benefits or risks of ownership of any ordinary shares, ADSs or other capital stock or any securities convertible into or exercisable or exchangeable for ordinary shares, ADSs or other capital stock.

For more detail on the lock-up agreements, see “Underwriting.”

### Rule 144

In general, under Rule 144 of the Securities Act and beginning 90 days after the date of this prospectus, a person who is not deemed to have been our affiliate at any time during the three months preceding a sale and who has beneficially owned “restricted securities” within the meaning of Rule 144 for more than six months would be entitled to sell an unlimited number of shares, subject only to the availability of current public information about us. A non-affiliate who has beneficially owned “restricted securities” for at least one year from the later of the date these shares were acquired from us or from our affiliate would be entitled to freely sell those shares.

A person who is deemed to be an affiliate of ours and who has beneficially owned “restricted securities” for at least six months would be entitled to sell, within any three-month period, a number of shares that is not more than the greater of:

- 1.0% of the number of our ordinary shares then outstanding; or
- the average weekly reported trading volume of our ordinary shares on NASDAQ during the four calendar weeks preceding the date on which a notice of the sale on Form 144 is filed with the SEC by such person.

Sales under Rule 144 of the Securities Act by persons who are deemed to be our affiliates are also subject to manner-of-sale provisions, notice requirements and the availability of current public information about us as specified in Rule 144. In addition, in each case, these shares would remain subject to lock-up arrangements and would only become eligible for sale when the lock-up period expires.

### **Regulation S**

Regulation S provides generally that sales made in offshore transactions are not subject to the registration or prospectus delivery requirements of the Securities Act.

### **Rule 701**

In general, under Rule 701 of the Securities Act, each of our employees, consultants or advisors who purchases our ordinary shares from us in connection with a compensatory stock plan or other written agreement executed prior to the completion of this offering is eligible to resell such ordinary shares in reliance on Rule 144, but without compliance with some of the restrictions, including the holding period, contained in Rule 144.

### **Equity Incentive Plans**

We intend to file with the SEC a registration statement on Form S-8 under the Securities Act covering the ordinary shares reserved for issuance under our equity incentive plans. The registration statement is expected to be filed and become effective as soon as practicable after the closing of this offering. Accordingly, shares registered under the Form S-8 registration statement will be available for sale in the open market following the registration statement's effective date, subject to Rule 144 volume limitations and the lock-up agreements described above, if applicable.

## TAXATION

*The following is a summary of material U.S. federal and Australian income tax considerations to U.S. holders, as defined below, of the acquisition, ownership and disposition of ordinary shares and ADSs. This discussion is based on the laws in force as of the date of this registration statement, and is subject to changes in the relevant income tax law, including changes that could have retroactive effect. The following summary does not take into account or discuss the tax laws of any country or other taxing jurisdiction other than the United States and Australia. Holders are advised to consult their tax advisors concerning the overall tax consequences of the acquisition, ownership and disposition of ordinary shares and ADSs in their particular circumstances. This discussion is not intended, and should not be construed, as legal or professional tax advice.*

*This summary does not address the 3.8% U.S. Federal Medicare Tax on net investment income, the effects of U.S. federal estate and gift tax laws, the alternative minimum tax, or any state and local tax considerations within the United States, and is not a comprehensive description of all U.S. federal or Australian income tax considerations that may be relevant to a decision to acquire or dispose of ordinary shares or ADSs. Furthermore, this summary does not address U.S. federal or Australian income tax considerations relevant to holders subject to taxing jurisdictions other than, or in addition to, the United States and Australia, and does not address all possible categories of holders, some of which may be subject to special tax rules.*

### U.S. Federal Income Tax Considerations

The following summary describes the material U.S. federal income tax consequences to U.S. holders (as defined below) of the acquisition, ownership and disposition of our ordinary shares and ADSs as of the date hereof. Subject to the qualifications, assumptions and limitations set forth herein, this discussion of the material U.S. federal income tax consequences to U.S. holders of our ordinary shares and ADSs represents the opinion of Baker & McKenzie LLP, our U.S. counsel. Except where noted, this summary deals only with ordinary shares or ADSs acquired in the initial offering and held as capital assets within the meaning of Section 1221 of the Internal Revenue Code of 1986, as amended (the “Code”). This section does not discuss the tax consequences to any particular holder, nor any tax considerations that may apply to holders subject to special tax rules, such as:

- insurance companies;
- financial institutions;
- individual retirement and other tax-deferred accounts;
- regulated investment companies;
- real estate investment trusts;
- individuals who are former U.S. citizens or former long-term U.S. residents;
- brokers or dealers in securities or currencies;
- traders that elect to use a mark-to-market method of accounting;
- investors in pass-through entities for U.S. federal income tax purposes;
- tax-exempt entities;
- persons that hold ordinary shares or ADSs as a position in a straddle or as part of a hedging, constructive sale or conversion transaction for U.S. federal income tax purposes;
- persons that have a functional currency other than the U.S. dollar;
- persons that own (directly, indirectly or constructively) 10% or more of our equity; or
- persons that are not U.S. holders (as defined below).

In this section, a “U.S. holder” means a beneficial owner of ordinary shares or ADSs that is, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation created or organized in or under the laws of the United States or any state thereof or the District of Columbia;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust (i) the administration of which is subject to the primary supervision of a court in the United States and for which one or more U.S. persons have the authority to control all substantial decisions or (ii) that has an election in effect under applicable income tax regulations to be treated as a U.S. person.

As used in this section, a “non-U.S. holder” is a beneficial owner of ordinary shares or ADSs that is not a U.S. holder or an entity or arrangement treated as a partnership for U.S. federal income tax purposes.

The discussion below is based upon the provisions of the Code, and the U.S. Treasury regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be replaced, revoked or modified, possibly with retroactive effect, so as to result in U.S. federal income tax consequences different from those discussed below. In addition, this summary is based, in part, upon representations made by the depository to us and assumes that the deposit agreement, and all other related agreements, will be performed in accordance with their terms.

If an entity or arrangement treated as a partnership for U.S. federal income tax purposes acquires, owns or disposes of ordinary shares or ADSs, the U.S. federal income tax treatment of a partner generally will depend on the status of the partner and the activities of the partnership. Partners of partnerships that acquire, own or dispose of ordinary shares or ADSs should consult their tax advisors.

***You are urged to consult your own tax advisor with respect to the U.S. federal, as well as state, local and non-U.S., tax consequences to you of acquiring, owning and disposing of ordinary shares or ADSs in light of your particular circumstances, including the possible effects of changes in U.S. federal and other tax laws.***

#### **ADSs**

If you hold ADSs, you generally will be treated, for U.S. federal income tax purposes, as the owner of the underlying ordinary shares that are represented by such ADSs. Accordingly, deposits or withdrawals of ordinary shares for ADSs will not be subject to U.S. federal income tax.

#### **Distributions**

Subject to the passive foreign investment company rules discussed below, U.S. holders generally will include as dividend income the U.S. dollar value of the gross amount of any distributions of cash or property (without deduction for any withholding tax), other than certain pro rata distributions of ordinary shares, with respect to ordinary shares to the extent the distributions are made from our current or accumulated earnings and profits, as determined for U.S. federal income tax purposes. A U.S. holder will include the dividend income on the day actually or constructively received by the holder, in the case of ordinary shares, or by the depository, in the case of ADSs. To the extent, if any, that the amount of any distribution by us exceeds our current and accumulated earnings and profits, as so determined, the excess will be treated first as a tax-free return of the U.S. holder’s tax basis in the ordinary shares or ADSs and thereafter as capital gain. Notwithstanding the foregoing, we do not intend to maintain calculations of earnings and profits, as determined for U.S. federal income tax purposes. Consequently, any distributions generally will be reported as dividend income for U.S. information reporting purposes. See “Backup Withholding Tax and Information Reporting Requirements” below. Dividends paid by us will not be eligible for the dividends-received deduction generally allowed to U.S. corporate shareholders.



Subject to certain exceptions for short-term and hedged positions, the U.S. dollar amount of dividends received by an individual, trust or estate with respect to the ordinary shares or ADSs will be subject to taxation at a maximum rate of 20% if the dividends are “qualified dividends.” Dividends will be treated as qualified dividends (a) if certain holding period requirements are satisfied, (b) if the Treaty is a qualified treaty and we are eligible for benefits under the Agreement between the Government of the United States of America and the Government of Australia for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with Respect to Taxes on Income (the “Treaty”) or our ordinary shares or ADSs are readily tradable on a U.S. securities market, and (c) provided that we were not, in the taxable year prior to the year in which the dividend was paid, and are not, in the taxable year in which the dividend is paid, a PFIC. The Treaty has been approved for the purposes of the qualified dividend rules and we have applied to list the ADSs on NASDAQ. We do not believe we were a PFIC in 2014 and do not expect to be a PFIC for 2015. However, our status in the current year and future years will depend in part upon our use of the funds from the offering, as well as our income and assets (which for this purpose depends in part on the market value of our shares) in those years. See the discussion below under “—Passive Foreign Investment Company”. You should consult your tax adviser regarding the availability of the reduced tax rate on qualified dividends.

Includible distributions paid in Australian dollars, including any Australian withholding taxes, will be included in the gross income of a U.S. holder in a U.S. dollar amount calculated by reference to the spot exchange rate in effect on the date of actual or constructive receipt, regardless of whether the Australian dollars are converted into U.S. dollars at that time. If Australian dollars are converted into U.S. dollars on the date of actual or constructive receipt, the tax basis of the U.S. holder in those Australian dollars will be equal to their U.S. dollar value on that date and, as a result, a U.S. holder generally should not be required to recognize any foreign exchange gain or loss.

If Australian dollars so received are not converted into U.S. dollars on the date of receipt, the U.S. holder will have a basis in the Australian dollars equal to their U.S. dollar value on the date of receipt. Any gain or loss on a subsequent conversion or other disposition of the Australian dollars generally will be treated as ordinary income or loss to such U.S. holder and generally will be income or loss from sources within the United States for foreign tax credit limitation purposes.

Dividends received by a U.S. holder with respect to ordinary shares or ADSs will be treated as foreign source income, which may be relevant in calculating the holder’s foreign tax credit limitation. The limitation on foreign taxes eligible for credit is calculated separately with respect to specific classes of income. For these purposes, dividends generally will be categorized as “passive” or “general” income depending on a U.S. holder’s circumstance.

Subject to certain complex limitations, a U.S. holder generally will be entitled, at its option, to claim either a credit against its U.S. federal income tax liability or a deduction in computing its U.S. federal taxable income in respect of any Australian taxes withheld. If a U.S. holder elects to claim a deduction, rather than a foreign tax credit, for Australian taxes withheld for a particular taxable year, the election will apply to all foreign taxes paid or accrued by or on behalf of the U.S. holder in the particular taxable year.

You may not be able to claim a foreign tax credit (and instead may claim a deduction) for non-U.S. taxes imposed on dividends paid on the ordinary shares or ADSs if you (i) have held the ordinary shares or ADSs for less than a specified minimum period during which you are not protected from risk of loss with respect to such shares, or (ii) are obligated to make payments related to the dividends (for example, pursuant to a short sale).

The availability of the foreign tax credit and the application of the limitations on its availability are fact specific and are subject to complex rules. You are urged to consult your own tax advisor as to the consequences of Australian withholding taxes and the availability of a foreign tax credit or deduction. See “Australian Tax Considerations—*Taxation of Dividends*.”

### ***Sale, Exchange or other Disposition of Ordinary Shares or ADSs***

Subject to the passive foreign investment company rules discussed below, a U.S. holder generally will, for U.S. federal income tax purposes, recognize capital gain or loss on a sale, exchange or other disposition of ordinary shares or ADSs equal to the difference between the amount realized on the disposition and the U.S. holder's tax basis (in U.S. dollars) in the ordinary shares or ADSs. This recognized gain or loss will generally be long-term capital gain or loss if the U.S. holder has held the ordinary shares or ADSs for more than one year. Generally, for U.S. holders who are individuals (as well as certain trusts and estates), long-term capital gains are subject to U.S. federal income tax at preferential rates. For foreign tax credit limitation purposes, gain or loss recognized upon a disposition generally will be treated as from sources within the United States. However, in limited circumstances, the Treaty can re-source U.S. source income as Australian source income. The deductibility of capital losses is subject to limitations for U.S. federal income tax purposes.

You should consult your own tax advisor regarding the availability of a foreign tax credit or deduction in respect of any Australian tax imposed on a sale or other disposition of ordinary shares or ADSs. See "Australian Tax Considerations—*Tax on Sales or other Dispositions of Shares.*"

### ***Passive Foreign Investment Company***

The Code provides special, generally adverse, rules regarding certain distributions received by U.S. holders with respect to, and sales, exchanges and other dispositions, including pledges, of, shares of stock of a PFIC. A foreign corporation will be a PFIC for any taxable year if at least 75% of its gross income for the taxable year is passive income or at least 50% of its gross assets during the taxable year, based on a quarterly average and generally by value, produce or are held for the production of passive income. Passive income for this purpose generally includes, among other things, dividends, interest, rents, royalties, gains from commodities and securities transactions and gains from the disposition of assets that produce or are held for the production of passive income. In determining whether a foreign corporation is a PFIC, a pro-rata portion of the income and assets of each corporation in which it owns, directly or indirectly, at least a 25% interest (by value) is taken into account.

Based on our business results for the last fiscal year and the composition of our assets, we believe that we were not a PFIC for U.S. federal income tax purposes for the taxable year ended June 30, 2014. Similarly, based on our business projections and the anticipated composition of our assets for the current and future years, we expect that we will also not be a PFIC for the taxable year ending June 30, 2015. However, the determination of PFIC status is a factual determination that must be made annually at the close of each taxable year and therefore, there can be no certainty as to our status for a taxable year until the close of that taxable year. Our status could change depending, among other things, upon a decrease in the trading price of our ordinary shares or ADSs, how quickly we make use of the proceeds from the offering, as well as changes in the composition and relative values of our assets and the composition of our income. Moreover, the rules governing whether certain assets are active or passive are complex and in some cases their application can be uncertain. If we were a PFIC in any year during a U.S. holder's holding period for the ordinary shares or ADSs, we generally would continue to be treated as a PFIC for each subsequent year during which the U.S. holder owned the ordinary shares or ADSs.

If we are a PFIC for any taxable year during which a U.S. holder holds ordinary shares or ADSs, any "excess distribution" that the holder receives and any gain realized from a sale or other disposition (including a pledge) of such ordinary shares or ADSs will be subject to special tax rules, unless the holder makes a mark-to-market election or qualified electing fund election, as discussed below. Any distribution in a taxable year that is greater than 125% of the average annual distribution received by a U.S. holder during the shorter of the three preceding taxable years or such holder's holding period for the ordinary shares or ADSs will be treated as an excess distribution. Under these special tax rules:

- the excess distribution or gain will be allocated ratably over the U.S. holder's holding period for the ordinary shares or ADSs;

- the amount allocated to the current taxable year, and any taxable year prior to the first taxable year in which we were a PFIC in the U.S. holder's holding period, will be treated as ordinary income arising in the current taxable year; and
- the amount allocated to each other year will be subject to income tax at the highest rate in effect for that year and the interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to each such year.

The tax liability for amounts allocated to years prior to the year of disposition or excess distribution cannot be offset by any net operating loss, and gains (but not losses) realized on the transfer of the ordinary shares or ADSs cannot be treated as capital gains, even if the ordinary shares or ADSs are held as capital assets. In addition, non-corporate U.S. holders will not be eligible for reduced rates of taxation on any dividends that we pay if we are a PFIC for either the taxable year in which the dividend is paid or the preceding year. Furthermore, unless otherwise provided by the U.S. Treasury Department, each U.S. holder of a PFIC is required to file an annual report containing such information as the U.S. Treasury Department may require.

If we are a PFIC for any taxable year during which any of our non-U.S. subsidiaries is also a PFIC, a U.S. holder of ordinary shares or ADSs during such year would be treated as owning a proportionate amount (by value) of the shares of the lower-tier PFIC for purposes of the application of these rules to such subsidiary. You should consult your tax advisors regarding the tax consequences if the PFIC rules apply to any of our subsidiaries.

In certain circumstances, in lieu of being subject to the special tax rules discussed above, you may make an election to include gain on the stock of a PFIC as ordinary income under a mark-to-market method, provided that such stock is regularly traded on a qualified exchange. Under current law, the mark-to-market election may be available to U.S. holders of ADSs if the ADSs are listed on NASDAQ, which constitutes a qualified exchange, although there can be no assurance that the ADSs will be "regularly traded" for purposes of the mark-to-market election. It should also be noted that it is intended that only the ADSs and not the ordinary shares will be listed on NASDAQ. While we would expect the Australian Stock Exchange, on which the ordinary shares are listed, to be considered a qualified exchange, no assurance can be given as to whether the Australian Stock Exchange is a qualified exchange, or that the ordinary shares would be traded in sufficient frequency to be considered regularly traded for these purposes. Additionally, because a mark-to-market election cannot be made for equity interests in any lower-tier PFIC that we may own, a U.S. holder that makes a mark-to-market election with respect to us may continue to be subject to the PFIC rules with respect to any indirect investments held by us that are treated as an equity interest in a PFIC for U.S. federal income tax purposes. If you make an effective mark-to-market election, you will include in each year that we are a PFIC as ordinary income the excess of the fair market value of your ordinary shares or ADSs at the end of your taxable year over your adjusted tax basis in the ordinary shares or ADSs. You will be entitled to deduct as an ordinary loss in each such year the excess of your adjusted tax basis in the ordinary shares or ADSs over their fair market value at the end of the year, but only to the extent of the net amount previously included in income as a result of the mark-to-market election. If you make an effective mark-to-market election, any gain you recognize upon the sale or other disposition of your ordinary shares or ADSs in a year that we are a PFIC will be treated as ordinary income and any loss will be treated as ordinary loss, but only to the extent of the net amount previously included in income as a result of the mark-to-market election. Any gain or loss you recognize upon the sale or other disposition of your ordinary shares or ADSs in a year when we are not a PFIC will be a capital gain or loss. See "—Sale, Exchange or other Disposition of Ordinary shares or ADSs" above for the treatment of capital gains and losses.

