

### Biotechnology

**BLT - ASX**

March 3, 2015

<b>Closing Price 03/2/2015</b>	<b>\$0.87</b>
Rating:	Buy
12-Month Target Price:	\$4.00
52-Week Range:	\$0.52 - \$2.20
Market Cap (\$M):	\$100
Shares O/S:	116
Float:	79.7%
Avg. Daily Volume (000):	193
Dividend Yield:	0.00%
Dividend:	\$0.00
Risk Profile:	High
Fiscal Year End:	June

#### Total Revenues ('000)

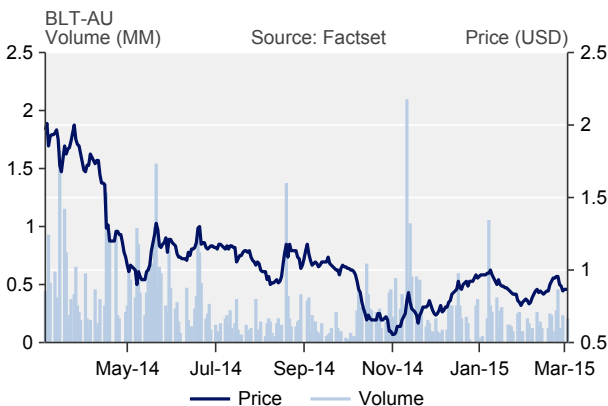
	2014E	2015E	2016E
H1	0A	0	0
H2	0	0	0
FY	0	0	0

#### GAAP Net Income (loss) ('000)

	2014E	2015E	2016E
H1	(4,193)A	(5,250)	(6,750)
H2	(4,193)	(5,250)	(6,750)
FY	(8,386)	(10,500)	(13,500)

#### GAAP EPS

	2014E	2015E	2016E
H1	(0.03)A	(0.04)	(0.05)
H2	(0.03)	(0.04)	(0.05)
FY	(0.07)	(0.09)	(0.11)



## Benitec BioPharma Ltd

Buy

### One Shot, One Cure – The Next Cohort in HCV Trial Advances

#### Summary

- Benitec reported that the DSMB has reviewed safety data from the third patient treated with TT034, who experienced no adverse events. The board has approved the next level of "safety" dosing at  $1.25 \times 10^{11}$  vg/kg (a half log higher than the first three patients received), but still below that believed to be therapeutically effective and inhibit viral replication.
- Benitec's approach to RNAi differentiates it from competing RNAi technologies, since it uses a virus to deliver DNA that encodes the antisense RNA that will target unwanted mRNA (i.e., HCV, HBV).
- RNAi has broad applications, ranging from infectious diseases to cancer and genetic diseases. Though RNAi seems to be a straightforward concept (i.e., gene silencing), there are different molecular pathways that lead to a cell's RNAi machinery to induce gene silencing. Benitec (ddRNAi), Tekmira (nanoparticle RNAi trigger delivery; TKMR - Buy), and Regulus Therapeutics (targeted anti-micro RNA to silence host microRNA; RGLS - \$18.81 - NR) are attacking HCV and HBV with RNAi, but all are different (below).
- 1H14 update (fiscal year ends in June), spending \$5M and closing the year with \$26.8M in cash. The company is funded through multiple data inflection points.

#### Details

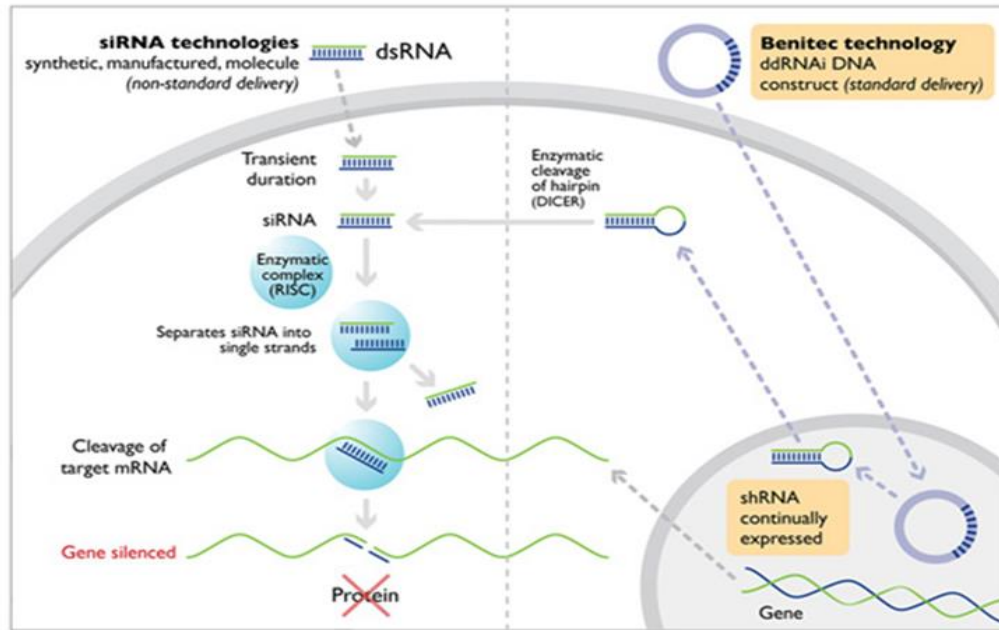
**TT-034 DNA-directed RNAi (ddRNAi).** Benitec uses circular DNA that encodes short hairpin (sh)RNAs delivered using a virus. This type of RNA essentially folds over on itself to make double-stranded RNA. The shRNA, which is specific for conserved regions of HCV mRNA, is fed into the RNAi pathway to then destroy HCV mRNA and, thus, end viral replication. The advantage over other methods lies in using a DNA vector that becomes a part of the hepatocyte genome, where it can remain for years. The shRNA will continuously be produced and, in a sense, is always hunting for any HCV mRNA that might appear. Benitec is also using ddRNAi to target HBV.