Your adjusted tax basis in the ordinary shares or ADSs will be increased by the amount of any income inclusion and decreased by the amount of any deductions under the mark-to-market rules. If you make a mark-to-market election it will be effective for the taxable year for which the election is made and all subsequent taxable years unless the ordinary shares or ADSs are no longer regularly traded on a qualified exchange or the IRS consents to the revocation of the election. You are urged to consult your tax advisors about the availability of the mark-to-market election, and whether making the election would be advisable in your particular

circumstances. In the case of a valid mark-to-market election, any distributions we make would generally be subject to the rules discussed above under “—*Taxation of Dividends*,” except the reduced rates of taxation on any dividends received from us would not apply.

Alternatively, you can sometimes avoid the PFIC rules described above by electing to treat us as a “qualified electing fund” under Section 1295 of the Code. However, this option will not be available to you because we do not intend to comply with the requirements necessary to permit you to make this election.

U.S. holders are urged to contact their own tax advisors regarding the determination of whether we are a PFIC and the tax consequences of such status.

### ***Backup Withholding Tax and Information Reporting Requirements***

Payments of dividends with respect to the ordinary shares or ADSs and proceeds from the sale, exchange or other disposition of the ordinary shares or ADSs, by a U.S. paying agent or other U.S. intermediary, or made into the United States, will be reported to the IRS and to the U.S. holder as may be required under applicable Treasury regulations. Backup withholding may apply to these payments if the U.S. holder fails to provide an accurate taxpayer identification number or certification of exempt status or fails to comply with applicable certification requirements. Certain U.S. holders (including, among others, corporations) are not subject to backup withholding and information reporting. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a U.S. holder will be refunded (or credited against such U.S. holder’s U.S. federal income tax liability, if any), provided the required information is timely furnished to the IRS. Prospective investors should consult their own tax advisors as to their qualification for exemption from backup withholding and the procedure for establishing an exemption.

Certain individual U.S. holders (and under proposed Treasury regulations, certain entities) may be required to report to the IRS information with respect to their investment in the ordinary shares or ADSs not held through an account with a U.S. financial institution. U.S. holders who fail to report required information could become subject to substantial penalties. U.S. holders are encouraged to consult with their own tax advisors regarding foreign financial asset reporting requirements with respect to their investment in the ordinary shares or ADSs.

U.S. holders who acquire any of the ordinary shares or ADSs for cash may be required to file an IRS Form 926 (Return by a U.S. Transferor of Property to a Foreign Corporation) with the IRS and to supply certain additional information to the IRS if (i) immediately after the transfer, the U.S. holder owns directly or indirectly (or by attribution) at least 10% of our total voting power or value or (ii) the amount of cash transferred to us in exchange for the ordinary shares or ADSs when aggregated with all related transfers under applicable regulations, exceeds US\$100,000. Substantial penalties may be imposed on a U.S. holder that fails to comply with this reporting requirement. Each U.S. holder is urged to consult with its own tax advisor regarding this reporting obligation.

***The discussion above is not intended to constitute a complete analysis of all tax considerations applicable to an investment in ordinary shares or ADSs. You should consult with your own tax advisor concerning the tax consequences to you in your particular situation.***

### **Australian Tax Considerations**

In this section, we discuss the material Australian income tax, stamp duty and goods and services tax considerations related to the acquisition, ownership and disposal by the absolute beneficial owners of the ordinary shares or ADSs. This discussion represents the opinion of Baker & McKenzie, Australian counsel to Benitec.

It is based upon existing Australian tax law as of the date of this registration statement, which is subject to change, possibly retrospectively. This discussion does not address all aspects of Australian tax law which may be

important to particular investors in light of their individual investment circumstances, such as shares held by investors subject to special tax rules (for example, financial institutions, insurance companies or tax exempt organizations). In addition, this summary does not discuss any foreign or state tax considerations, other than stamp duty and goods and services tax.

Prospective investors are urged to consult their tax advisors regarding the Australian and foreign income and other tax considerations of the acquisition, ownership and disposition of the shares. As used in this summary a “Non-Australian Shareholder” is a holder that is not an Australian tax resident and is not carrying on business in Australia through a permanent establishment.

#### ***Nature of ADSs for Australian Taxation Purposes***

Ordinary shares represented by ADSs held by a U.S. holder will be treated for Australian taxation purposes as held under a “bare trust” for such holder. Consequently, the underlying ordinary shares will be regarded as owned by the ADS holder for Australian income tax and capital gains tax purposes. Dividends paid on the underlying ordinary shares will also be treated as dividends paid to the ADS holder, as the person beneficially entitled to those dividends. Therefore, in the following analysis we discuss the tax consequences to Non-Australian Shareholders of ordinary shares for Australian taxation purposes. We note that the holder of an ADS will be treated for Australian tax purposes as the owner of the underlying ordinary shares that are represented by such ADSs.

#### ***Taxation of Dividends***

Australia operates a dividend imputation system under which dividends may be declared to be “franked” to the extent of tax paid on company profits. Fully franked dividends are not subject to dividend withholding tax. An exemption for dividend withholding tax can also apply to unfranked dividends that are declared to be conduit foreign income, or CFI, and paid to Non-Australian Shareholders. Dividend withholding tax will be imposed at 30%, unless a shareholder is a resident of a country with which Australia has a double taxation agreement and qualifies for the benefits of the treaty. Under the provisions of the current Double Taxation Convention between Australia and the United States, the Australian tax withheld on unfranked dividends that are not declared to be CFI paid by us to a resident of the United States which is beneficially entitled to that dividend is limited to 15% where that resident is a qualified person for the purposes of the Double Taxation Convention between Australia and the United States.

If a Non-Australian Shareholder is a company and owns a 10% or more interest, the Australian tax withheld on dividends paid by us to which a resident of the United States is beneficially entitled is limited to 5%. In limited circumstances the rate of withholding can be reduced to zero.

#### ***Tax on Sales or other Dispositions of Shares—Capital gains tax***

Non-Australian Shareholders will not be subject to Australian capital gains tax on the gain made on a sale or other disposal of ordinary shares, unless they, together with associates, hold 10% or more of our issued capital, at the time of disposal or for 12 months of the last 2 years prior to disposal.

Non-Australian Shareholders who own a 10% or more interest would be subject to Australian capital gains tax if more than 50% of our direct or indirect assets, determined by reference to market value, consists of Australian land, leasehold interests or Australian mining, quarrying or prospecting rights. The Double Taxation Convention between the United States and Australia is unlikely to limit Australia’s right to tax any gain in these circumstances. Net capital gains are calculated after reduction for capital losses, which may only be offset against capital gains.

### ***Tax on Sales or other Dispositions of Shares—Shareholders Holding Shares on Revenue Account***

Some Non-Australian Shareholders may hold shares on revenue rather than on capital account for example, share traders. These shareholders may have the gains made on the sale or other disposal of the shares included in their assessable income under the ordinary income taxing provisions of the income tax law, if the gains are sourced in Australia.

Non-Australian Shareholders assessable under these ordinary income provisions in respect of gains made on shares held on revenue account would be assessed for such gains at the Australian tax rates for non-Australian residents, which start at a marginal rate of 32.5%. This rate does not include the Temporary Budget Repair Levy of 2% that applies in certain circumstances. Some relief from Australian income tax may be available to Non-Australian Shareholders under the Double Taxation Convention between the United States and Australia.

To the extent an amount would be included in a Non-Australian Shareholder's assessable income under both the capital gains tax provisions and the ordinary income provisions, the capital gain amount would generally be reduced, so that the shareholder would not be subject to double tax on any part of the income gain or capital gain.

### ***Dual Residency***

If a shareholder is a resident of both Australia and the United States under those countries' domestic taxation laws, that shareholder may be subject to tax as an Australian resident. If, however, the shareholder is determined to be a U.S. resident for the purposes of the Double Taxation Convention between the United States and Australia, the Australian tax would be subject to limitation by the Double Taxation Convention. Shareholders should obtain specialist taxation advice in these circumstances.

### ***Stamp Duty***

No stamp duty is payable by Australian residents or non-Australian residents on the issue and trading of shares that are quoted on the ASX or NASDAQ at all relevant times and the shares do not represent 90% or more of all of our issued shares.

### ***Australian Death Duty***

Australia does not have estate or death duties. As a general rule, no capital gains tax liability is realized upon the inheritance of a deceased person's shares. The disposal of inherited shares by beneficiaries may, however, give rise to a capital gains tax liability if the gain falls within the scope of Australia's jurisdiction to tax.

### ***Goods and Services Tax***

The issue or transfer of shares to a non-Australian resident investor will not incur Australian goods and services tax.

## UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement, dated \_\_\_\_\_, 2015, with respect to the ADSs being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of ADSs indicated in the following table. BMO Capital Markets Corp. is the representative of the underwriters.

<u>Underwriters</u>	<u>Number of ADSs</u>
BMO Capital Markets Corp. ....	_____
Maxim Group LLC .....	_____
Roth Capital Partners, LLC .....	_____
Total .....	_____

The underwriters are committed to take and pay for all of the ADSs being offered, if any are taken, other than the ADSs covered by the option described below unless and until that option is exercised. If an underwriter fails or refuses to purchase any of its committed ADSs, the purchase commitments of the non-defaulting underwriters may be increased or the offering may be terminated.

The underwriters have an option to buy up to an additional \_\_\_\_\_ ADSs from us to cover sales by the underwriters of a greater number of ADSs than the total number set forth in the table above. They may exercise this option for 30 days. If any ADSs are purchased pursuant to this option, the underwriters will severally purchase ADSs in approximately the same proportion as set forth in the table above, and the underwriters will offer the additional ADSs on the same terms as those on which the ADSs are being offered.

The underwriters propose to offer the ADSs representing an interest in our ordinary shares directly to the public at the public offering price set forth on the cover of this prospectus and to certain dealers at such offering price less a concession not in excess of US\$ \_\_\_\_\_ per ADS. After the public offering of the ADSs, the offering price and the selling concession may be changed by the underwriters.

The following table shows the per ADS and total underwriting discounts and commissions to be paid by us to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional ADSs.

	<u>No Exercise</u>	<u>Full Exercise</u>
Per ADS .....	US\$	US\$
Total .....	US\$	US\$

We estimate that the total expenses of the offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding underwriting discounts and commissions, will be approximately \$ \_\_\_\_\_, all of which will be paid by us. We have agreed to reimburse the underwriters for certain of their expenses incurred in connection with the clearance of this offering with the Financial Industry Regulatory Authority, Inc.

We and our officers and directors agreed with the underwriters that, for a period of 180 days after the date of this prospectus, subject to certain exceptions, we and they will not (1) offer, sell, pledge, contract to sell, purchase any option to sell, grant any option for the purchase of, lend, or otherwise dispose of, or require us to file with the SEC a registration statement under the Securities Act to register, any shares of our ordinary shares or ADSs or any securities convertible into, exercisable for or exchangeable for our ordinary shares or ADSs of which such officer, director or holder is now, or may in the future become, the beneficial owner (within the meaning of Rule 13d-3 under the Exchange Act), or (2) enter into any swap or other derivative transaction that transfers to another, in whole or in part, any of the economic benefits or risks of ownership of ordinary shares or

ADSs, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of ordinary shares, ADSs or other securities, in cash or otherwise, or publicly disclose the intention to enter into any transaction described in clause (1) or (2) above, except with the prior written consent of BMO Capital Markets Corp.; provided that BMO Capital Markets Corp. on behalf of the underwriters, has agreed to notify us at least three business days before the effective date of any release or waiver granted to one of our officers or directors, and we have agreed to announce the impending release or waiver by issuing a press release through a major news service at least two business days before the effective date of the release or waiver.

The restrictions above do not apply to the following, subject to certain limitations set forth in the lock-up agreements:

- transfers of securities as a bona fide gift;
- transfers or dispositions of securities to any trust for the direct or indirect benefit of the lock-up signatory or any member of the immediate family of the lock-up signatory;
- transfers of securities to affiliates;
- transfers of securities by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the lock-up signatory;
- transfers or dispositions of shares of our ordinary shares or ADSs acquired in open market purchases after the completion of this offering; or
- entry into any trading plan established pursuant to Rule 10b5-1 under the Exchange Act.

See “Shares Eligible for Future Sale” for a discussion of certain transfer restrictions.

Prior to this offering, the ADSs have not been listed on any stock exchange in the United States. Our ordinary shares are listed on the Australian Securities Exchange, or ASX, under the symbol “BLT.” The public offering price of the ADSs will be determined by negotiations between us and the underwriters taking into account the most recent closing price of our ordinary shares on the ASX prior to the pricing date as well as other factors, including: prevailing market conditions, our historical performance, estimates of our business potential and earnings prospects, an assessment of our management and the consideration of the above factors in relation to market valuation of companies in related businesses.

We have applied to have our ADSs listed on The NASDAQ Global Select Market under the symbol “BNTC.”

In connection with the offering, the underwriters may purchase and sell ADSs in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of ADSs than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A “covered short position” is a short position that is not greater than the amount of additional ADSs for which the underwriters’ option described above may be exercised. The underwriters may cover any covered short position by either exercising their option to purchase additional ADSs or purchasing ADSs in the open market. In determining the source of ADSs to cover the covered short position, the underwriters will consider, among other things, the price of ADSs available for purchase in the open market as compared to the price at which they may purchase additional ADSs pursuant to the option described above. “Naked” short sales are any short sales that create a short position greater than the amount of additional ADSs for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing ADSs in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the ADSs in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of ADSs made by the underwriters in the open market prior to the completion of the offering.



The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representative has repurchased ADSs sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the ADSs, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the ADSs. As a result, the price of our ADSs may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on The NASDAQ Global Select Market, in the over-the-counter market or otherwise.

In connection with this offering, the underwriters may engage in passive market making transactions in the ADSs on The NASDAQ Select Market in accordance with Rule 103 of Regulation M under the Exchange Act during a period before the commencement of offers or sales of ADSs and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded. Passive market making may cause the price of our ADSs to be higher than the price that otherwise would exist in the open market in the absence of those transactions. The underwriters are not required to engage in passive market making and may end passive market making activities at any time.

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act and to contribute to payments that the underwriters may be required to make for these liabilities.

A prospectus in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The representative may agree to allocate a number of ADSs to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representative to underwriters that may make Internet distributions on the same basis as other allocations.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to the issuer and to persons and entities with relationships with the issuer, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities and/or instruments of the issuer (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with the issuer. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

## **Offer Restrictions Outside the United States**

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the ADSs offered by this prospectus in any jurisdiction where action for that purpose is required. The ADSs offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such ADSs be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any ADSs offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

### ***Australia***

This prospectus is not a disclosure document under Chapter 6D of the Australian Corporations Act, has not been lodged with the Australian Securities and Investments Commission and does not purport to include the information required of a disclosure document under Chapter 6D of the Australian Corporations Act. Accordingly, (i) the offer of the ADSs under this prospectus is only made to persons to whom it is lawful to offer the ADSs without disclosure under Chapter 6D of the Australian Corporations Act under one or more exemptions set out in section 708 of the Australian Corporations Act, (ii) this prospectus is made available in Australia only to those persons as set forth in clause (i) above, and (iii) the offeree must be sent a notice stating in substance that by accepting this offer, the offeree represents that the offeree is such a person as set forth in clause (i) above, and, unless permitted under the Australian Corporations Act, agrees not to sell or offer for sale within Australia any of the ADSs sold to the offeree within 12 months after its transfer for the offeree under this prospectus.

### ***China***

The information in this document does not constitute a public offer of the ADSs, whether by way of sale or subscription, in the People's Republic of China, or PRC, (excluding, for purposes of this paragraph, Hong Kong Special Administrative Region, Macau Special Administrative Region and Taiwan). The ADSs may not be offered or sold directly or indirectly in the PRC to legal or natural persons other than directly to "qualified domestic institutional investors."

### ***European Economic Area—Belgium, Germany, Luxembourg and Netherlands***

The information in this document has been prepared on the basis that all offers of ADSs will be made pursuant to an exemption under the Directive 2003/71/EC, or Prospectus Directive, as amended and implemented in Member States of the European Economic Area, each a Relevant Member State, from the requirement to produce a prospectus for offers of securities.

An offer to the public of ADSs has not been made, and may not be made, in a Relevant Member State except pursuant to one of the following exemptions under the Prospectus Directive as implemented in that Relevant Member State:

- to any legal entity that is authorized or regulated to operate in the financial markets or whose main business is to invest in financial instruments;
- to any legal entity that satisfies two of the following three criteria: (i) balance sheet total of at least €20,000,000; (ii) annual net turnover of at least €40,000,000 and (iii) own funds of at least €2,000,000 (as shown on its last annual unconsolidated or consolidated financial statements);
- to any person or entity who has requested to be treated as a professional client in accordance with the EU Markets in Financial Instruments Directive (Directive 2004/39/EC, "MiFID"); or
- to any person or entity who is recognized as an eligible counterparty in accordance with Article 24 of the MiFID.

### ***France***

This document is not being distributed in the context of a public offering of financial securities (*offre au public de titres financiers*) in France within the meaning of Article L.411-1 of the French Monetary and Financial Code (*Code monétaire et financier*) and Articles 211-1 et seq. of the General Regulation of the French *Autorité des marchés financiers*, or AMF. The ADSs have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France.

This document and any other offering material relating to the ADSs has not been, and will not be, submitted to the AMF for approval in France and, accordingly, may not be distributed or caused to be distributed, directly or indirectly, to the public in France.

This document and any other offering material relating to the ADSs have not been, and will not be, submitted to the AMF for approval in France and, accordingly, may not be distributed (directly or indirectly) to the public in France. Such offers, sales and distributions have been and shall only be made in France to qualified investors (*investisseurs qualifiés*) acting for their own account, as defined in and in accordance with Articles L.411-2-II-2, D.411-1, L.533-16, L.533-20, D.533-11, D.533-13, D.744-1, D.754-1 and D.764-1 of the French Monetary and Financial Code and any implementing regulation.

Pursuant to Article 211-3 of the General Regulation of the AMF, investors in France are informed that the ADSs cannot be distributed (directly or indirectly) to the public by the investors otherwise than in accordance with Articles L.411-1, L.411-2, L.412-1 and L.621-8 to L.621-8-3 of the French Monetary and Financial Code.

### ***Ireland***

The information in this document does not constitute a prospectus under any Irish laws or regulations and this document has not been filed with or approved by any Irish regulatory authority as the information has not been prepared in the context of a public offering of securities in Ireland within the meaning of the Irish Prospectus (Directive 2003/71/EC) Regulations 2005 (the “Prospectus Regulations”). The ADSs have not been offered or sold, and will not be offered, sold or delivered directly or indirectly in Ireland by way of a public offering, except to qualified investors as defined in Regulation 2(l) of the Prospectus Regulations.

### ***Israel***

The ADSs offered by this prospectus have not been approved or disapproved by the Israeli Securities Authority, or ISA, nor have such ADSs been registered for sale in Israel. The ADSs may not be offered or sold, directly or indirectly, to the public in Israel, absent the publication of a prospectus. The ISA has not issued permits, approvals or licenses in connection with the offering or publishing the prospectus; nor has it authenticated the details included herein, confirmed their reliability or completeness, or rendered an opinion as to the quality of the ADSs being offered. Any resale in Israel, directly or indirectly, to the public of the ADSs offered by this prospectus is subject to restrictions on transferability and must be effected only in compliance with the Israeli securities laws and regulations.

### ***Italy***

The offering of the ADSs in the Republic of Italy has not been authorized by the Italian Securities and Exchange Commission (*Commissione Nazionale per le Società e la Borsa*, or *CONSOB*), pursuant to the Italian securities legislation and, accordingly, no offering material relating to the ADSs may be distributed in Italy and such ADSs may not be offered or sold in Italy in a public offer within the meaning of Article 1.1(t) of Legislative Decree No. 58 of 24 February 1998 (“Decree No. 58”), other than:

- to Italian qualified investors, as defined in Article 100 of Decree no. 58 by reference to Article 34-ter of CONSOB Regulation no. 11971 of 14 May 1999 (“Regulation no. 11971”) as amended (“Qualified Investors”); and

- in other circumstances that are exempt from the rules on public offer pursuant to Article 100 of Decree No. 58 and Article 34-ter of Regulation No. 11971 as amended.

Any offer, sale or delivery of the ADSs or distribution of any offer document relating to the ADSs in Italy (excluding placements where a Qualified Investor solicits an offer from the issuer) under the paragraphs above must be:

- made by investment firms, banks or financial intermediaries permitted to conduct such activities in Italy in accordance with Legislative Decree No. 385 of 1 September 1993 (as amended), Decree No. 58, CONSOB Regulation No. 16190 of 29 October 2007 and any other applicable laws; and
- in compliance with all relevant Italian securities, tax and exchange controls and any other applicable laws.

Any subsequent distribution of the ADSs in Italy must be made in compliance with the public offer and prospectus requirement rules provided under Decree No. 58 and the Regulation No. 11971 as amended, unless an exception from those rules applies. Failure to comply with such rules may result in the sale of such ADSs being declared null and void and in the liability of the entity transferring the ADSs for any damages suffered by the investors.

### ***Japan***

The ADSs have not been and will not be registered under Article 4, paragraph 1 of the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948), as amended (the “FIEL”), pursuant to an exemption from the registration requirements applicable to a private placement of securities to Qualified Institutional Investors (as defined in and in accordance with Article 2, paragraph 3 of the FIEL and the regulations promulgated thereunder). Accordingly, the ADSs may not be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan other than Qualified Institutional Investors. Any Qualified Institutional Investor who acquires the ADSs offered hereby may not resell them to any person in Japan that is not a Qualified Institutional Investor, and acquisition by any such person of the ADSs is conditional upon the execution of an agreement to that effect.

### ***Portugal***

This document is not being distributed in the context of a public offer of financial securities (*oferta pública de valores mobiliários*) in Portugal, within the meaning of Article 109 of the Portuguese Securities Code (*Código dos Valores Mobiliários*). The ADSs offered hereby have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in Portugal. This document and any other offering material relating to the ADSs has not been, and will not be, submitted to the Portuguese Securities Market Commission (*Comissão do Mercado de Valores Mobiliários*) for approval in Portugal and, accordingly, may not be distributed or caused to be distributed, directly or indirectly, to the public in Portugal, other than under circumstances that are deemed not to qualify as a public offer under the Portuguese Securities Code. Such offers, sales and distributions of ADSs in Portugal are limited to persons who are “qualified investors” (as defined in the Portuguese Securities Code). Only such investors may receive this document and they may not distribute it or the information contained in it to any other person.

### ***Sweden***

This document has not been, and will not be, registered with or approved by Finansinspektionen (the Swedish Financial Supervisory Authority). Accordingly, this document may not be made available, nor may the ADSs be offered for sale in Sweden, other than under circumstances that are deemed not to require a prospectus under the Swedish Financial Instruments Trading Act (1991:980) (Sw. lag (1991:980) *om handel med finansiella instrument*). Any offering of the ADSs in Sweden is limited to persons who are “qualified investors” (as defined in the Financial Instruments Trading Act). Only such investors may receive this document and they may not distribute it or the information contained in it to any other person.

### ***Switzerland***

The ADSs may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering material relating to the ADSs may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering material relating to the ADSs has been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of ADSs will not be supervised by, the Swiss Financial Market Supervisory Authority, or FINMA.

This document is personal to the recipient only and not for general circulation in Switzerland.

### ***United Arab Emirates***

Neither this document nor the ADSs have been approved, disapproved or passed on in any way by the Central Bank of the United Arab Emirates or any other governmental authority in the United Arab Emirates, nor have we received authorization or licensing from the Central Bank of the United Arab Emirates or any other governmental authority in the United Arab Emirates to market or sell the ADSs within the United Arab Emirates. This document does not constitute and may not be used for the purpose of an offer or invitation. No services relating to the ADSs, including the receipt of applications and/or the allotment or redemption of such ADSs, may be rendered within the United Arab Emirates by us.

No offer or invitation to subscribe for ADSs is valid or permitted in the Dubai International Financial Centre.

### ***United Kingdom***

Neither the information in this document nor any other document relating to the offer has been delivered for approval to the Financial Services Authority in the United Kingdom and no prospectus (within the meaning of section 85 of the Financial Services and Markets Act 2000, as amended, or FSMA, has been published or is intended to be published in respect of the ADSs. This document is issued on a confidential basis to “qualified investors” (within the meaning of section 86(7) of FSMA) in the United Kingdom, and the ADSs may not be offered or sold in the United Kingdom by means of this document, any accompanying letter or any other document, except in circumstances that do not require the publication of a prospectus pursuant to section 86(1) FSMA. This document should not be distributed, published or reproduced, in whole or in part, nor may its contents be disclosed by recipients to any other person in the United Kingdom.

Any invitation or inducement to engage in investment activity (within the meaning of section 21 of FSMA) received in connection with the issue or sale of the ADSs has only been communicated or caused to be communicated and will only be communicated or caused to be communicated in the United Kingdom in circumstances in which section 21 (1) of FSMA does not apply to us.

In the United Kingdom, this document is being distributed only to, and is directed at, persons (i) who have professional experience in matters relating to investments falling within Article 19(5) (investment professionals) of the Financial Services and Markets Act 2000 (Financial Promotions) Order 2005, or FPO, (ii) who fall within the categories of persons referred to in Article 49(2)(a) to (d) (high net worth companies, unincorporated associations, etc.) of the FPO or (iii) to whom it may otherwise be lawfully communicated (together “relevant persons”). The investments to which this document relates are available only to, and any invitation, offer or agreement to purchase will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

## EXPENSES RELATING TO THIS OFFERING

Set forth below is an itemization of the estimated expenses, excluding underwriting discounts, that are expected to be incurred in connection with our offer and sale of the ADSs. Expenses for the offering will be borne by us.

SEC registration fee .....	\$
NASDAQ listing fee .....	
Financial Industry Regulatory Authority Inc. filing fee .....	
Printing expenses .....	
Legal fees and expenses .....	
Accounting fees and expenses .....	
Roadshow expenses .....	
Other fees and expenses .....	
Total .....	<u>\$</u>

## LEGAL MATTERS

The validity of the ordinary shares represented by the ADSs to be issued in this offering will be passed upon for us by Baker & McKenzie, our Australian counsel. Certain matters as to U.S. federal law and New York state law will be passed upon for us by Baker & McKenzie LLP, our U.S. counsel. Cooley LLP will be serving as U.S. counsel to the underwriters.

## EXPERTS

The audited financial statements included in this prospectus and elsewhere in the registration statement have been so included in reliance upon the report of Grant Thornton Audit Pty Ltd., independent registered public accountants, upon the authority of said firm as experts in accounting and auditing.

## ENFORCEABILITY OF CIVIL LIABILITIES

We are a public limited company incorporated under the laws of Australia. Certain of our directors are non-residents of the United States and substantially all of their assets are located outside the United States. As a result, it may not be possible for you to:

- effect service of process within the United States upon our non-U.S. resident directors or on us;
- enforce in U.S. courts judgments obtained against our non-U.S. resident directors or us in the United States courts in any action, including actions under the civil liability provisions of U.S. securities laws;
- enforce in U.S. courts judgments obtained against our non-U.S. resident directors or us in courts of jurisdictions outside the United States in any action, including actions under the civil liability provisions of U.S. securities laws; or
- bring an original action in an Australian court to enforce liabilities against our non-U.S. resident directors or us based solely upon U.S. securities laws.

You may also have difficulties enforcing in courts outside the United States judgments that are obtained in U.S. courts against any of our non-U.S. resident directors or us, including actions under the civil liability provisions of the U.S. securities laws.

With that noted, there are no treaties between Australia and the United States that would affect the recognition or enforcement of foreign judgments in Australia. We also note that investors may be able to bring an original action in an Australian court against us to enforce liabilities based in part upon U.S. federal securities laws.

The disclosure in this section is not based on the opinion of counsel.

We have appointed Tacere Therapeutics, Inc., our wholly owned U.S. subsidiary, as our agent to receive service of process with respect to any action brought against us in the U.S. District Court for the Southern District of New York under the federal securities laws of the United States or any action brought against us in the Supreme Court of the State of New York in the County of New York under the securities laws of the State of New York.

### **WHERE YOU CAN FIND ADDITIONAL INFORMATION**

We have filed with the SEC a registration statement on Form F-1, including relevant exhibits and schedules, under the Securities Act with respect to the ordinary shares to be sold in this offering. This prospectus, which constitutes a part of the registration statement, summarizes material provisions of contracts and other documents that we refer to in this prospectus. Since this prospectus does not contain all of the information contained in the registration statement, you should read the registration statement and its exhibits and schedules for further information with respect to us and our ordinary shares represented by ADSs. Statements contained in this prospectus regarding the contents of any agreement, contract or other document referred to are not necessarily complete and reference is made in each instance to the copy of the contract or document filed as an exhibit to the registration statement. All information we file with the SEC is available through the SEC's Electronic Data Gathering, Analysis and Retrieval system, which may be accessed through the SEC's website at [www.sec.gov](http://www.sec.gov). Information filed with the SEC may also be inspected and copied at the public reference room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You can request copies of these documents upon payment of a duplicating fee, by writing to the SEC. Please visit the SEC's website at [www.sec.gov](http://www.sec.gov) for further information on the SEC's public reference room.

Immediately upon completion of this offering, we will become subject to periodic reporting and other informational requirements of the Exchange Act as applicable to foreign private issuers. Our annual reports on Form 20-F for the year ending June 30, 2015 and subsequent years will be due within four months following the fiscal year end. We are not required to disclose certain other information that is required from U.S. domestic issuers. As a foreign private issuer, we are exempt under the Exchange Act from, among other things, the rules prescribing the furnishing and content of proxy statements, and our executive officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act and Regulation FD (Fair Disclosure), which was adopted to ensure that select groups of investors are not privy to specific information about an issuer before other investors.

We are, however, still subject to the anti-fraud and anti-manipulation rules of the SEC, such as Rule 10b-5. Since many of the disclosure obligations required of us as a foreign private issuer are different than those required by companies filing as a domestic issuer, our shareholders, potential shareholders and the investing public in general should not expect to receive information about us in the same amount and at the same time as information is received from, or provided by, companies filing as a domestic issuer. We are liable for violations of the rules and regulations of the SEC, which do apply to us as a foreign private issuer.

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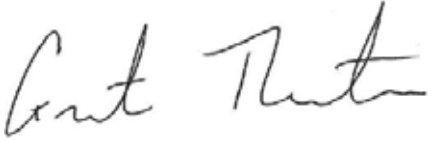
## **REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

### **BOARD OF DIRECTORS AND SHAREHOLDERS BENITEC BIOPHARMA LIMITED**

We have audited the accompanying consolidated statements of financial position of Benitec Biopharma Limited and its controlled entities (the “Group”) as of 30 June 2014 and 2013, and the related consolidated statements of profit or loss and other comprehensive income, statements of changes in equity, and statements of cash flows for each of the two years in the period ended 30 June 2014. These financial statements are the responsibility of the Group’s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Group’s internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Group’s internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Benitec Biopharma Limited and its' controlled entities as of 30 June 2014 and 2013 and the results of their operations and their cash flows for each of the two years in the period ended 30 June 2014 and 2013 in conformity with International Financial Reporting Standards, as issued by the International Accounting Standards Board.

A handwritten signature in black ink, appearing to read "Grant Thornton", is positioned above the printed name of the firm.

GRANT THORNTON AUDIT PTY LTD  
Chartered Accountants

Sydney, 1 May 2015

**Consolidated Statement of Profit or Loss and Other Comprehensive Income  
For the Year Ended 30 June 2014**

	Note	2014	2013
		\$	\$
<b>Continuing Operations</b>			
Revenue .....	2	597,940	639,849
Other income .....	2	775,833	824,333
		1,373,773	1,464,182
Royalties & licence fees .....		(192,753)	(30,000)
Research and development .....		(3,757,869)	(1,280,012)
Employment related .....		(2,444,015)	(1,832,065)
Share based expense .....		(355,116)	(518,749)
Impairment costs .....		—	(1,503,296)
Travel related costs .....		(585,359)	(345,826)
Consultants costs .....		(652,839)	(336,570)
Occupancy costs .....		(121,582)	(100,153)
Corporate expenses .....		(646,315)	(531,686)
Foreign exchange translation .....		(111,399)	1,526,215
Total expenses .....		(8,867,247)	(4,952,142)
Loss before income tax .....		(7,493,474)	(3,487,960)
Income tax benefit .....	4	454,365	—
<b>Loss for the year attributable to members of the parent entity</b> .....		<b>(7,039,109)</b>	<b>(3,487,960)</b>
Other Comprehensive Income:			
<i>Items that may be reclassified subsequently to profit and loss</i>			
Other Comprehensive Income for the year, Foreign exchange translation, net of tax .....		7,747	(1,313,792)
<b>Total Comprehensive Income for the year</b> .....		<b>(7,031,362)</b>	<b>(4,801,752)</b>
<b>Total Comprehensive Income attributable to members of the parent entity</b> .....		<b>(7,031,362)</b>	<b>(4,801,752)</b>
<i>Earnings per share (cents per share):</i>			
Basic and diluted loss for the year attributable to ordinary equity holders of the parent entity			
Cents per share, with the comparative adjusted for the share consolidation at 25:1 in July 2013 .....	6	(7.81)	(8.25)

This statement should be read in conjunction with the notes to the financial statements.

**Consolidated Statement of Financial Position**  
**As at 30 June 2014**

	<u>Note</u>	<u>2014</u>	<u>2013</u>
		\$	\$
<b>CURRENT ASSETS</b>			
Cash and cash equivalents . . . . .	8	31,359,199	1,587,299
Trade and other receivables . . . . .	9	121,587	105,073
Other current assets . . . . .	10	2,966,739	30,218
<b>TOTAL CURRENT ASSETS . . . . .</b>		<b><u>34,447,525</u></b>	<b><u>1,722,590</u></b>
<b>NON-CURRENT ASSETS</b>			
Property, plant and equipment . . . . .	12	47,677	28,120
<b>TOTAL NON-CURRENT ASSETS . . . . .</b>		<b><u>47,677</u></b>	<b><u>28,120</u></b>
<b>TOTAL ASSETS . . . . .</b>		<b><u>34,495,202</u></b>	<b><u>1,750,710</u></b>
<b>CURRENT LIABILITIES</b>			
Trade and other payables . . . . .	14	788,169	1,011,733
Provisions . . . . .	15	166,511	98,637
<b>TOTAL CURRENT LIABILITIES . . . . .</b>		<b><u>954,680</u></b>	<b><u>1,110,370</u></b>
<b>TOTAL LIABILITIES . . . . .</b>		<b><u>954,680</u></b>	<b><u>1,110,370</u></b>
<b>NET ASSETS . . . . .</b>		<b><u>33,540,522</u></b>	<b><u>640,340</u></b>
<b>EQUITY</b>			
Contributed equity . . . . .	16	129,185,676	89,609,248
Reserves . . . . .	17	640,773	277,910
Accumulated losses . . . . .		(96,285,927)	(89,246,818)
<b>TOTAL EQUITY . . . . .</b>		<b><u>33,540,522</u></b>	<b><u>640,340</u></b>

This statement should be read in conjunction with the notes to the financial statements.