**TT-034: Why less is more.** Delivering RNA in an RNAi therapy model is difficult because of the unstable nature of the RNA. By using a stable DNA vector inside a virus, Benitec is avoiding degradation and manipulation of the RNA to enhance stability, which can alter its performance as a therapeutic. Further, since the DNA enters the nucleus and integrates into the genome, a cell only needs a few copies of the RNA encoding sequence to generate therapeutic levels of shRNA. Other methods that deliver high doses of RNA to achieve a gene silencing effect can result in "off-target effects." This ddRNAi technology may hold the ability to permanently silence the target genes. As such, it may prove to be possible, in a single dose, to cure certain conditions, such as hepatitis C or B. The promise of such a cure could lead to the next paradigm shift in the space beyond direct-acting antivirals (DAAV).

**Beyond HCV: ddRNAi is particularly attractive for HBV.** Unlike HCV, the HBV virus deposits its DNA genome into the hepatocyte nucleus, where it can remain for years making viral mRNA. The mRNA is copied to make new viral particles (the site of nucleotide analogue interference) as well as excess viral proteins. The viral products (HBsAg and HBeAg antigens) get into the blood and prevent seroconversion by completely absorbing all available anti-HBV antibodies that would otherwise neutralize the virus. The ddRNAi becomes a permanent resident of the hepatocyte genome, just like HPV, and, thus, will always be on guard to protect the cell.

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**Exhibit 1. Where Benitec’s ddRNAi enters the RNAi pathway.** ddRNAi stands for DNA-directed RNA interference. The HCV or HBV mRNA target is encoded into a DNA vector that is delivered to hepatocytes using a virus. The DNA enters the cell, where it migrates into the nucleus and integrates into the host genome. Once integrated, the mRNA target that is encoded in the DNA is transcribed into short hairpin (sh) mRNAs that get transported to the cytosol, where they are processed and enter the RNAi pathway. The short complimentary pieces to viral mRNA are used to seek out viral mRNA and destroy it. The DNA can reside in the nucleus for years, thus providing a permanent defense system against HCV and HBV.