**Consolidated Statement of Cash Flows**  
**For the year ended 30 June 2014**

	<u>Note</u>	<u>2014</u>	<u>2013</u>
		\$	\$
<b>CASH FLOWS FROM OPERATING ACTIVITIES</b>			
Receipts from customers .....		260,310	566,754
Research and development grants .....		775,833	824,333
Interest received .....		321,116	133,011
Income tax benefit .....		454,365	—
Payments to suppliers and employees .....		<u>(11,081,963)</u>	<u>(4,256,694)</u>
<b>Net cash used in operating activities .....</b>	<b>8</b>	<b><u>(9,270,339)</u></b>	<b><u>(2,732,596)</u></b>
<b>CASH FLOWS FROM INVESTING ACTIVITIES</b>			
Business acquisition .....	26	—	143,603
Purchase of property, plant and equipment .....		<u>(32,365)</u>	<u>(9,889)</u>
<b>Net cash provided/(used) by investing activities .....</b>		<b><u>(32,365)</u></b>	<b><u>133,714</u></b>
<b>CASH FLOWS FROM FINANCING ACTIVITIES</b>			
Net proceeds from issue of shares .....		<u>39,075,618</u>	<u>1,086,844</u>
<b>Net cash provided by financing activities .....</b>		<b><u>39,075,618</u></b>	<b><u>1,086,844</u></b>
<b>Net decrease in cash held .....</b>		<b><u>29,772,914</u></b>	<b><u>(1,512,038)</u></b>
Exchange differences on cash and cash equivalents .....		(1,014)	23,457
Cash and cash equivalents, beginning of year .....		<u>1,587,299</u>	<u>3,075,880</u>
<b>Cash and cash equivalents, end of year .....</b>	<b>8</b>	<b><u>31,359,199</u></b>	<b><u>1,587,299</u></b>

This statement should be read in conjunction with the notes to the financial statements.

**Consolidated Statement of Changes in Equity**  
**For the year ended 30 June 2014**

	<u>Contributed Equity</u>	<u>Share-based Payments Reserve</u>	<u>Foreign exchange translation reserve</u>	<u>Accumulated Losses</u>	<u>Total</u>
	\$	\$	\$	\$	\$
<b>Balance at 1 July 2012</b> .....	<b>87,348,819</b>	<b>1,394,142</b>	<b>—</b>	<b>(86,080,047)</b>	<b>2,662,914</b>
Loss for the year .....	—	—	—	(3,487,960)	(3,487,960)
Other comprehensive income for year .....	—	—	(1,313,792)	—	(1,313,792)
Total comprehensive income for year .....	—	—	(1,313,792)	(3,487,960)	(4,801,752)
Share issue to Tacere on business acquisition .....	1,173,585	—	—	—	1,173,585
Transfer to Accumulated Losses the Share Based Payments Reserve no longer required .....	—	(321,189)	—	321,189	—
Share Based Payments .....	—	518,749	—	—	518,749
Share issues, net of transaction costs .....	1,086,844	—	—	—	1,086,844
Transactions with owners .....	2,260,429	197,560	—	321,189	2,779,178
<b>Balance 30 June 2013</b> .....	<b>89,609,248</b>	<b>1,591,702</b>	<b>(1,313,792)</b>	<b>(89,246,818)</b>	<b>640,340</b>
Loss for the year .....	—	—	—	(7,039,109)	(7,039,109)
Other comprehensive income for year .....	—	—	7,747	—	7,747
Total comprehensive income for year .....	—	—	7,747	(7,039,109)	(7,031,362)
Share Based Payments .....	—	355,116	—	—	355,116
Share issues, net of transaction costs .....	39,576,428	—	—	—	39,576,428
Transactions with owners .....	39,576,428	355,116	—	—	39,931,544
<b>Balance 30 June 2014</b> .....	<b>129,185,676</b>	<b>1,946,818</b>	<b>(1,306,045)</b>	<b>(96,285,927)</b>	<b>33,540,522</b>

This statement should be read in conjunction with the notes to the financial statements.

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

### Note 1: Summary of significant accounting policies

#### (a) Basis of Preparation

The financial report covers Benitec Biopharma Limited and its controlled entities as a consolidated entity (“Group”). Benitec Biopharma Limited is a listed public company, incorporated and domiciled in Australia. All amounts are stated in Australian dollars.

The consolidated general purpose financial statements of the Group have been prepared in accordance with the requirements of the *Corporations Act 2001*, International Accounting Standards and other authoritative pronouncements of the International Accounting Standards Board. Compliance with International Accounting Standards results in full compliance with the International Financial Reporting Standards (IFRS) as issued by the International Accounting Standards Board (IASB). Benitec Biopharma Limited is a for-profit entity for the purpose of preparing financial statements.

The consolidated financial statements for the year ended 30 June 2014 (including comparatives) were approved and authorised for issue by the board of directors on 1 May 2015.

The consolidated financial statements have been prepared using the measurement bases specified by International Accounting Standards for each type of asset, liability, income and expense. The measurement bases are more fully described in the accounting policies below.

#### (b) Principles of Consolidation

A controlled entity is any entity controlled by Benitec Biopharma Limited whereby Benitec Biopharma Limited has the power to control the financial and operating policies of an entity so as to obtain benefits from its activities.

All inter-company balances and transactions between entities in the consolidated entity, including any unrealised profits or losses, have been eliminated on consolidation. Accounting policies of controlled entities have been changed where necessary to ensure consistencies with those policies applied by the parent entity.

Where controlled entities have entered or left the consolidated entity during the year, their operating results have been included/excluded from the date control was obtained or until the date control ceased.

A list of controlled entities is contained in note 11 to the financial statements. All controlled entities have a June financial year-end except for Benitec Ltd (UK) which has a December year-end.

#### (c) Accounting Standards

##### *New and revised standards that are effective for these financial statements*

A number of new and revised standards are effective for annual periods beginning on or after 1 July 2013. Information on these new standards is presented below.

##### Amendments to IFRS 8 Operating Segments

The 2012 amendment to IFRS 8 Operating Segments requires the disclosure of judgments made by management in applying the aggregation criteria.

##### IFRS 10 Consolidated Financial Statements

IFRS 10 supersedes IAS 27 *Consolidated and Separate Financial Statements IFRS 10*. IFRS 10 revises the definition of control and provides extensive new guidance on its application. These new requirements have the

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

potential to affect which of the Group's investees are considered to be subsidiaries and therefore to change the scope of consolidation. The requirements on consolidation procedures, accounting for changes in non-controlling interests and accounting for loss of control of a subsidiary are unchanged.

Management has reviewed its control assessments in accordance with IFRS 10 and has concluded that there is no effect on the classification (as subsidiaries or otherwise) of any of the Group's investees held during the period or comparative periods covered by these financial statements.

### IFRS 11 Joint Arrangements

IFRS 11 supersedes IAS 31 *Interests in Joint Ventures*. IFRS 11 revises the categories of joint arrangement, and the criteria for classification into the categories, with the objective of more closely aligning the accounting with the investor's rights and obligations relating to the arrangement. In addition, IAS 31's option of using proportionate consolidation for arrangements classified as jointly controlled entities under that Standard has been eliminated. IFRS 11 now requires the use of the equity method for arrangements classified as joint ventures (as for investments in associates).

### IFRS 13 Fair Value Measurement

IFRS 13 clarifies the definition of fair value and provides related guidance and enhanced disclosures about fair value measurements. It does not affect which items are required to be fair-valued. The scope of IFRS 13 is broad and it applies for both financial and non-financial items for which other International Accounting Standards require or permit fair value measurements or disclosures about fair value measurements, except in certain circumstances.

IFRS 13 applies prospectively for annual periods beginning on or after 1 January 2013. Its disclosure requirements need not be applied to comparative information in the first year of application. The Group has however included as comparative information the IFRS 13 disclosures that were required previously by IFRS 7 *Financial Instruments: Disclosures*.

### Amendments to IAS 19 Employee Benefits

The 2011 amendments to IAS 19 made a number of changes to the accounting for employee benefits. The amendments which impact the Group related to the following:

- Under the amendments, employee benefits 'expected to be settled wholly' (as opposed to 'due to be settled' under the superseded version of IFRS 19) within 12 months after the end of the reporting period are short-term benefits, and are therefore not discounted when calculating leave liabilities. As the Group does not expect all annual leave for all employees to be used wholly within 12 months of the end of reporting period, annual leave is included in 'other long-term benefit' and discounted when calculating the leave liability. This change has had no impact on the presentation of annual leave as a current liability in accordance with IAS 1 *Presentation of Financial Statements*.

Management have assessed the impact of this change and noted that it is not material to the Group for the years ended 30 June 2013 and 30 June 2014.

### ***Accounting Standards issued but not yet effective and not been adopted early by the Group***

At the date of authorisation of these financial statements, certain new standards, amendments and interpretations to existing standards have been published but are not yet effective, and have not been adopted



## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

early by the Group. Management anticipates that all of the relevant pronouncements will be adopted in the Group's accounting policies for the first period beginning after the effective date of the pronouncement. Information on new standards, amendments and interpretations that are expected to be relevant to the Group's financial statements is provided below. Certain other new standards and interpretations have been issued but are not expected to have a material impact on the Group's financial statements.

### Accounting for Acquisitions of Interests in Joint Operations

The amendments to IFRS 11 state that an acquirer of an interest in a joint operation in which the activity of the joint operation constitutes a 'business', as defined in IFRS 3 Business Combinations, should:

- apply all of the principles on business combinations accounting in IFRS 3 and other IFRSs except principles that conflict with the guidance of IFRS 11. This requirement also applies to the acquisition of additional interests in an existing joint operation that results in the acquirer retaining joint control of the joint operation (note that this requirement applies to the additional interest only, i.e. the existing interest is not remeasured) and to the formation of a joint operation when an existing business is contributed to the joint operation by one of the parties that participate in the joint operation; and
- provide disclosures for business combinations as required by IFRS 3 and other IFRSs.

### IFRS 9 Financial Instruments

IFRS 9 introduces new requirements for the classification and measurement of financial assets and liabilities. These requirements improve and simplify the approach for classification and measurement of financial assets compared with the requirements of IAS 39. The main changes are:

(a) Financial assets that are debt instruments will be classified based on (1) the objective of the entity's business model for managing the financial assets; and (2) the characteristics of the contractual cash flows.

(b) Allows an irrevocable election on initial recognition to present gains and losses on investments in equity instruments that are not held for trading in other comprehensive income (instead of in profit or loss). Dividends in respect of these investments that are a return on investment can be recognised in profit or loss and there is no impairment or recycling on disposal of the instrument.

(c) Financial assets can be designated and measured at fair value through profit or loss at initial recognition if doing so eliminates or significantly reduces a measurement or recognition inconsistency that would arise from measuring assets or liabilities, or recognising the gains and losses on them, on different bases.

(d) Where the fair value option is used for financial liabilities the change in fair value is to be accounted for as follows:

- The change attributable to changes in credit risk are presented in other comprehensive income (OCI); and
- The remaining change is presented in profit or loss.

If this approach creates or enlarges an accounting mismatch in the profit or loss, the effect of the changes in credit risk are also presented in profit or loss.

### (d) Revenue

Revenue from the granting of licenses is recognised in accordance with the terms of the relevant agreements and is usually recognised on an accruals basis, unless the substance of the agreement provides evidence that it is

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

more appropriate to recognise revenue on some other systematic rational basis. Interest revenue is recognised on a proportional basis taking into account the interest rates applicable to the financial assets. Revenue from the rendering of a service is recognised upon the delivery of the service to the customers. All revenue is stated net of the amount of goods and services tax (GST).

Government grants are recognised at fair value where there is reasonable assurance that the grant will be received and all grant conditions will be met. Grants relating to expense items are recognised as income over the periods necessary to match the grant costs they are compensating. Grants relating to assets are credited to deferred income at fair value and are credited to income over the expected useful life of the asset on a straight line basis.

Research and Development Grant revenue is recognised as income when it is received.

### (e) Income Tax

The charge for current income tax expense is based on the loss for the year adjusted for any non-assessable or disallowed items. It is calculated using tax rates that have been enacted or are substantially enacted by reporting date.

Deferred tax is accounted for using the liability method in respect of temporary differences arising between the tax bases of assets and liabilities and their carrying amounts in the financial statements. No deferred income tax will be recognised from the initial recognition of an asset or liability, excluding a business combination, where there is no effect on accounting or taxable profit or loss.

Deferred tax is calculated at the tax rates that are expected to apply to the period when the asset is realised or liability is settled. Deferred tax is credited in the statement of comprehensive income except where it relates to items that may be credited directly to equity, in which case the deferred tax is adjusted directly against equity. Deferred income tax assets are recognised to the extent that it is probable that future tax profits will be available against which deductible temporary differences can be utilised.

The amount of benefits brought to account or which may be realised in the future is based on the assumption that no adverse change will occur in income taxation legislation and the anticipation that the consolidated entity will derive sufficient future assessable income to enable the benefit to be realised and comply with the conditions of deductibility imposed by the law.

Benitec Biopharma Limited and its wholly-owned Australian subsidiary has formed an income tax consolidated group under the Tax Consolidation Regime. Benitec Biopharma Limited is responsible for recognising the current and deferred tax assets and liabilities for the tax consolidated group. The Group notified the ATO on 12 February 2004 that it had formed an income tax consolidated group to apply from 1 July 2002. No tax sharing agreement has been entered between entities in the tax consolidated group.

### (f) Critical Accounting Estimates and Judgments

The Directors evaluate estimates and judgments incorporated into the financial report based on historical knowledge and best available current information. Estimates assume a reasonable expectation of future events and are based on current trends and economic data, obtained both externally and within the Group.

### Key estimates—share-based payments transactions

The Group measures the cost of equity-settled transactions with employees by reference to the fair value of the equity instruments at the date at which they are granted. The fair value is determined using a Black-Scholes model, using the assumptions detailed in note 21.

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

### Key judgements—tax losses

Given the company's and each individual entities' history of recent losses, the Group has not recognised a deferred tax asset with regard to unused tax losses and other temporary differences, as it has not been determined whether the company or its subsidiaries will generate sufficient taxable income against which the unused tax losses and other temporary differences can be utilised.

### Key judgements—compound financial instruments

The Group measures the fair value of the liability component using the prevailing market interest rate for similar convertible instruments.

### (g) Impairment of Non-Financial Assets

The Group assesses at each reporting date whether there is an indication that an asset may be impaired. If any such indication exists, or when annual impairment testing for an asset is required (i.e. Goodwill, intangible assets with indefinite useful lives and intangible assets not yet available for use), the Group makes an estimate of the asset's recoverable amount. An asset's recoverable amount is the higher of its fair value less costs to sell and its value in use and is determined for an individual asset, unless the asset does not generate cash inflows that are largely independent of those from other assets or groups of assets and the asset's value in use cannot be estimated to be close to its fair value. In such cases the asset is tested for impairment as part of the cash generating unit to which it belongs. When the carrying amount of an asset or cash-generating unit exceeds its recoverable amount, the asset or cash-generating unit is considered impaired and is written down to its recoverable amount.

In assessing value in use, the estimated future cash flows are discounted to their present value using a pre-tax discount rate that reflects current market assessments of the time value of money and the risks specific to the asset. Impairment losses relating to continuing operations are recognised in those expense categories consistent with the function of the impaired asset unless the asset is carried at revalued amount (in which case the impairment loss is treated as a revaluation decrease).

### (h) Cash and Cash Equivalents

Cash and cash equivalents includes cash on hand, deposits held at call with banks, other short-term highly liquid investments with original maturities of three months or less, and bank overdrafts. Bank overdrafts are shown within short term borrowings in current liabilities on the statement of financial position.

### (i) Trade and Other Receivables

Trade receivables, which generally have 30 day terms, are recognised and carried at original invoice amount less an allowance for any uncollectible amounts. An estimate for doubtful debts is made when collection of the full amount is no longer probable. Bad debts are written off when identified.

### (j) Property, Plant and Equipment

Each class of property, plant and equipment is carried at cost or fair value less, where applicable, any accumulated depreciation and impairment losses.

### Plant and equipment

Plant and equipment are measured on the cost basis less depreciation and impairment losses. The carrying amount of plant and equipment is reviewed annually by directors to ensure it is not in excess of the recoverable

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

amount from these assets. The recoverable amount is assessed on the basis of the expected net cash flows that will be received from the assets employment and subsequent disposal. The expected net cash flows have been discounted to their present values in determining recoverable amounts.

Subsequent costs are included in the asset's carrying amount or recognised as a separate asset, as appropriate, only when it is probable that future economic benefits associated with the item will flow to the Group and the cost of the item can be measured reliably. All other repairs and maintenance are charged to the statement of comprehensive income during the financial period in which they are incurred.

### Depreciation

The depreciable amount of all fixed assets including capitalised lease assets is depreciated on a diminishing value basis over their useful lives to the consolidated entity commencing from the time the asset is held ready for use. Leasehold improvements are depreciated over the shorter of either the unexpired period of the lease or the estimated useful lives of the improvements.

The depreciation rates used for plant and equipment were 20-33%. The assets' residual values and useful lives are reviewed, and adjusted if appropriate, at each reporting date. An asset's carrying amount is written down immediately to its recoverable amount if the asset's carrying amount is greater than its estimated recoverable amount.

Gains and losses on disposals are determined by comparing proceeds with the carrying amount. These gains and losses are included in the statement of comprehensive income. When assets which have been revalued are sold, amounts included in the revaluation reserve relating to that asset are transferred to retained earnings.

### (k) Leases

Leases of fixed assets are classified as finance leases where the Group has substantially all the risks and benefits incidental to the ownership of the asset, but not the legal ownership.

Finance leases are capitalised by recording an asset and a liability at the lower of the amounts equal to the fair value of the leased property or the present value of the minimum lease payments, including any guaranteed residual values. Lease payments are allocated between the reduction of the lease liability and the lease interest expense for the period. Leased assets are depreciated on a straight-line basis over their estimated useful lives where it is likely that the consolidated entity will obtain ownership of the asset or over the term of the lease. Lease payments for operating leases, where substantially all the risks and benefits remain with the lessor, are charged as expenses in the periods in which they are incurred.

Lease incentives under operating leases are recognised as a liability and amortised on a straight-line basis over the life of the lease term.

### (l) Financial Instruments

#### Recognition

Financial instruments are initially measured at cost on trade date, which includes transaction costs, when the related contractual rights or obligations exist. Subsequent to initial recognition these instruments are measured as set out below.

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

### Loans and receivables

Loans and receivables are non-derivative financial assets with fixed or determinable payments that are not quoted in an active market and are stated at amortised cost using the effective interest rate method.

### Financial liabilities

Non-derivative financial liabilities are recognised at amortised cost, comprising original debt less principal payments and amortisation.

### Compound instruments

The component parts of compound instruments issued by the Group are classified separately as financial liabilities and equity in accordance with the substance of the contractual arrangement. The liability component is recorded on an amortised cost basis using the effective interest method until extinguished upon conversion or at the instrument's maturity date. The equity component is determined by deducting the amount of the liability component from the fair value of the compound instrument as a whole. This is recognised and included in equity, net of income tax effects, and is not subsequently remeasured.

### Fair value

Fair value is determined based on current bid prices for all quoted investments. Valuation techniques are applied to determine the fair value for all unlisted securities, including recent arm's length transactions, reference to similar instruments and option pricing models.

### Impairment

At each reporting date, the Group assess whether there is objective evidence that a financial instrument has been impaired. In the case of available-for-sale financial instruments, a prolonged or significant decline in the value of the instrument is considered to determine whether impairment has arisen. Impairment losses are recognised in the statement of comprehensive income.

### (m) Intangibles

#### Research and development

Expenditure during the research phase of a project is recognised as an expense when incurred. Development costs are capitalised only when technical feasibility studies identify that the project will deliver future economic benefits and these benefits can be measured reliably.

Development costs have a finite life and are amortised on a systematic basis matched to the future economic benefits over the useful life of the project.

#### Goodwill

Goodwill, representing the excess of the cost of acquisition over the fair value of the identifiable assets, liabilities and contingent liabilities acquired, is recognised as an asset and not amortised, but tested at least annually for impairment and whenever there is an indication that the goodwill may be impaired. Any impairment is recognised immediately in profit or loss and is not subsequently reversed.

Refer to Note 1 (g) for a description of impairment testing procedures.

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

### **(n) Trade and Other Payables**

Trade payables and other payables are carried at amortised costs and represent liabilities for goods and services provided to the Group prior to the end of the financial year that are unpaid and arise when the Group becomes obliged to make future payments in respect of the purchase of these goods and services.

### **(o) Employee Benefits**

Provision is made for the Group's liability for employee benefits arising from services rendered by employees to reporting date. Employee benefits that are expected to be settled within one year have been measured at the amounts expected to be paid when the liability is settled, plus related on-costs. Employee benefits payable later than one year have been measured at the present value of the estimated future cash outflows to be made for those benefits.

### **(p) Provisions**

Provisions are recognised when the Group has a legal or constructive obligation, as a result of past events, for which it is probable that an outflow of economic benefits will result and that outflow can be reliably measured.

### **(q) Contributed Equity**

Ordinary shares are classified as equity. Incremental costs directly attributable to the issue of new shares or options are shown in equity as a deduction, net of tax, from the proceeds.

### **(r) Share-based Payment Transactions**

Benefits are provided to employees of the Group in the form of share-based payment transactions, whereby employees render services in exchange for shares or rights over shares ('equity-settled transactions'). The plan currently in place to provide these benefits is the Employee Share Option Plan (ESOP), which provides benefits to senior executives.

The cost of these equity-settled transactions with employees is measured by reference to the fair value at the date at which they are granted. The fair value is determined using a Black-Scholes model. In valuing equity-settled transactions, no account is taken of any performance conditions, other than conditions linked to the price of the shares of Benitec Biopharma Limited ('market conditions').

The cost of equity-settled transactions is recognised, together with a corresponding increase in equity, over the period in which the performance conditions are fulfilled, ending on the date on which the relevant employees become fully entitled to the award ('vesting date').

The cumulative expense recognised for equity-settled transactions at each reporting date until vesting date reflects (i) the extent to which the vesting period has expired and (ii) the number of awards that, in the opinion of the directors of the Group, will ultimately vest. This opinion is formed based on the best available information at reporting date. No adjustment is made for the likelihood of market performance conditions being met as the effect of these conditions is included in the determination of fair value at grant date.

No expense is recognised for awards that do not ultimately vest, except for awards where vesting is conditional upon a market condition.

Where the terms of an equity-settled award are modified, as a minimum an expense is recognised as if the terms had not been modified. In addition, an expense is recognised for any increase in the value of the transaction as a result of the modification, as measured at the date of modification. Where an equity-settled award is cancelled, it is treated as if it had vested on the date of cancellation, and any expense not yet recognised for the

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

award is recognised immediately. However, if a new award is substituted for the cancelled award, and designated as a replacement award on the date that it is granted, the cancelled and new award are treated as if they were a modification of the original award, as described in the previous paragraph.

The dilutive effect, if any, of outstanding options is reflected as additional share dilution in the computation of earnings per share.

### (s) Earnings per Share

Basic earnings per share is calculated as net profit attributable to members of the parent, adjusted to exclude any costs of servicing equity (other than dividends) and preference share dividends, divided by the weighted average number of ordinary shares, adjusted for any bonus element.

Diluted earnings per share is calculated as net profit attributable to members of the parent, adjusted for:

- costs of servicing equity (other than dividends) and preference share dividends;
- the after tax effect of dividends and interest associated with dilutive potential ordinary shares that have been recognised as expenses; and
- other non-discretionary changes in revenues or expenses during the period that would result from the dilution of potential ordinary shares;

divided by the weighted average number of ordinary shares and dilutive potential ordinary shares, adjusted for any bonus element.

### (t) Foreign Currency Transactions and Balances

#### Functional and presentation currency

The functional currency of each of the Group's entities is measured using the currency of the primary economic environment in which that entity operates. The consolidated financial statements are presented in Australian dollars which is the parent entity's functional and presentation currency.

#### Transaction and balances

Foreign currency transactions are translated into functional currency using the exchange rates prevailing at the date of the transaction. Foreign currency monetary items are translated at the year-end exchange rate. Non-monetary items measured at historical cost continue to be carried at the exchange rate at the date of the transaction. Non-monetary items measured at fair value are reported at the exchange rate at the date when fair values were determined.

Exchange differences arising on the translation of monetary items are recognised in the statement of comprehensive income, except where deferred in equity as a qualifying cash flow or net investment hedge. Exchange differences arising on the translation of non-monetary items are recognised directly in equity to the extent that the gain or loss is directly recognised in equity, otherwise the exchange difference is recognised in the statement of comprehensive income.

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

### Group companies

The financial results and position of foreign operations whose functional currency is different from the Group's presentation currency are translated as follows:

- Assets and liabilities are translated at year-end exchange rates prevailing at that reporting date.
- Income and expenses are translated at average exchange rates for the period.
- Retained profits are translated at the exchange rates prevailing at the date of the transaction.

### (u) Goods and Services Tax (GST)

Revenues, expenses and assets are recognised net of the amount of GST, except where the amount of GST incurred is not recoverable from the Australian Tax Office. In these circumstances the GST is recognised as part of the cost of acquisition of the asset or as part of an item of the expense. Receivables and payables in the statement of financial position are shown inclusive of GST.

Cash flows are presented in the statement of cash flows on a gross basis, except for the GST component of investing and financing activities, which are disclosed as operating cash flows.

### (v) Comparative Figures

When required by Accounting Standards, comparative figures have been adjusted to conform to changes in presentation for the current financial year.

### (w) Going Concern

The directors have prepared the financial statements on a going concern basis after taking into consideration the net loss for the year of \$7,039,109 and the cash and cash equivalents balance of \$31,359,199. The directors have recognised the capital raisings in 2013 and 2014, performed a review of the cash flow forecasts, considered the cash flow needs of the Group, and believe that the strategies in place are appropriate to generate funding which will be sufficient to maintain the going concern status of the Group. If these strategies are unsuccessful then the Group may need to realise its assets and extinguish liabilities other than in the ordinary course of business and at amounts different to those disclosed in the financial report.

### Note 2: Revenue from continuing operations

	2014	2013
	\$	\$
<b>Revenue</b>		
Licensing revenue and royalties . . . . .	276,824	521,140
Finance income—interest received . . . . .	321,116	118,709
	597,940	639,849
<b>Other income</b>		
Federal Government Research and Development Grants . . . . .	775,833	824,333
Total revenue and other income . . . . .	1,373,773	1,464,182



Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

**Note 3: Loss for the year**

**(a) Expenses incurred by continuing operations**

**Items included in Statement of Comprehensive Income**

	<u>2014</u>	<u>2013</u>
	\$	\$
<b>Depreciation</b>		
<i>Included in Occupancy expenses</i>		
Depreciation of plant and equipment .....	12,808	29,794
<b>Employee benefits expense</b>		
<i>Included in Employment related expenses</i>		
Wages and salaries .....	2,109,860	1,759,745
Superannuation costs .....	89,090	72,320

**(b) Expenses**

Research and development expenses costs consist of:

	<u>2014</u>	<u>2013</u>
	\$	\$
Project expenses .....	3,310,014	1,075,844
Other IP related expenses .....	447,855	204,168
	<u>3,757,869</u>	<u>1,280,012</u>

**Note 4: Income tax expense**

(a) The prima facie tax on loss from ordinary activities before income tax is reconciled to the income tax as follows:

	<u>2014</u>	<u>2013</u>
	\$	\$
Prima facie tax payable on loss from ordinary activities before income tax at 30% (2013: 30%) .....	(2,248,042)	(1,046,388)
<i>Add Tax effect of:</i>		
Non-deductible share-based payment expense .....	106,535	155,625
Non-assessable foreign currency translation provision .....	(2,324)	457,865
Non-deductible legal fees .....	15,906	9,326
Capital items deductible .....	(231,942)	(58,863)
Other non-deductible items .....	19,500	46,842
Deductible items not included in operating result .....	4,800	(48,354)
Deferred tax asset not brought to account .....	<u>2,335,567</u>	<u>483,947</u>
Income tax benefit .....	<u>—</u>	<u>—</u>
Income tax benefit reported in the income statement .....	<u>454,365</u>	<u>—</u>

The income tax benefit was a cash refund of income tax in the US in Tacere Therapeutics Inc. (a wholly owned subsidiary) not previously recorded.

(b) The parent entity, acting as the Head Entity, notified the Australian Taxation Office on 12 February 2004 that it had formed a Tax Consolidated Group applicable as from 1 July 2002. No tax sharing agreement has been entered between entities in the tax consolidated group.

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

- (c) As at 30 June 2014, the Tax Consolidated Group has estimated carry-forward tax losses of \$13,103,412 (2013: \$11,751,713) calculated at 30% of the accumulated annual Australian tax losses. The tax losses have not been recognised in the financial statements and the capacity of the Tax Consolidated Group to use the tax losses will be subject to conforming with regulatory tests. The deferred tax asset relating to temporary differences (calculated at 30%) was \$49,953 (2013: \$29,591).

The Tax Consolidated Group also has Australian capital tax losses for which no deferred tax asset is recognised in the financial statements of \$381,588 (2013: \$381,588). The capacity of the Tax Consolidated Group to use the capital tax losses will be subject to conforming with regulatory tests.

The recoupment of available tax losses as at 30 June 2014 is contingent upon the following:

- (i) the Consolidated Group deriving future assessable income of a nature and of an amount sufficient to enable the benefit from the losses to be realised;
- (ii) the conditions for deductibility imposed by tax legislation continuing to be complied with; and
- (iii) there being no changes in tax legislation which would adversely affect the Tax Consolidated Group from realising the benefit from the losses.

### Note 5: Auditor's remuneration

	2014	2013
	\$	\$
<b>Audit Services</b>		
Remuneration of Grant Thornton Audit Pty Ltd for:		
—auditing or reviewing the financial report . . . . .	73,238	54,000
<b>Other Services</b>		
Remuneration of Grant Thornton Australia Limited for:		
—taxation compliance and corporate advisory services . . . . .	24,000	43,230

### Note 6: Earnings per share

Basic earnings per share is calculated by dividing the net loss for the year attributable to ordinary shareholders by the weighted average number of ordinary shares on issue during the year.

Diluted earnings per share amounts are calculated by dividing the net loss attributable to ordinary shareholders by the weighted average number of ordinary shares on issue during the year (adjusted for the effects of dilutive options) and the weighted average number of ordinary shares that would be issued on conversion of all dilutive potential ordinary shares.

	2014	2013
	\$	\$
Loss after income tax used in the calculation of basic EPS and dilutive EPS . . . . .	(7,039,109)	(3,487,960)
	<b>Number</b>	<b>Number</b>
Weighted average number of ordinary shares for basic and diluted earnings per share . . . . .	90,432,177	41,688,975
Weighted average number of converted, lapsed or cancelled potential ordinary shares included in diluted earnings per share . . . . .	—	—

Outstanding options to acquire ordinary shares are not considered dilutive for the years ended 30 June 2014 and 30 June 2013.

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

### *Classification of securities*

No securities were classified as potential ordinary shares under IAS33 and therefore have not been included in determination of dilutive EPS due to their anti-dilutive nature.

### **Note 7: Key management personnel**

#### **(a) Details of Key Management Personnel**

##### **(i) Non-Executive Directors**

Mr Peter Francis	Chairman—Non-Executive	Appointed on 23 February 2006
Dr John Chiplin	Director—Non-Executive	Appointed on 1 February 2010
Mr Iain Ross	Director—Non-Executive	Appointed on 1 June 2010
Mr Kevin Buchi	Director—Non-Executive	Appointed on 11 April 2014
Dr Mel Bridges	Director—Non-Executive	Appointed on 12 October 2007 Resigned 18 June 2014

##### **(ii) Specified Executives**

Dr Peter French	Managing Director and Chief Executive Officer	Appointed as Managing Director on 26 August 2014 Appointed Chief Executive Officer on 4 June 2010 Appointed Chief Scientific Officer on 4 August 2009
Dr Michael Graham	Chief Scientific Officer	Appointed on 1 January 2012
Mr Greg West	Company Secretary	Appointed on 26 May 2011
Mr Carl Stubbings	Chief Business Officer	Appointed on 2 July 2012
Dr David Suhy	Senior VP Research and Development	Appointed on 1 October 2012

#### **(b) Key management personnel remuneration includes the following expenses:**

	<u>2014</u>	<u>2013</u>
	\$	\$
Short term employee benefits		
Salaries including bonuses .....	1,859,719	1,252,095
Post-employment benefits		
Superannuation .....	71,100	61,935
Share-based payments .....	348,013	492,976
Total Remuneration .....	<u>2,278,832</u>	<u>1,807,006</u>

During the year no key management personnel exercised options which were granted either under ESOP or by a General Meeting of Members to Non-Executive Directors

### **Note 8: Cash and cash equivalents**

	<u>2014</u>	<u>2013</u>
	\$	\$
Cash at bank .....	288,945	614,746
Deposits at call .....	31,070,254	972,553
	<u>31,359,199</u>	<u>1,587,299</u>

**Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014**

**Reconciliation of Cash Flow from Operations with Loss after Income Tax**

	<u>2014</u>	<u>2013</u>
	\$	\$
Loss after Income Tax .....	(7,039,109)	(3,487,960)
<b>Non-cash flows included in operating loss:</b>		
Impairment .....	—	1,503,296
Foreign exchange on intercompany balances .....	—	(1,526,215)
Depreciation .....	12,808	29,794
Share-based payments .....	355,116	518,749
Foreign currency translation unrealised .....	8,761	(23,457)
<b>Changes in assets and liabilities:</b>		
(Increase)/decrease in other assets .....	(2,936,521)	(13,163)
Decrease in receivables .....	(16,514)	22,393
Decrease/(increase) in payables .....	277,246	200,452
Increase/(decrease) in employee provisions .....	67,874	43,515
Net cash flows from operations .....	<u>(9,270,339)</u>	<u>(2,732,596)</u>

**Note 9: Trade and other receivables**

	<u>2014</u>	<u>2013</u>
	\$	\$
CURRENT		
Sundry Debtors .....	<u>121,587</u>	<u>105,073</u>

**Note 10: Other assets**

	<u>2014</u>	<u>2013</u>
	\$	\$
CURRENT		
Prepayments .....	26,679	14,190
Prepaid clinical trials * .....	2,700,000	—
Other current assets .....	<u>240,060</u>	<u>16,028</u>
	<u>2,966,739</u>	<u>30,218</u>

\* Prepaid clinical trials—The Company announced on 3 June 2013 that it had committed to moving its non-small cell lung cancer therapeutic into clinical development. The Company is using European-based clinical research organisation Clinical Trials Group (CTGCRO) to manage both the initial clinical development and trials. The Company made prepayments in the September quarter 2013 in order to secure favourable commercial terms with CTGCRO for the conduct of the trials.

Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

**Note 11: Controlled entities**

**(a) Controlled entities:**

	<u>Country of Incorporation</u>	<u>Percentage Owned</u>	
		<u>2014</u>	<u>2013</u>
<b>Parent Entity:</b>			
Benitec Biopharma Limited .....	Australia		
<b>Controlled entities of Benitec Biopharma Limited:</b>			
Benitec Australia Limited .....	Australia	100%	100%
Benitec Biopharma Limited .....	United Kingdom	100%	100%
Benitec, Inc. ....	USA	100%	100%
Benitec LLC .....	USA	100%	100%
RNAi Therapeutics, Inc. ....	USA	100%	100%
Tacere Therapeutics, Inc. ....	USA	100%	100%

**(b) Controlled entities acquired or disposed:**

No controlled entities were acquired or disposed during the 2014 financial year.

**Note 12: Property, plant and equipment**

	<u>2014</u>	<u>2013</u>
	\$	\$
At cost .....	127,795	95,431
Accumulated depreciation .....	(80,118)	(67,311)
Total Property, Plant and Equipment .....	<u>47,677</u>	<u>28,120</u>

*Movements in Carrying Amounts*

Movement in the carrying amounts for each class of property, plant and equipment between the beginning and the end of the current financial year.