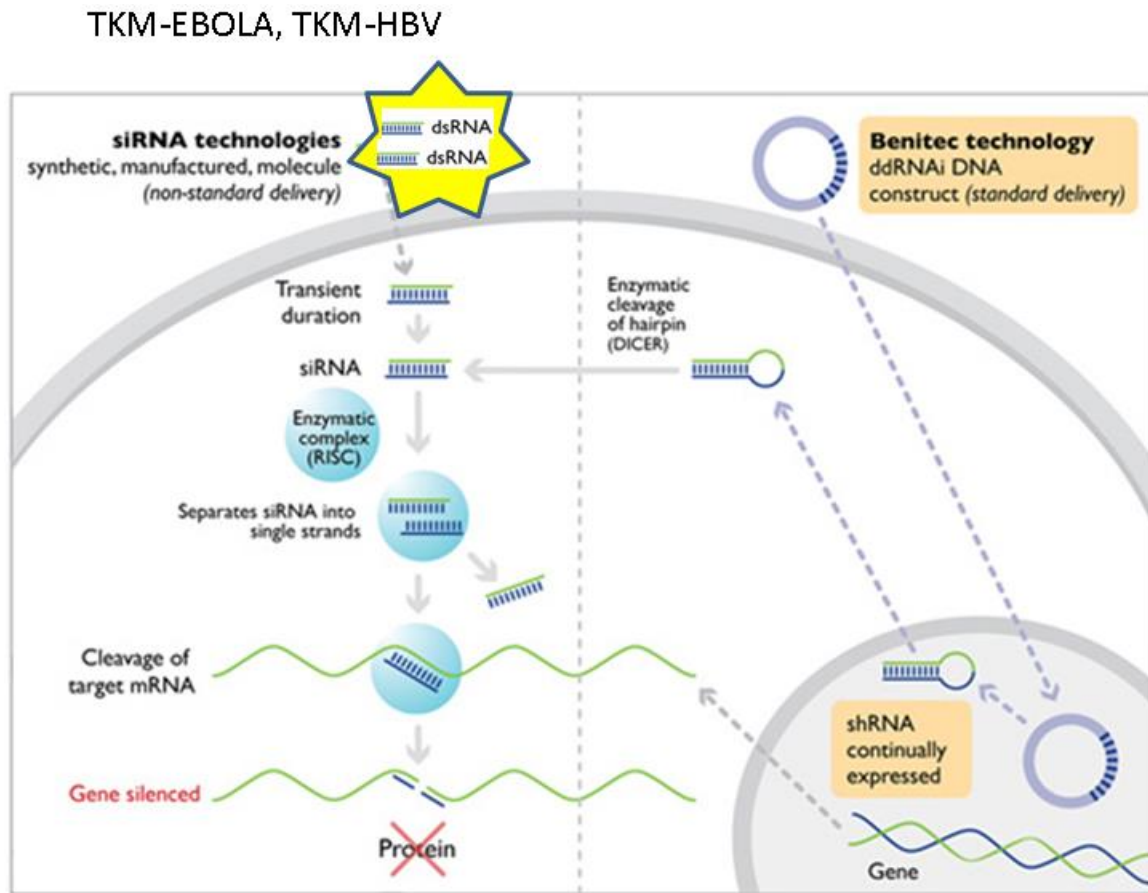
Source: Benitec Presentation

**Exhibit 2. Synthetic RNAi versus expressed RNAi.** Benitec uses integrated DNA carrying instructions for expressing RNAi. Other approaches to RNAi rely on synthesizing RNA and delivering it using targeted vehicles (i.e., Tekmira’s TKM-HBV and TKM-Ebola).

Criterion	siRNA	shRNA
Nomenclature	Small Interfering RNA	Short Hairpin RNA
Source	Laboratory synthesis	Nuclear expression
Delivery to the cell	Via synthetic/natural polymers and lipids to the cytoplasm	Via viral and other gene therapy vectors to the nucleus.
Persistence	99% degraded after 48 hours	Expressed for up to 3 years.
Administration	Local or limited systemic injection	Local and systemic injection
Dosage	High (low nM)	Low (5 copies)
Likelihood of specific 'off target' effects	Higher than shRNA	Lower than siRNA
Likelihood of non-specific 'off targets' effects	Higher immune activation, inflammation and toxicity	Lower immune activation, inflammation and toxicity
Application	Acute disease conditions; Where high doses are tolerable	Chronic, life threatening diseases or disorders; Where low doses are desirable