	<u>Leasehold Improvement</u>	<u>Plant and Equipment</u>	<u>Total</u>
	\$	\$	\$
Balance at 30 June 2012 .....	11,760	19,043	30,803
Additions .....	—	27,111	27,111
Less Disposals .....	—	—	—
Depreciation expense .....	(1,550)	(28,244)	(29,794)
Balance at 30 June 2013 .....	<u>10,210</u>	<u>17,910</u>	<u>28,120</u>
Additions .....	—	32,365	32,365
Less Disposals .....	—	—	—
Depreciation expense .....	(1,550)	(11,258)	(12,808)
Balance at 30 June 2014 .....	<u>8,660</u>	<u>39,017</u>	<u>47,677</u>

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

### Note 13: Intangibles

The net carrying amount of intangibles can be analysed as follows:

	\$
<b>Gross carrying amount</b>	
Balance at 30 June 2012 .....	—
Acquired through business combination .....	<u>1,503,296</u>
Balance at 30 June 2013 .....	<u>1,503,296</u>
Acquired through business combination .....	—
Balance at 30 June 2014 .....	<u>1,503,296</u>
<b>Accumulated impairment</b>	
Balance at 30 June 2012 .....	—
Impairment loss recognised in the year .....	<u>(1,503,296)</u>
Balance at 30 June 2013 .....	<u>(1,503,296)</u>
Impairment loss recognised in the year .....	—
Balance at 30 June 2014 .....	<u>(1,503,296)</u>
<b>Net book value</b>	
At 30 June 2013 .....	—
As at 30 June 2014 .....	—

### Impairment

A review of the carrying value of the in-process research which arose on the acquisition of Tacere Therapeutics Inc. was undertaken in the 2013 financial year. The recoverable amounts of the cash generating units to which the in-process research was allocated were determined based on value-in-use calculations. This review identified that the full value of the in-process research should be impaired and as such a non-cash impairment charge of \$1,503,296 was booked in the 2013 financial year.

### Note 14: Trade and other payables

	<u>2014</u>	<u>2013</u>
	\$	\$
<b>CURRENT</b>		
<i>Unsecured liabilities</i>		
Trade creditors .....	572,557	279,994
Sundry creditors and accrued expenses .....	215,612	374,560
Deferred consideration—Tacere vendors .....	—	<u>357,179</u>
	<u>788,169</u>	<u>1,011,733</u>

### Note 15: Provisions

<b>CURRENT</b>		
Provision for employee benefits .....	<u>166,511</u>	<u>98,637</u>

### Note 16: Contributed equity

The share capital of the Company consists only of fully paid ordinary shares; the shares do not have a par value. All shares are equally eligible to receive dividends and the repayment of capital and represent one vote at

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

the shareholders' meeting of the Company. The Board monitors capital funding requirements in its competitive landscape and continues to actively manage its cash requirements as part of a broader capital management program to ensure adequate capital is in place to fund the company's operations.

### (a) Ordinary Shares, reported in post consolidation share numbers for 2014 and 2013

114,898,992 (2013: 46,076,562) issued and fully paid ordinary shares

	2014	2013
	\$	\$
Contributed Equity at the beginning of the reporting period, (after applying the 25:1 consolidation) .....	89,609,248	87,348,819
Placements in March to June 2013 .....	—	1,262,000
Placement in July 2013 .....	7,618,326	—
Share Purchase Plan August 2013 .....	2,820,000	—
Issued to Tacere shareholders on purchase of Tacere .....	—	1,173,585
Tacere escrow shares released October 2013 .....	357,190	—
Options exercised during the year .....	185,503	—
Placements in February and April 2014 .....	31,496,504	—
Transaction costs relating to share issues during the year .....	(2,901,095)	(175,156)
Contributed Equity at the close of the reporting period .....	129,185,676	89,609,248
	Number	Number
At the beginning of reporting period .....	46,076,562	38,825,141
Shares issued during the year .....	68,822,430	7,251,421
	114,898,992	46,076,562

### (b) Share options

At the end of the financial year, there were 23,320,173 unissued ordinary shares (2013: 17,594,313) over which options were outstanding.

	Expiry Date	Exercise Price		
Strategic Advisor warrants .....	4 August 2014	22.500	245,078	
ESOP Options .....	19 August 2014	0.510	260,000	
NED Options .....	19 August 2014	0.570	120,000	
Unlisted Options—placement .....	18 February 2015	0.325	662,767	
Unlisted other options .....	10 April 2015	2.500	480,000	
Unlisted other options .....	23 October 2015	4.250	78,125	
NED Options .....	26 September 2016	1.250	1,600,000	
ESOP Options .....	17 November 2016	1.250	1,800,000	
NED Options .....	26 September 2016	1.250	1,200,000	
ESOP Options .....	7 February 2017	1.250	168,000	
ESOP Options .....	18 July 2017	1.250	400,000	
ESOP Options .....	16 November 2017	1.250	400,000	
NED Options .....	18 May 2018	0.625	400,000	
ESOP Options .....	22 August 2018	1.250	2,080,000	
Unlisted options—placement .....	28 February 2019	1.260	13,246,203	
ESOP Options .....	15-May-19	1.500	180,000	
			23,320,173	

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

Since 30 June 2013, the following options were issued under the ESOP:

<u>Expiry date</u>	<u>Exercise price</u>	<u>Issue date</u>	<u>Number</u>	<u>Weighted average share price</u>	<u>Volatility</u>	<u>Risk free rate</u>
22 August 2018 .....	1.250	22 August 2013	2,080,000	\$0.29	112%	3.55%
15 May 2019 .....	1.500	15 May 2014	180,000	\$0.30	100%	2.60%
			<u>2,260,000</u>			

Rights over shares are provided to employees under the Employee Share Option Plan (ESOP). The cost of these equity-settled transactions with employees is measured by reference to the fair value at the date at which they are granted. The fair value is determined using a Black-Scholes model. In valuing equity-settled transactions, no account is taken of any performance conditions, other than conditions linked to the price of the shares of Benitec Biopharma Limited ('market conditions').

The following information was factored in to the Black-Scholes model for the options issued under ESOP this year:

- weighted average share price as shown above
- exercise prices were as shown above
- expected volatility was as shown above and was determined by reference to Bloomberg for the Benitec share price based on historical volatility
- option life is 5 years
- The risk-free interest rate used was as shown above

There were no options issued to staff or directors in the period from 30 June 2014 to the date this report was issued.

### Note 17: Reserves

	<u>2014</u>	<u>2013</u>
	\$	\$
<b>Share-based payments reserve</b>		
At the beginning of the reporting period .....	1,591,702	1,394,142
Share based payments .....	355,116	518,749
Transferred to Accumulated Losses Reserve no longer required .....	—	(321,189)
	<u>1,946,818</u>	<u>1,591,702</u>
<b>Foreign currency translation reserve</b>		
At the beginning of the reporting period .....	(1,313,792)	—
Foreign currency translation .....	7,747	(1,313,792)
	<u>(1,306,045)</u>	<u>(1,313,792)</u>
<b>Total Reserves</b>	<u><b>640,773</b></u>	<u><b>277,910</b></u>

### Nature and purpose of Reserves

#### *Share Based Payments Reserve*

The Share-based Payments Reserve represents the expense attributed to options based on a Black Scholes valuation method for vested options.



## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

### Foreign currency translation reserve

The Foreign currency translation reserve represents the currency translation movements of subsidiary company balances denominated in foreign currencies at year end.

### Note 18: Operating segments

#### Business Segments

The Group had only one business segment during the financial year, being the global commercialisation by licensing and partnering of patents and licences in biotechnology, more specifically in functional genomics, with applications in biomedical research and human therapeutics.

#### Geographical Segments

Business operations are principally conducted in Australia, with laboratory and other activities in the USA.

Geographical location	Segment Revenues		Segment Results		Carrying Amount of Segment Assets	
	2014	2013	2014	2013	2014	2013
	\$	\$	\$	\$	\$	\$
Australia . . . . .			(7,495,377)	(3,220,240)	34,433,803	1,507,350
External customers . . . . .	274,413	521,140				
Interest revenue . . . . .	321,116	118,709				
Other income . . . . .	775,833	823,354				
	<u>1,371,362</u>	<u>1,463,203</u>				
United States of America . . . . .			1,903	(267,720)	61,399	243,360
External customers . . . . .	2,411	—				
Interest revenue . . . . .	—	—				
Other income . . . . .	—	979				
	<u>2,411</u>	<u>979</u>				
	<u>1,373,773</u>	<u>1,464,182</u>	<u>(7,493,474)</u>	<u>(3,487,960)</u>	<u>34,495,202</u>	<u>1,750,710</u>

### Accounting Policies

Segment revenues and expenses are directly attributable to the identified segments and include joint venture revenue and expenses where a reasonable allocation basis exists. Segment assets include all assets used by a segment and consist mainly of cash, receivables, inventories, intangibles and property, plant and equipment, net of any allowances, accumulated depreciation and amortisation. Where joint assets correspond to two or more segments, allocation of the net carrying amount has been made on a reasonable basis to a particular segment. Segment liabilities include mainly accounts payable, employee entitlements, accrued expenses, provisions and borrowings. Deferred income tax provisions are not included in segment assets and liabilities.

### Note 19: Financial risk management objectives and policies

The Group's principal financial instruments comprise receivables, payables, cash and short-term deposits. The Group manages its exposure to key financial risks, including interest rate and currency risk in accordance with the Company financial risk management policy. The objective of the policy is to protect the assets and provide a solid return.

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

The main risks arising from the financial instruments are interest rate risk, liquidity risk, foreign currency risk and credit risk. The Board reviews and agrees policies for managing each of these risks and they are summarised below.

### Risk Exposures and Responses

#### Interest rate risk

The Group generates income from interest on surplus funds. At reporting date, the Group had the following mix of financial assets and liabilities exposed to Australian variable interest rate risk that are not designated in cash flow hedges:

	<u>2014</u>	<u>2013</u>
	\$	\$
Financial Assets		
Cash and cash equivalents . . . . .	31,359,199	1,587,299
Financial Liabilities . . . . .	<u>—</u>	<u>—</u>
Net Exposure . . . . .	<u>31,359,199</u>	<u>1,587,299</u>

The policy is to analyse the Company's interest rate exposure across the Group's financial assets and liabilities. Consideration is given to the return on funds invested, alternative financing, the mix of fixed and variable interest rates and hedging positions. The Group currently has short term deposits at variable interest rates. The average interest rate applying to cash deposits in the year was 3.67% (2013 4.00%).

The following sensitivity analysis is based on the interest rate risk exposures in existence at the reporting date:

At 30 June 2014, if interest rates had moved, as illustrated in the table below, with all other variables held constant, the judgment of reasonably possible movements in post-tax profit and equity would have been as follows:

	<u>Post Tax Result</u> <u>Higher/ (Lower)</u>		<u>Equity</u> <u>Higher/ (Lower)</u>	
	<u>2014</u>	<u>2013</u>	<u>2014</u>	<u>2013</u>
	\$	\$	\$	\$
+1% (100 basis points) . . . . .	143,625	12,797	143,625	12,797
-0.5% (50 basis points) . . . . .	(71,812)	(6,399)	(71,812)	(6,399)

#### Liquidity risk

The Group's objective is to obtain revenue from commercialisation and to continue to access funding markets. The Group has a pipeline of programs to take its research and development to the clinic and potentially originate licensing transactions with pharmaceutical companies. Trade payables and other financial liabilities originate from the financing of the ongoing research and development programs in addition to the operations of the business generally.

The table below reflects all contractually fixed pay-offs and receivables for settlement, repayments and interest resulting from recognised financial assets and liabilities as at 30 June 2014. Cash flows for financial assets and liabilities with fixed amount or timing are presented with their respective discounted cash flows for the respective upcoming fiscal years.

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

The remaining contractual maturities of the Group's financial liabilities are:

	2014	2013
	\$	\$
6 months or less .....	788,169	1,011,733
6-12 months .....	—	—
1-5 years .....	—	—
Over 5 years .....	—	—
	788,169	1,011,733

### Maturity analysis of financial assets and liabilities based on management's expectation

The table below reflects management's expectation of the maturity of financial assets and liabilities.

These assets are considered in the context of the Group's overall liquidity risk. The Group has established a risk reporting process overseen by the board which monitors existing financial assets and liabilities and provides information to enable effective risk management. The Board regularly evaluates managements rolling forecasts of liquidity which includes assessments of cash income and outgoings.

	≤ 6 months	6-12 months	1-5 years	>5 years	Total
	\$	\$	\$	\$	\$
<b>Financial assets</b>					
Cash and cash equivalents .....	23,359,199	8,000,000	—	—	31,359,199
Trade and other receivables .....	121,587	—	—	—	121,587
<b>Financial Liabilities</b>					
Trade and other payables .....	(788,169)	—	—	—	(788,169)
Net Maturity .....	22,692,617	8,000,000	—	—	30,692,617

### Foreign currency risk

The Group has transactional currency exposures. Such exposure arises from licensing fees and royalties as well as expenditure by the Group in currencies other than the unit's measurement currency. With the exception of unrealised movements on intercompany loans, foreign currency income and expenditure accounts for less than 15% of the Groups transactions and therefore management have assessed that movements in foreign exchange would not materially impact the financial statements.

### Credit risk

Credit risk arises from the financial assets of the Group, which comprise cash and cash equivalents, and trade and other receivables. The Group's exposure to credit risk arises from potential counter party payment default, with a maximum exposure equal to the carrying amount. Exposures at each reporting date are assessed and disclosed in the financial statements.

The Group does not hold any credit derivatives to offset its credit exposure. The Group trades only with recognised, creditworthy third parties and as such collateral is not requested. The Group does not securitise its trade and other receivables.

Customers who wish to trade on credit terms are subject to credit assessment procedures which may include an assessment of their independent credit rating, financial position, past experience and industry reputation. Receivable balances are regularly monitored. There are no significant concentrations of credit risk within the Group.

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

### Note 20: Financial instruments

#### Fair values

Fair values of financial assets and liabilities are equivalent to carrying values due their short term to maturity.

### Note 21: Share based payments

#### Benitec Biopharma Limited Employees Share Option Plan (ESOP):

##### Description of plan

The Group may from time to time issue employees options to acquire shares in the parent at a fixed price. Each option when exercised entitles the option holder to one share in the Company. Options are exercisable on or before an expiry date, do not carry any voting or dividend rights and are not transferable except on death of the option holder.

##### Share Options granted during the year

The following options were issued to executives by Benitec Biopharma Limited under its ESOP and are unlisted.

<u>Executive</u>	<u>Grant Date</u>	<u>Number</u>	<u>Exercise Price</u>	<u>Expiry Date</u>
Peter French .....	22 August 2013	1,400,000	\$1.250	22 August 2018
David Suhy .....	22 August 2013	200,000	\$1.250	22 August 2018
Greg West .....	22 August 2013	280,000	\$1.250	22 August 2018
Carl Stubbings .....	22 August 2013	200,000	\$1.250	22 August 2018
Tin Mao .....	15 May 2014	90,000	\$1.500	15 May 2019
Shin-chu Kao .....	15 May 2014	90,000	\$1.500	15 May 2019
		<u>2,260,000</u>		

There were no options issued to directors in the year to 30 June 2014. The closing market price of an ordinary share of Benitec Biopharma Limited (ASX Code: BLT) on the Australian Securities Exchange at 30 June 2014 was \$1.15 (30 June 2013: \$0.375, after adjusting for the securities consolidation in July 2013)

The following table shows the number and weighted average exercise price (WAEP) of share options issued under the ESOP:

	<u>2014 Number</u>	<u>2014 WAEP</u>	<u>2013 Number</u>	<u>2013 WAEP</u>
Outstanding at the beginning of the year .....	3,028,000	1.200	2,440,000	1.147
Granted during the year .....	2,260,000	1.270	800,000	1.250
Exercised during the year .....	—	—	—	—
Lapsed or forfeited during the year .....			<u>(212,000)</u>	0.792
Outstanding at the end of the year .....	<u>5,288,000</u>	1.229	<u>3,028,000</u>	1.200
Options exercisable at the end of the year .....	<u>2,178,667</u>		<u>1,456,000</u>	

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

### Details of ESOP share options outstanding as at end of year:

<u>Grant Date</u>	<u>Expiry Date</u>	<u>Exercise Price</u>	<u>2014 Number</u>	<u>2013 Number</u>
13 July 2010 .....	19 August 2014	\$0.510	260,000	260,000
17 November 2011 .....	17 November 2016	\$1.250	1,800,000	1,800,000
7 February 2012 .....	7 February 2017	\$1.250	168,000	168,000
18 July 2012 .....	18 July 2017	\$1.250	400,000	400,000
16 November 2012 .....	16 November 2017	\$1.250	400,000	400,000
22 August 2013 .....	22 August 2018	\$1.250	2,080,000	—
28 May 2014 .....	18 May 2019	\$1.500	180,000	—
			<u>5,288,000</u>	<u>3,028,000</u>

The weighted average remaining life of the options issued under the ESOP at 30 June 2014 was 3 years and 3 months. (2013: 3 years and 4 months)

### Note 22: Events subsequent to reporting date

No matters or circumstances have arisen since 30 June 2014 which have significantly affected or may significantly affect the operations of the Group, the results of those operations or the state of affairs of the Group, in subsequent financial years.

### Note 23: Contingent liabilities

In January 2010, the Company reached a settlement with the CSIRO to replace the existing Licence Agreement and Commercial Agreement with a new exclusive Licence Agreement for the use of intellectual property and the Capital Growth Agreement with the issue of ordinary shares. As part of the settlement, a Transition Agreement was put in place in order to facilitate the change from the old agreements to the new agreement and to deal with a number of other matters.

Under the terms of the Transition Agreement, the Company agreed to pay CSIRO an amount of \$297,293 for past patent costs only in the event of a trigger event, being either a corporate transaction or an insolvency event.

### Scientific work on the therapeutic programs

On 18 December 2012 Benitec announced the appointment of Synteract Inc. as the Company's Clinical Research Organisation responsible for the progression of TT-034 into Phase I/II (a) Clinical Trials in the USA. Benitec has negotiated a contract with favourable commercial terms, in some instances requiring prepayment, for Synteract to continue to manage the Clinical Trials throughout 2013 and 2014.

Benitec announced plans on 3 June 2014 to progress its non-small cell lung cancer (NSCLC) therapeutic Tribetarna™ into Phase II clinical trials in late 2014 calendar year. The Company had reached agreement to use European-based clinical research organisation Clinical Trials Group (CTGCRO) to manage the trial, and subsequently negotiated favourable commercial terms which included prepayments covering the clinical trial and consulting services.

The Company has contracted for scientific work on the therapeutic programs, as described above, and payments due within the next twelve months total approximately \$2,092,500 (2013: \$4,178,261).

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

### Note 24: Capital management policies and procedures

The Group's capital management objectives are to ensure the Group has the ability to fund its activities, to continue as a going concern; and to provide value to shareholders.

The Group's capital management plan targets appropriate cash levels to service expected future cash flow needs based on the forecasts for current and future programs and business running costs. Management assesses the Group's capital requirements in order to maintain an efficient overall financing structure. The Group manages the capital structure and makes adjustments to it in the light of changes in access to funding, business conditions and the risk characteristics of the business. In order to maintain appropriate funding the Group may issue new shares. The amounts managed as capital by the Group for the reporting periods under review are as shown in the statement of financial position.

### Note 25: Related party transactions

	2014	2013
	\$	\$
Transactions with Directors and Director-related Entities:		
Legal services paid / payable to Francis Abourizk Lightowlers, a law firm in which Mr Peter Francis is a partner and has a beneficial interest. . . . .	108,913	103,492
Consultancy fees for executive duties paid/payable to NewStar Ventures Ltd, a corporation in which Dr John Chiplin is a director and has a beneficial interest. . . . .	40,000	40,000

Transactions between related parties are on normal commercial terms and the conditions no more favourable than those available to other non-related parties. There are no outstanding balances as at 30 June 2014 (2013: nil)

### Note 26: Business combination—Tacere Therapeutics Inc. acquisition in October 2012

Benitec announced an agreement to acquire the US-based RNA interference (RNAi) therapeutics company Tacere Therapeutics Inc. ('Tacere') on 11 October 2012. The acquisition was completed on 30 October 2012 when Benitec acquired 100% of the issued share capital and voting rights of Tacere, a company based in the United States. Tacere was a privately held drug development company with a Phase I/II ready program in hepatitis C (HCV) that uses Benitec's novel gene silencing technology.

Benitec acquired Tacere's extensive HCV program data and materials, as well as an advanced preclinical program for the eye disease macular degeneration, The Tacere acquisition provided Benitec with the opportunity to commence Phase I/II clinical trials in 2014.

The consideration for the acquisition was an issue of shares in Benitec Biopharma Limited for USD \$1,530,765 plus a potential cash royalty on future licensing revenue. The shares issued as consideration represented 9.5% of the issued capital at the time of the acquisition.

Further, the agreements with the Tacere vendors provided for AUD \$357,179 Benitec Biopharma Limited shares (included in the acquisition consideration) be treated as reserve shares and not issued to the Tacere vendors for a period of 12 months from acquisition. The reserve shares are accounted for as a creditor in 2013 (refer to note 6). The reserve shares were established by an agreement with the Tacere vendors for the purposes of satisfying indemnities to Benitec, if required. The Tacere Vendors also provided a cash escrow of USD \$360,000 to provide Benitec with additional security should certain pre-acquisition liabilities emerge.

Impairment costs, relating to the in-process research on the acquisition of Tacere of \$1,503,296 were recognised in the 2013 financial year. The Tacere acquisition in-process research is deemed to be the excess of the consideration over the fair value of the identifiable assets acquired less liabilities assumed. The immediate

## Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014

write off of the in-process research, following the impairment review, was considered to be the most appropriate accounting treatment as the intellectual property is a preclinical trial and hence the future economic benefit is uncertain.

Financial details of the business combination made in the previous financial year (year ended 30 June 2013) were:

	\$
<b>Fair value of consideration transferred</b>	
Consideration for the acquisition in October 2012 was the issue of 102,321,345 (pre-consolidation) shares in Benitec Biopharma Limited, plus a potential cash royalty on future licensing revenue . . .	<u>1,530,765</u>
Recognised amounts of identifiable net assets	
Property, plant and equipment . . . . .	17,567
Cash and cash equivalents . . . . .	138,760
Amount owing to Benitec Biopharma Limited . . . . .	(126,882)
Other liabilities . . . . .	<u>(1,976)</u>
Identifiable net assets . . . . .	27,469
Goodwill on acquisition impaired in the June 2013 financial statements . . . . .	<u>1,503,296</u>
Net cash inflow on acquisition . . . . .	143,603
Acquisition related costs recognised as an expense in the Group corporate expenses . . . . .	77,104
Post-acquisition loss of Tacere in the period to 30 June 2013 . . . . .	267,720
Post-acquisition loss of Tacere in the period to 30 June 2014 . . . . .	1,903

### Note 27: Benitec Biopharma Limited parent company information

	Parent Entity	
	2014	2013
	\$	\$
<b>ASSETS</b>		
Current assets . . . . .	34,386,167	1,478,422
Non-current assets . . . . .	181,547	48,999
<b>TOTAL ASSETS</b> . . . . .	<u>34,567,714</u>	<u>1,527,421</u>
<b>LIABILITIES</b>		
Current liabilities . . . . .	1,311,608	1,165,652
Non-current liabilities . . . . .	—	—
<b>TOTAL LIABILITIES</b> . . . . .	<u>1,311,608</u>	<u>1,165,652</u>
<b>NET ASSETS</b> . . . . .	<u>33,256,106</u>	<u>361,769</u>
<b>EQUITY</b>		
Contributed equity . . . . .	129,185,675	89,609,248
Share based payments reserve . . . . .	2,096,818	1,591,702
Accumulated losses . . . . .	<u>(98,026,387)</u>	<u>(90,839,181)</u>
<b>TOTAL EQUITY</b> . . . . .	<u>33,256,106</u>	<u>361,769</u>
<b>FINANCIAL PERFORMANCE</b>		
Loss for the year . . . . .	(7,037,206)	(4,885,852)
Other comprehensive income . . . . .	—	—
<b>TOTAL COMPREHENSIVE INCOME</b> . . . . .	<u>(7,037,206)</u>	<u>(4,885,852)</u>

## **Notes to the Consolidated Financial Statements for the Year Ended 30 June 2014**

### *Contingent liabilities*

The parent entity had no contingent liabilities as at 30 June 2014 (2013: nil), other than the contingent liabilities described in note 22.

### *Capital commitments*

The parent entity has no capital commitments as at 30 June 2014 (2013: nil).

### *Significant accounting policies*

The accounting policies of the parent are consistent with those of the consolidated entity (Note 1)



**Consolidated Statement of Profit or Loss and Other Comprehensive Income  
FOR THE HALF-YEAR ENDED DECEMBER 31, 2014**

	<u>Notes</u>	HALF-YEAR	
		December 2014	December 2013
		\$ (unaudited)	\$ (unaudited)
Revenue .....	2	639,167	223,917
Royalties and licence fees .....		(40,000)	(5,596)
Research and development costs .....		(2,210,023)	(1,850,012)
Employment related expenses .....		(2,343,524)	(1,243,816)
Travel related expenses .....		(516,528)	(209,772)
Consultants costs .....		(400,305)	(304,341)
Occupancy costs .....		(131,364)	(61,785)
Corporate expenses .....		(436,353)	(386,415)
Foreign exchange translation .....		391,955	14,625
Total expenses .....		(5,686,142)	(4,047,112)
Loss before income tax .....	2	(5,046,975)	(3,823,195)
Income tax benefit .....	2	—	454,365
Loss for the half year .....		(5,046,975)	(3,368,830)
Other comprehensive income .....		24,457	9,887
<b>Total comprehensive loss for the half year .....</b>		<b>(5,022,518)</b>	<b>(3,358,943)</b>
<b>Total comprehensive loss for the half year attributable to members of Benitec Biopharma Limited .....</b>		<b>(5,022,518)</b>	<b>(3,358,943)</b>
Earnings per share (cents per share) for loss attributable to the ordinary equity holders of the consolidated entity:			
Basic earnings (loss) for the half-year .....		(4.4)	(4.3)
Diluted earnings (loss) for the half-year .....		(4.4)	(4.3)

The above consolidated statement of profit or loss and other comprehensive income should be read in conjunction with the accompanying notes.

**Consolidated Statement of Financial Position  
FOR THE HALF-YEAR ENDED DECEMBER 31, 2014**

	<u>Notes</u>	<u>December 2014</u>	<u>June 2014</u>
		\$ (unaudited)	\$ (unaudited)
<b>ASSETS</b>			
<b>Current Assets</b>			
Cash and cash equivalents .....		26,827,488	31,359,199
Trade and other receivables .....		73,054	121,587
Other assets and prepaid clinical trials .....		3,017,347	2,966,739
<b>Total Current Assets</b> .....		<u><b>29,917,889</b></u>	<u><b>34,447,525</b></u>
<b>Non-current Assets</b>			
Plant and equipment .....		418,206	47,677
<b>Total Non-current Assets</b> .....		<u><b>418,206</b></u>	<u><b>47,677</b></u>
<b>TOTAL ASSETS</b> .....		<u><b>30,336,095</b></u>	<u><b>34,495,202</b></u>
<b>LIABILITIES</b>			
<b>Current Liabilities</b>			
Trade and other payables .....	5	541,758	788,169
Provisions .....		177,092	166,511
<b>Total Current Liabilities</b> .....		<u><b>718,850</b></u>	<u><b>954,680</b></u>
<b>TOTAL LIABILITIES</b> .....		<u><b>718,850</b></u>	<u><b>954,680</b></u>
<b>NET ASSETS</b> .....		<u><b>29,617,245</b></u>	<u><b>33,540,522</b></u>
<b>EQUITY</b>			
Contributed equity .....	6	129,551,591	129,185,676
Reserves .....		1,395,041	640,773
Accumulated losses .....		(101,329,387)	(96,285,927)
<b>TOTAL EQUITY</b> .....		<u><b>29,617,245</b></u>	<u><b>33,540,522</b></u>

The above consolidated statement of financial position should be read in conjunction with the accompanying notes.

**Consolidated Statement of Changes in Equity  
FOR THE HALF-YEAR ENDED DECEMBER 31, 2014**

	Issued capital	Share-based Payments Reserve	Foreign exchange translation reserve	Accumulated Losses	Total equity
	\$	\$	\$	\$	\$
	(unaudited)	(unaudited)	(unaudited)	(unaudited)	(unaudited)
<b>At 30 June 2013</b> .....	<b>89,609,248</b>	<b>1,591,702</b>	<b>(1,313,792)</b>	<b>(89,246,818)</b>	<b>640,340</b>
Loss for the period .....	—	—	—	(3,368,830)	(3,368,830)
Other comprehensive income .....	—	—	9,887	—	9,887
<b>Total comprehensive income</b> .....	—	—	<b>9,887</b>	<b>(3,368,830)</b>	<b>(3,358,943)</b>
Share issues, net of transaction costs, for the acquisition of Tacere Therapeutics Inc. . . .	357,179	—	—	—	357,179
Share based payments .....	—	116,091	—	—	116,091
Share issues, net of transaction costs .....	9,936,288	—	—	—	9,936,288
<b>At 31 December 2013</b> .....	<b>99,902,715</b>	<b>1,707,793</b>	<b>(1,303,905)</b>	<b>(92,615,648)</b>	<b>7,690,955</b>
Loss for the period .....	—	—	—	(3,670,279)	(3,670,279)
Other comprehensive income .....	—	—	(2,140)	—	(2,140)
<b>Total comprehensive income</b> .....	—	—	<b>(2,140)</b>	<b>(3,670,279)</b>	<b>(3,672,419)</b>
Share issues, net of transaction costs .....	29,282,961	—	—	—	29,282,961
Share based payments .....	—	239,025	—	—	239,025
<b>At 30 June 2014</b> .....	<b>129,185,676</b>	<b>1,946,818</b>	<b>(1,306,045)</b>	<b>(96,285,927)</b>	<b>33,540,522</b>
Loss for the period .....	—	—	—	(5,046,975)	(5,046,975)
Other comprehensive income .....	—	—	—	—	—
<b>Total comprehensive income</b> .....	—	—	—	<b>(5,046,975)</b>	<b>(5,046,975)</b>
Share issues, net of transaction costs .....	257,615	—	—	—	257,615
Foreign exchange translation reserve .....	—	—	24,457	—	24,457
Share based payments .....	—	841,626	—	—	841,626
Transfer of expired share based payments ..	—	(3,515)	—	3,515	—
Transfer to share capital for options exercised .....	108,300	(108,300)	—	—	—
<b>At 31 December 2014</b> .....	<b>129,551,591</b>	<b>2,676,629</b>	<b>(1,281,588)</b>	<b>(101,329,387)</b>	<b>29,617,245</b>

The above consolidated statement of changes in equity should be read in conjunction with the accompanying notes.

**Consolidated Statement of Cash Flows  
FOR THE HALF-YEAR ENDED DECEMBER 31, 2014**

	<b>HALF-YEAR</b>		
	<b>Notes</b>	<b>December 2014</b>	<b>December 2013</b>
		<b>\$</b>	<b>\$</b>
		<b>(unaudited)</b>	<b>(unaudited)</b>
<b>Cash flows from operating activities</b>			
Receipts from customers . . . . .		253,761	170,723
Payments to suppliers and employees . . . . .		(5,493,311)	(6,328,953)
Interest income . . . . .		452,603	53,194
Net cash outflows from operating activities . . . . .		<u>(4,786,947)</u>	<u>(6,105,036)</u>
<b>Cash flows from investing activities</b>			
Purchase of plant and equipment . . . . .		(394,334)	—
Net cash inflows from investing activities . . . . .		<u>(394,334)</u>	<u>—</u>
<b>Cash flows from financing activities</b>			
Proceeds from issue of shares . . . . .		257,615	9,703,483
Net cash inflows from financing activities . . . . .		<u>257,615</u>	<u>9,703,483</u>
Net (decrease)/ increase in cash and cash equivalents . . . . .		(4,923,666)	3,598,447
Effects of exchange rate changes on cash and cash equivalents . . . . .		391,955	(1,892)
Cash and cash equivalents at beginning of the half-year . . . . .		31,359,199	1,587,299
<b>Cash and cash equivalents at end of half-year . . . . .</b>		<b><u>26,827,488</u></b>	<b><u>5,183,854</u></b>

The above consolidated statement of cash flows should be read in conjunction with the accompanying notes.

**Notes to the Consolidated Financial Statements  
FOR THE HALF-YEAR ENDED 31 December 2014**

**1. BASIS OF PREPARATION OF THE CONSOLIDATED FINANCIAL REPORT**

The condensed interim consolidated financial statements (the interim financial statements) of the Group are for the six months ended 31 December 2014 and are presented in Australian dollars (\$), which is the functional currency of the parent company. These general purpose interim financial statements have been prepared in accordance with the requirements of the *Corporations Act 2001* and AASB 134 *Interim Financial Reporting*. They do not include all of the information required in annual financial statements in accordance with International Accounting Standards, and should be read in conjunction with the consolidated financial statements of the Group for the year ended 30 June 2014 and any public announcements made by the Group during the half-year in accordance with continuous disclosure requirements arising under the Australian Stock Exchange Listing Rules and the *Corporations Act 2001*.

The interim financial statements have been approved and authorised for issue by the Board of Directors on 27 February 2015.

**(a) Basis of accounting**

The half-year financial report is a general-purpose financial report, which has been prepared in accordance with the requirements of the Corporations Act 2001, applicable Accounting Standards including AASB 134 “Interim Financial Reporting” and other mandatory professional reporting requirements.

This financial report has been prepared on a going concern basis.

During the half year ended 31 December 2014, the consolidated entity incurred a loss of \$5,046,975 (2013 comparative period: loss \$3,358,943) and had net operating cash outflows of \$4,795,062 (2013 comparative period \$6,105,036).

The ability of the consolidated entity to continue as a going concern has been determined by directors on the following basis:

- i. consistent with start-up biotechnology companies, the consolidated entity’s operations are subject to considerable risks, primarily due to the nature of program development and commercialisation being undertaken; and
- ii. to allow the consolidated entity to execute its long-term plans, it may be necessary to raise additional capital, and generate further income from commercialising the consolidated entity’s intellectual property.

The financial report does not contain any adjustments to the amounts or classifications of recorded assets or liabilities that might be necessary if the consolidated entity does not continue as a going concern.

The financial statements take no account of the consequences, if any, of the effects of unsuccessful product development or commercialisation, nor of the inability of the consolidated entity to obtain adequate funding in the future.

The half-year financial report has been prepared in accordance with the historical convention. For the purpose of preparing the half-year financial report, the half-year has been treated as a discrete reporting period.

**(b) Summary of significant accounting policies**

The interim financial statements have been prepared in accordance with the accounting policies adopted in the Group’s last annual financial statements for the year ended 30 June 2014.

**Notes to the Consolidated Financial Statements  
FOR THE HALF-YEAR ENDED 31 December 2014**

**(c) Estimates**

When preparing the interim financial statements, management undertakes a number of judgements, estimates and assumptions about recognition and measurement of assets, liabilities, income and expenses. The actual results may differ from the judgements, estimates and assumptions made by management, and will seldom equal the estimated results.

The judgements, estimates and assumptions applied in the interim financial statements, including the key sources of estimation uncertainty were the same as those applied in the consolidated entity's last annual financial statements for the year ended 30 June 2014.

**(d) Significant events and transactions**

Key highlights of the interim reporting period to 31 December 2014 include the following:

- **Multiple patients dosed in Benitec's 'first in human' trial for TT034, a hepatitis C therapeutic, designed as a single-shot cure for hepatitis C**

Benitec Biopharma continues to advance its ddRNAi gene silencing technology into the clinic with the dosing of a third patient in the Company's phase I/II(a) clinical trial for TT-034, a potential single-shot cure for hepatitis C. The success of this 'first in human' trial is an important element in the Group's strategy for commercialising ddRNAi and validating the other indications in the Group's pipeline. Demonstration of safety and efficacy of ddRNAi as treatment for hepatitis C, based on industry comparators, will be a significant value inflection point for the Group.