Source: Benitec Presentation

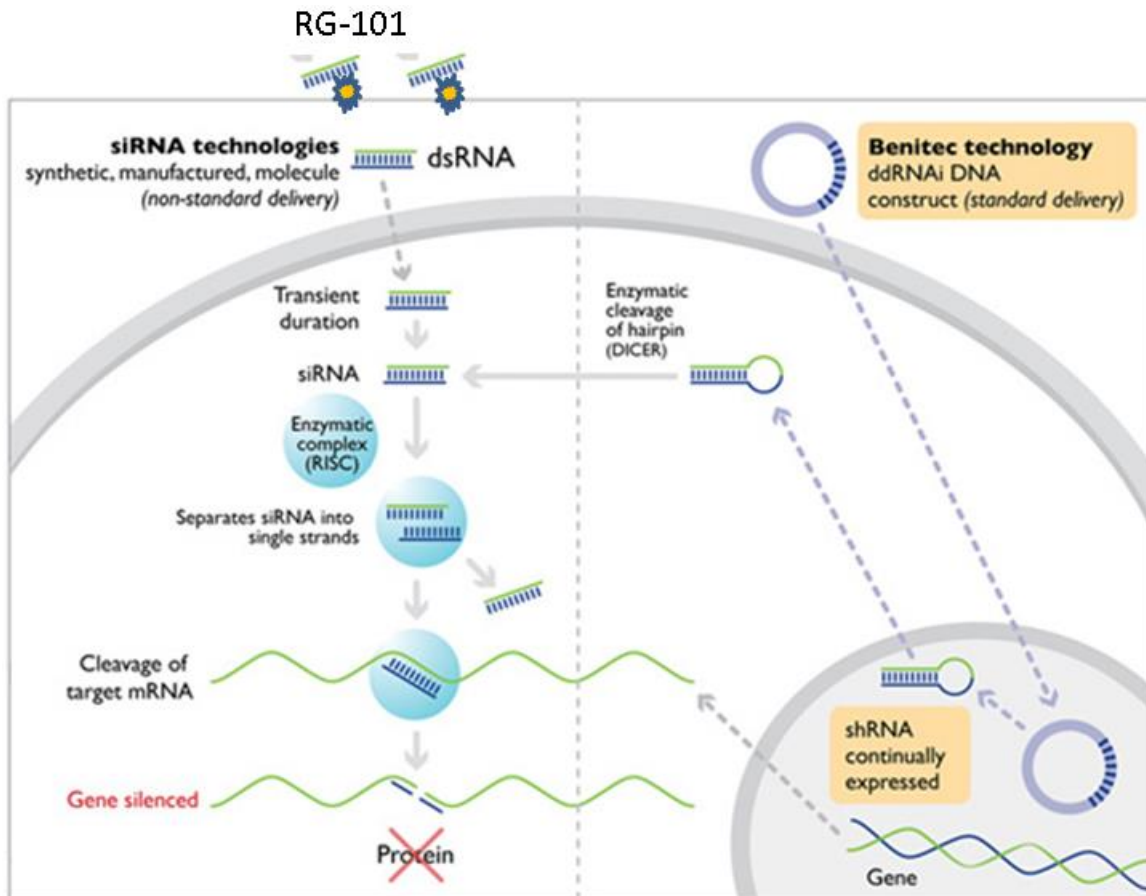
**Exhibit 3. Tekmira and TKM-EBOLA, TKM-HBV.** Both of Tekmira's antisense products in clinical development use synthetic anti-sense RNA that is delivered using proprietary lipid nanoparticles to target specific cell types. The lipid nanoparticles fuse to the cell membrane and are endocytosed. The RNA cargo is released and enters the RNAi pathway to target and destroy viral mRNA.



Source: Modified from Benitec presentation

**Exhibit 4. Regulus Therapeutics turns host endogenous gene silencing against HCV.** The company's lead product, RG-101, takes a different approach to RNAi by targeting the host microRNAs (miRNAs). miRNAs are short, 20-25 nucleotide sequences that are encoded in the introns (non-coding) of larger RNA molecules. The role of microRNA is to control expression of proteins by controlling the level of mRNA available for protein translation. The basic concept is that the cell needs to turn a gene on to have a response or perform a function (ultimately with a functional protein/enzyme). However, the cell must also control how much protein is made. One mechanism to regulate control is by expression of microRNAs that target specific mRNAs (and thus proteins) for degradation through the RNAi pathway by binding to create double-stranded RNA (the feature that initiates the RNAi pathway). miRNAs are single-stranded, and more than 800 have been discovered in the last 10 years.

RG-101 targets miRNA 122 (miR122), the most abundant miRNA in hepatocytes. miR122 has an unusual feature in that it binds to very conserved regions of HCV mRNA and actually stimulates viral replication, suggesting that the HCV has adapted to the hepatocyte environment. Conversely, binding of miR122 to HBV inhibits expression and replication of the virus. Regulus uses antisense miRNAs specific for miR122 to shut down the host miR122 that is contributing to HCV survival. miR122 is modified with targeting molecules to deliver miR122 to the hepatocyte.



Source: Modified from Benitec presentation

**Related Companies Mentioned in this Report**

Company	Ticker	Rating	12 Month Price Target	Price 03/02/15
Tekmira Pharmaceuticals Corp	TKMR	Buy	\$27.00	\$17.93

**DISCLOSURES**

**Benitec BioPharma Ltd Rating History as of 03/02/2015**

powered by: BlueMatrix



**Tekmira Pharmaceuticals Corp Rating History as of 03/02/2015**

powered by: BlueMatrix



<b>Maxim Group LLC Ratings Distribution</b>		<b>As of: 03/02/15</b>	
		<b>% of Coverage Universe with Rating</b>	<b>% of Rating for which Firm Provided Banking Services in the Last 12 months</b>
<b>Buy</b>	Fundamental metrics and/or identifiable catalysts exist such that we expect the stock to outperform its relevant index over the next 12 months.	<b>78%</b>	<b>38%</b>
<b>Hold</b>	Fundamental metrics are currently at, or approaching, industry averages. Therefore, we expect this stock to neither significantly outperform nor underperform its relevant index over the next 12 months.	<b>20%</b>	<b>15%</b>
<b>Sell</b>	Fundamental metrics and/or identifiable catalysts exist such that we expect the stock to underperform its relevant index over the next 12 months.	<b>2%</b>	<b>0%</b>

*\*See valuation section for company specific relevant indices*

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The research analyst(s) primarily responsible for the preparation of this research report have received compensation based upon various factors, including the firm's total revenues, a portion of which is generated by investment banking activities.

**Maxim Group makes a market in Benitec BioPharma Ltd and Tekmira Pharmaceuticals Corp**

**Maxim Group managed/co-managed/acted as placement agent for an offering of the securities for Benitec BioPharma Ltd in the past 12 months.**

**Maxim Group received compensation for investment banking services from Benitec BioPharma Ltd and Tekmira Pharmaceuticals Corp in the past 12 months.**

**Maxim Group expects to receive or intends to seek compensation for investment banking services from Benitec BioPharma Ltd and Tekmira Pharmaceuticals Corp in the next 3 months.**

**BLT:** For Benitec, we use the BTK (NYSE Biotechnology Index) as the relevant index.

**TKMR:** For Tekmira, we use the BTK (NYSE Biotechnology Index) as the relevant index.

**Valuation Methods**

**BLT:** We assume that the clinical development of any single product to proof-of-concept studies will trigger a valuation increase. For modeling purposes, we assume that commercialization of the first product (HCV/NSCLC/HBV/AMD) begins in 2019. We use a maximum risk rate of 30% in our modeling assumptions. Using these metrics, we model the market potential and discount back in our FCF, discounted-EPS, and sum-of-the-parts models to arrive our price target.

**TKMR:** Tekmira's technology represents a new paradigm, siRNA. The company's partner progress (Alnylam) is a factor, as Tekmira receives a royalty on the commercialization of its lead product. We see the ever-rising evidence of the viability of siRNA and the platform required to deliver the product, which Tekmira provides as a key element in this space. We see upside to the DoD platform with other indications, such as Marburg. Using these metrics, we model the market and discount back using a 15% rate in our FCFF, discounted-EPS, and sum-of-the-parts models, which triangulate to arrive at our price target.

**Price Target and Investment Risks**

**BLT:** Benitec faces multiple risks, which include: (1) developmental risk: the DNA-directed RNAi platform is still in early clinical development; (2) regulatory risk: RNAi is not an approved therapy yet, and the path to approval may not favor Benitec; and (3) financial risk: the company may need multiple capital raises to operate while their products are in development.

**TKMR:** Tekmira faces multiple risks, which include the clinical efficacy of the product; the management of the clinical trial process; the manufacturing of the product; the company's ability to raise capital; the competitive landscape for this product; the decisions of regulatory bodies, such as the European Union and FDA; and the reimbursement environment. Small, capitalized biotechnology companies possess unique risks and can be very volatile. Our ability to "predict" data based on small and limited patient numbers in early (phase I) trials is limited. As such, investors should expect these risks, which are typically commensurate with the reward potential.

**RISK RATINGS**

Risk ratings take into account both fundamental criteria and price volatility.



**Speculative – Fundamental Criteria:** This is a risk rating assigned to early-stage companies with minimal to no revenues, lack of earnings, balance sheet concerns, and/or a short operating history. Accordingly, fundamental risk is expected to be significantly above the industry. Price Volatility: Because of the inherent fundamental criteria of the companies falling within this risk category, the price volatility is expected to be significant with the possibility that the investment could eventually be worthless. Speculative stocks may not be suitable for a significant class of individual investors.

**High – Fundamental Criteria:** This is a risk rating assigned to companies having below-average revenue and earnings visibility, negative cash flow, and low market cap or public float. Accordingly, fundamental risk is expected to be above the industry. Price Volatility: The price volatility of companies falling within this category is expected to be above the industry. High-risk stocks may not be suitable for a significant class of individual investors.

**Medium – Fundamental Criteria:** This is a risk rating assigned to companies that may have average revenue and earnings visibility, positive cash flow, and is fairly liquid. Accordingly, both price volatility and fundamental risk are expected to approximate the industry average.

**Low – Fundamental Criteria:** This is a risk rating assigned to companies that may have above-average revenue and earnings visibility, positive cash flow, and is fairly liquid. Accordingly, both price volatility and fundamental risk are expected to be below the industry.

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