- **In-house laboratory capabilities established through the opening of the 'Bremner Lab' in Northern California**

Setting up Benitec's own laboratory (called the Bremner Lab) under the leadership of Dr David Suhy, the inventor of TT-034, is an important step in enabling the Group to advance its other programs. Dr Suhy has built a team of scientists in Benitec's California facility, the Group prioritising three of the Group's programs to advance towards the clinic—hepatitis B, non-small cell lung cancer and age related macular degeneration (AMD). Using Benitec's in-house expertise the Group will expand and modify each of these programs.

- **Executed an agreement with 4D Molecular Therapeutics for development of next generation novel vectors—enabling advancement of the AMD program**

The execution of an agreement with 4D Molecular Therapeutics was an important step in the advancement of Benitec's AMD program. The engagement with 4D aims to develop novel vectors with increased tissue specificity, a vital component in building a long lasting cure for this important disease.

- **Licensed ddRNAi to Circuit Therapeutics for the development of treatments for intractable pain**

The recent license agreement executed with Circuit Therapeutics for the development of a treatment for intractable pain, targeting the Nav1.7 sodium ion channel offers the Group another opportunity to extend its pipeline of programs.

Benitec is actively engaged in the development of novel therapies with its ddRNAi platform and has commenced a Phase I/IIa clinical trial in its lead HCV program.

**Notes to the Consolidated Financial Statements  
FOR THE HALF-YEAR ENDED 31 December 2014**

Benitec expects to continue to record negative operating cashflow in the medium term. Benitec has a capital management program to ensure adequate capital is in place to fund the Group's operations. Benitec has presented to institutional and sophisticated investors as part of its capital management plan, and is always considering further funding opportunities, whether domestically or internationally.

**2. REVENUE AND EXPENSES**

		HALF-YEAR	
		December 2014	December 2013
		\$	\$
<b>(a)</b>	<b>(i) Revenue</b>		
	Licensing revenue .....	186,564	170,723
	Finance income .....	452,603	53,194
		639,167	223,917
	<b>(ii) Expenses</b>		
	Depreciation .....	23,804	6,924
	Share-based payments .....	841,626	116,091
	Foreign exchange fluctuation .....	(391,955)	14,625
	US tax refund .....	—	(454,365)

**(b) Seasonality of Operations**

There is no discernible seasonality in the operations of the consolidated entity.

**3. OPERATING SEGMENTS**

*Business Segments*

The Group had only one business segment during the period, being the global commercialisation by licensing and partnering of patents and licences in biotechnology, with applications in biomedical research and human therapeutics.

*Geographical Segments*

Business operations are conducted in Australia. However there are controlled entities based in the USA and United Kingdom. The United Kingdom entity has no segment revenues, results or assets.

Geographical location	Segment Revenues from External Customers		Segment Results		Carrying Amount of Segment Assets	
	Dec 2014	Dec 2013	Dec 2014	Dec 2013	Dec 2014	June 2014
	\$	\$	\$	\$	\$	\$
Australia .....	639,167	223,971	(4,333,576)	(3,617,151)	29,956,867	34,433,803
United States of America .....	—	—	(713,399)	258,208	379,228	61,399
	639,167	223,971	(5,046,975)	(3,358,943)	30,336,095	34,495,202

*Accounting Policies*

Segment revenues and expenses are directly attributable to the identified segments and include joint venture revenue and expenses where a reasonable allocation basis exists. Segment assets include all assets used by a

**Notes to the Consolidated Financial Statements  
FOR THE HALF-YEAR ENDED 31 December 2014**

segment and consist mainly of cash, receivables, inventories, intangibles and property, plant and equipment, net of any allowances, accumulated depreciation and amortisation. Where joint assets correspond to two or more segments, allocation of the net carrying amount has been made on a reasonable basis to a particular segment. Segment liabilities include mainly accounts payable, employee entitlements, accrued expenses, provisions and borrowings. Deferred income tax provisions are not included in segment assets and liabilities.

**4 EVENTS AFTER THE BALANCE SHEET DATE**

There were no significant events after balance date.

**5. TRADE AND OTHER PAYABLES**

	<u>December 2014</u>	<u>June 2014</u>
	\$	\$
Trade creditors .....	241,053	572,557
Sundry creditors and accrued expenses .....	300,705	215,612
	<u>541,758</u>	<u>788,169</u>

**6. ISSUED CAPITAL**

	<u>No. of Shares</u>	<u>\$</u>
<i>Ordinary shares</i>		
Issued and fully paid at the beginning of the period .....	114,898,992	129,185,676
Options exercised .....	664,618	257,615
Transfer from share based payments for options exercised .....	—	108,300
At 31 December 2014 .....	<u>115,563,610</u>	<u>129,551,591</u>
The weighted average number of shares on issue during the period was .....	<u>115,218,666</u>	

**Share options outstanding**

<u>Details</u>	<u>Expiry Date</u>	<u>Exercise Price</u>	<u>Dec 2014</u> <u>Number of options</u>
Unlisted Options—placement .....	18 February 2015	0.3250	318,153
Other Options .....	10 April 2015	2.5000	480,000
Other Options .....	23 October 2015	4.2500	78,125
NED Options .....	26 September 2016	1.2500	1,600,000
ESOP Options .....	17 November 2016	1.2500	1,800,000
NED Options .....	26 September 2016	1.2500	1,200,000
ESOP Options .....	7 February 2017	1.2500	168,000
ESOP Options .....	18 July 2017	1.2500	400,000
ESOP Options .....	16 November 2017	1.2500	400,000
NED Options .....	18 May 2018	0.6250	400,000
ESOP Options .....	22 August 2018	1.2500	2,080,000
Unlisted Options—placement .....	28 February 2019	1.2600	13,246,203
ESOP Options .....	15 May 2019	1.5000	180,000
ESOP Options .....	17 December 2014	1.2500	3,334,000
			<u>25,684,481</u>



**Notes to the Consolidated Financial Statements  
FOR THE HALF-YEAR ENDED 31 December 2014**

**7. CONTINGENT LIABILITIES**

In January 2010, the Company reached a settlement with the CSIRO to replace the existing Licence Agreement and Commercial Agreement with a new exclusive Licence Agreement for the use of intellectual property and the Capital Growth Agreement with the issue of ordinary shares. As part of the settlement, a Transition Agreement was put in place in order to facilitate the change from the old agreements to the new agreement and to deal with a number of other matters.

Under the terms of the Transition Agreement, the Company agreed to pay CSIRO an amount of \$297,293 for past patent costs only in the event of a trigger event, being either a corporate transaction or an insolvency event.

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**American Depositary Shares  
Representing Ordinary Shares**



**Benitec Biopharma Limited**

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PRELIMINARY PROSPECTUS

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**BMO Capital Markets  
Maxim Group LLC**

**Roth Capital Partners**

, 2015

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Until \_\_\_\_\_, 2015 (the 25th day after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

**PART II**  
**INFORMATION NOT REQUIRED IN PROSPECTUS**

**Item 6. Indemnification of Directors and Officers**

*Australian law.* Australian law provides that a company or a related body corporate of the company may provide for indemnification of officers and directors, except to the extent of any of the following liabilities incurred as an officer or director of the company:

- a liability owed to the company or a related body corporate of the company;
- a liability for a pecuniary penalty order made under section 1317G or a compensation order under section 961M, 1317H, 1317HA or 1317HB of the Australian Corporations Act 2001;
- a liability that is owed to someone other than the company or a related body corporate of the company and did not arise out of conduct in good faith; or
- legal costs incurred in defending an action for a liability incurred as an officer or director of the company if the costs are incurred:
  - in defending or resisting proceedings in which the officer or director is found to have a liability for which they cannot be indemnified as set out above;
  - in defending or resisting criminal proceedings in which the officer or director is found guilty;
  - in defending or resisting proceedings brought by the Australian Securities & Investments Commission or a liquidator for a court order if the grounds for making the order are found by the court to have been established (except costs incurred in responding to actions taken by the Australian Securities & Investments Commission or a liquidator as part of an investigation before commencing proceedings for a court order); or
  - in connection with proceedings for relief to the officer or a director under the Corporations Act, in which the court denies the relief.

*Constitution.* Our Constitution provides, except to the extent prohibited by the law and the Corporations Act, for the indemnification of every person who is or has been an officer or a director of the company against liability (other than legal costs that are unreasonable) incurred by that person as an officer or director. This includes any liability incurred by that person in their capacity as an officer or director of a subsidiary of the company where the company requested that person to accept that appointment.

*Indemnification Agreements.* Pursuant to Deeds of Access, Insurance and Indemnity, the form of which is filed as Exhibit 10.9 to this registration statement, we have agreed to indemnify our directors against certain liabilities and expenses incurred by such persons in connection with claims made by reason of their being such a director.

*SEC Position.* Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling us pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Pursuant to the underwriting agreement for this offering, the form of which is filed as Exhibit 1.1 to this registration statement, the underwriters will agree to indemnify our directors and officers and persons controlling us, within the meaning of the Securities Act, against certain liabilities that might arise out of or are based upon certain information furnished to us by any such underwriter.

## Item 7. Recent Sales of Unregistered Securities

Over the past three years, we have issued and sold to third parties the securities listed below without registering the securities under the Securities Act of 1933, as amended (the “Securities Act”). None of these transactions involved any public offering. All our securities were sold through private placement either (i) outside the United States or (ii) in the United States to a limited number of investors in transactions not involving any public offering. As discussed below, we believe that each issuance of these securities was exempt from, or not subject to, registration under the Securities Act.

1. On October 30, 2012, we issued 78,446,306 ordinary shares to the vendors of Tacere Therapeutics Inc. as part of the consideration under an acquisition agreement, at an issue price of A\$0.01496 per share. This issuance was exempt from registration under the Securities Act in reliance on Section 4(a)(2).
2. On March 11, 2013, we issued 43,846,155 ordinary shares as part of a private placement at A\$0.013 per share to institutional and professional investors outside the United States. Participants in the placement received two free options for every five shares subscribed for in the placement and, as a result, we issued 17,538,462 options with an exercise price of A\$0.013 per share. These issuances were exempt from registration under the Securities Act in reliance on Regulation S.
3. On March 28, 2013, we issued 13,846,154 ordinary shares as part of a private placement at A\$0.013 per share to institutional and professional investors outside the United States. Participants in the placement received two free options for every five shares subscribed for in the placement and, as a result, we issued 5,538,462 options with an exercise price of A\$0.013 per share. These issuances were exempt from registration under the Securities Act in reliance on Regulation S.
4. On May 28, 2013, we issued 7,692,308 ordinary shares as part of a private placement at A\$0.013 per share to institutional and professional investors outside the United States. Participants in the placement received two free options for every five shares subscribed for in the placement and, as a result, we issued 3,076,923 options with an exercise price of A\$0.013 per share. These issuances were exempt from registration under the Securities Act in reliance on Regulation S.
5. On June 14, 2013, we issued 37,454,591 ordinary shares as part of a private placement at A\$0.011 per share to institutional and professional investors outside the United States. This issuance was exempt from registration under the Securities Act in reliance on Regulation S.
6. On July 23, 2013, we issued 27,229,089 ordinary shares as part of a private placement at A\$0.275 per share to institutional and professional investors outside the United States. This issuance was exempt from registration under the Securities Act in reliance on Regulation S.
7. On July 23, 2013, we issued 400,000 ordinary shares at A\$0.325 per share to directors resident outside the United States. Participants in the placement received two free options for every five shares subscribed for in the placement and, as a result, we issued 160,000 unlisted options with an exercise price of A\$0.013 per share. These issuances were exempt from registration under the Securities Act in reliance on Regulation S.
8. On August 6, 2013, we issued 10,254,696 ordinary shares at A\$0.275 per share to shareholders resident in Australia or New Zealand under a share purchase plan. This issuance was exempt from registration under the Securities Act in reliance on Regulation S.
9. On October 30, 2013, we issued 955,002 ordinary shares to the vendors of Tacere Therapeutics Inc. as part of the consideration under an acquisition agreement. The consideration was A\$350,000. This issuance was exempt from registration under the Securities Act in reliance on Section 4(a)(2).
10. On February 28, 2014, we issued 14,717,995 ordinary shares and 6,623,098 unlisted options, as the first tranche of a private placement transacted over two tranches to institutional investors in Australia and the United States. Consideration received from the issue of the ordinary shares was A\$15,748,255. Maxim Group LLC acted as U.S. placement agent. This issuance was exempt from registration under the Securities Act in reliance on Section 4(a)(2) and Regulation S.

11. On April 15, 2014, we issued 14,717,999 ordinary shares and 6,623,105 unlisted options, as the second tranche of a private placement transacted over two tranches to institutional investors in Australia and the United States. Consideration received from the issue of the ordinary shares was A\$15,748,259. Maxim Group LLC acted as U.S. placement agent. This issuance was exempt from registration under the Securities Act in reliance on Section 4(a)(2) and Regulation S.

Since July 1, 2012, we have granted options to employees, directors and consultants under our Employee Share Option Plan covering an aggregate of 5,822,000 ordinary shares, with exercise prices ranging from A\$0.51 to A\$1.50 per share. As of March 31, 2015, 60,000 of these options have been exercised, while none of these options have been forfeited and cancelled without being exercised. We believe that the issuance of these securities were exempt from registration under the Securities Act in reliance upon Regulation S or Rule 701 of the Securities Act as transactions pursuant to written compensatory plans or pursuant to a written contract relating to compensation. No underwriters were employed in connection with the foregoing option grants.

#### **Item 8. Exhibits and Financial Statement Schedules**

- (a) Exhibits

See Exhibit Index beginning on page II-7 of this registration statement.

- (b) Financial Statement Schedules

Schedules have been omitted because the information required to be set forth therein is not applicable or is shown in the Consolidated Financial Statements or the Notes thereto.

#### **Item 9. Undertakings**

The undersigned registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreements, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than payment by a registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question of whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned registrant hereby undertakes that:

- (1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and this offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

## SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form F-1 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in Sydney, Australia on June 22, 2015.

### Benitec Biopharma Limited

By: /s/ Peter French

Name: Peter French

Title: Chief Executive Officer and Managing Director

## POWER OF ATTORNEY

Each person whose signature appears below does hereby constitute and appoint Peter French and Greg West, and each of them singly (with full power to act alone), as his true and lawful attorneys-in-fact and agents, each with full power of substitution and re-substitution, for him and in his name, place and stead, in any and all capacities, in connection with this registration statement, including to sign and file in the name and on behalf of the undersigned as director or officer of the registrant, any and all amendments and supplements (and any and all prospectus supplements, stickers and post-effective amendments) to this registration statement with all exhibits thereto, and sign any registration statement for the same offering covered by this registration statement that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933, as amended, and all post-effective amendments thereto and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, and any applicable securities exchange, securities self-regulatory body or other regulatory entity, granting unto said attorneys-in-fact and agents, and each of them (with full power to act alone) full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith and in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his substitutes may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Peter Francis</u> Name: Peter Francis	Chairman	June 22, 2015
<u>/s/ Peter French</u> Name: Peter French	Chief Executive Officer and Managing Director (principal executive officer)	June 22, 2015
<u>/s/ Greg West</u> Name: Greg West	Chief Financial Officer and Company Secretary (principal financial officer and principal accounting officer)	June 22, 2015
<u>/s/ John Chiplin</u> Name: John Chiplin	Director	June 22, 2015

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<hr/> <i>/s/ Iain Ross</i> Name: Iain Ross	Director	June 22, 2015
<hr/> <i>/s/ J. Kevin Buchi</i> Name: J. Kevin Buchi	Director	June 22, 2015

**SIGNATURE OF AUTHORIZED REPRESENTATIVE IN THE UNITED STATES**

Pursuant to the Securities Act of 1933, as amended, the undersigned, the duly authorized representative in the United States of Benitec Biopharma Limited, has signed this registration statement or amendment thereto in Hayward, California on June 22, 2015.

Authorized U.S. Representative

**TACERE THERAPEUTICS, INC.**

By: /s/ John Chiplin \_\_\_\_\_

Name: John Chiplin

Title: Director



## EXHIBIT INDEX

<u>Exhibits</u>	<u>Description</u>
1.1	Form of Underwriting Agreement*
3.1	Constitution of Benitec Biopharma Limited
4.1	Form of Deposit Agreement between Benitec Biopharma Limited and The Bank of New York Mellon, as depositary, and Owners and Holders of the American Depositary Shares*
4.2	Form of American Depositary Receipt evidencing American Depositary Shares (included in Exhibit 4.1)*
5.1	Opinion of Baker & McKenzie regarding the validity of the ordinary shares being issued*
8.1	Opinion of Baker & McKenzie LLP regarding material U.S. tax matters
8.2	Opinion of Baker & McKenzie regarding material Australian tax matters
10.1	License Agreement, dated December 23, 2009, between Commonwealth Scientific and Industrial Research Organisation (“CSIRO”) and Benitec
10.2	Research and Collaboration Agreement–Overall Project, dated July 11, 2014, between Biomics Biotech Co., Ltd and Benitec
10.3	Commercial License Agreement–Amended and Restated, dated December 3, 2014, between NewSouth Innovations Pty Limited and Benitec Australia Limited
10.4	Collaborative Research and License Agreement, dated November 11, 2014, between 4D Molecular Therapeutics, LLC and Benitec*
10.5	Lease Agreement, dated May 12, 2014, between Hayward Point Eden 1 Limited Partnership and Benitec
10.6	First Amendment to Lease Agreement, dated May 7, 2015, between Hayward Point Eden 1 Limited Partnership and Benitec
10.7	Commercial Lease Agreement, dated August 5, 2014, between Mary Montague and Janice Leong and Benitec
10.8	Form of Executive Employment Agreement for executive officers
10.9	Form of Deed of Access, Insurance and Indemnity for Directors and Officers
21.1	List of significant subsidiaries of Benitec Biopharma Limited
23.1	Consent of Baker & McKenzie (see Exhibit 5.1)*
23.2	Consent of Baker & McKenzie LLP (see Exhibit 8.1)
23.3	Consent of Baker & McKenzie (see Exhibit 8.2)
23.4	Consent of Grant Thornton Audit Pty Ltd
24.1	Power of Attorney (contained on the signature page to this registration statement)

\* To be filed by amendment