



Benitec Biopharma (BLT)

Mechanism of Action of Beta III-Tubulin in Drug Resistance Defined

BUY

Risk: High

Key Information

Price (\$ps)	0.77
Target Price (\$ps)	3.00
Market Cap (\$M)	89
GICS Sector	Pharma, Biotech & Life
52 week Hi-Lo (\$ps)	2.38 - 0.50
Daily Vol (M, mth avg)	0.6
Weight of S&P 200 Index (%)	0.00
Cash (\$m)	\$31M
Debt (\$m)	\$0M
Gearing (ND/ND+E) (%)	Net Cash
Forecast Total Return (%)	289.6%

Investment Fundamentals

YE 30 June	FY13	FY14	FY15F	FY16F
Sales (\$m)	1.3	1.1	1.2	60.1
EBITDA (\$m)	-3.6	-7.8	-11.8	39.3
Margin (%)	-2.7	-7.4	-9.8	0.7
NPAT (\$m)	-3.5	-7.0	-3.1	34.1
EPS (cps)	-5.3	-6.1	-2.7	29.6
EPS Growth (%)	-51.6%	15.0%	-55.3%	1183.5%
DPS (cps)	0.0	0.0	0.0	0.0
Franking (%)	100%	100%	100%	100%

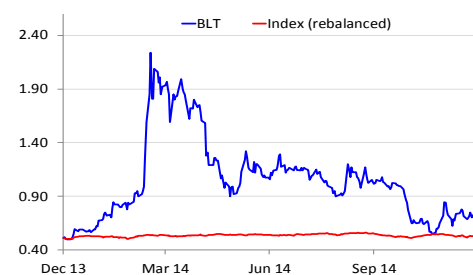
Source: Shaw Stockbroking

Ratio Analysis

YE 30 June	FY13	FY14	FY15F	FY16F
PE (x)	-14.5	-12.6	-28.2	2.6
PE Rel (x)	-1.0	-0.8	-1.9	0.2
Yield	0.0%	0.0%	0.0%	0.0%
ROE	-211.0%	-41.2%	-9.4%	101.6%
P/BV (x)	78.9x	2.6x	3.2x	1.4x

PE Rel is compared to the Market (Industrials + Resources)

BLT vs S&P/ASX Market Index



Performance	1 Mth	3 Mth	12 Mth
Absolute (BLT)	41.2%	0.0%	-4.4%
Rel to Market	38.5%	0.0%	0.0%

Company Activities

BLT is a biotechnology company focused on the development of treatments for chronic and life-threatening human conditions based on its patented gene-silencing technology, ddRNAi.

Major Shareholders

Shareholding	
RA Capital Management, LLC	12.2%
Christopher Bremner	7.0%
Dalit	5.0%

Directors and Management

Peter French (MD)
Kevin Buchi
Ian Ross
John Chiplin
Melvyn Bridges
Peter Francis (Ch)

Event

BLT has announced that its collaboration partner, the University of NSW, has determined the mechanism of action of beta III-tubulin in drug resistance in cancer. This is a very important step in validating the use of ddRNAi to silence the gene responsible for chemotherapy resistance in non small-cell lung cancer (NSCLC).

Key points

- Mode of action confirmed.** The University of NSW research has added to earlier animal studies that demonstrated resistance to chemotherapy in NSCLC is strongly associated with overexpression of β III-tubulin, providing an understanding of mechanism of action that had not previously been established. The significance of the enhanced understanding is in the further independent validation of BLT's lung cancer program aimed at silencing the beta III-tubulin gene using ddRNAi.
- Understanding the mode of action could also potentially help BLT look at a wider range of cancer targets for its ddRNAi technology further down the track.
- Trials to follow.** BLT has contracted European-based clinical research organisation Clinical Trials Group (CTGCRO) to manage the initial clinical development of Tribetarna™ for NSCLC BLT is undertaking biodistribution and toxicology studies in animal models prior to commencing a clinical trial. In parallel with these studies BLT is developing a companion diagnostic to stratify patients prior to human trials.

Recommendation - BUY

Validation of BLT's platform technology (which has a wide array of potential uses in fighting viruses, cancers and gene disorders) is progressing. In preclinical models, BLT's technology has cleared viruses such as Hepatitis C and caused chemotherapy resistant lung cancer to again become sensitive to chemotherapy. BLT has compelling animal data, a four patient human HIV trial that showed safety (via its sub-licensee Calimmune) and recently the FDA gave the go-ahead for BLT's hepatitis C clinical trial to commence (TT-034), which, when it reports, will potentially validate not just the HCV program, but more significantly, BLT's technology platform, in particular its hepatitis B program.

Achieving this milestone should generate further US investor interest given BLT's capitalisation (\$89mn) is undemanding for a company with its positioning, especially when compared to similar US companies that have market caps in the \$ billions. This supports our 12 month TP of \$3.00 and our view that, longer term, BLT has the potential to go much higher.



Financial Summary

Consolidated P&L (A\$m)	FY12	FY13	FY14	FY15F	FY16F	Key Financials	FY12	FY13	FY14	FY15F	FY16F
Operating revenues	0.3	1.3	1.1	1.2	60.1	Diluted average shares	37.5	65.6	115.2	115.2	115.2
Non operating revenues	0.0	0.0	0.0	0.0	0.0	Reported EPS	-11.0	-7.3	-6.1	-2.7	29.6
Total revenues	0.3	1.3	1.1	1.2	60.1	Reported EPS (diluted)	-11.0	-7.3	-6.1	-2.7	29.6
Total operating expenses	4.6	4.9	8.9	13.0	20.8	Cash EPS (diluted)	-11.0	-5.3	-6.1	-2.7	29.6
EBITDA	-4.3	-3.6	-7.8	-11.8	39.3	EPS growth	-30%	-52%	15%	-55%	1183%
Depreciation of assets	0.0	0.0	0.0	-0.1	-0.2	PER (x)	-7.0x	-14.5x	-12.6x	-28.2x	2.6x
Amortisation goodwill	0.0	0.0	0.0	0.0	0.0	DPS (cps)	0.0	0.0	0.0	0.0	0.0
Amortisation other	0.0	0.0	0.0	0.0	0.0	Payout ratio (%)	0.0%	0.0%	0.0%	0.0%	0.0%
EBIT	-4.3	-3.6	-7.8	-12.0	39.2	Dividend yield (net)	0.0%	0.0%	0.0%	0.0%	0.0%
Interest charges	0.0	0.0	0.0	0.0	0.0	Franking	100%	100%	100%	100%	100%
Interest received	0.2	0.1	0.3	1.1	1.2	Dividend yield (gross)	0.0%	0.0%	0.0%	0.0%	0.0%
Share of net profits of asso	0.0	0.0	0.0	0.0	0.0	Key Operational Financials	FY12	FY13	FY14	FY15F	FY16F
Profit before tax	-4.1	-3.5	-7.5	-10.9	40.4	EBITDA margin (%)	-1269.5%	-265.7%	-741.2%	-983.4%	65.5%
Tax	0.0	0.0	0.5	7.8	-6.3	EBIT margin (%)	-1273.3%	-267.9%	-742.4%	-994.5%	65.2%
OEI	0.0	0.0	0.0	0.0	0.0	NPAT margin (%)	-1226.4%	-259.1%	-668.7%	-261.1%	56.7%
Normalised NPAT	-4.1	-3.5	-7.0	-3.1	34.1	Tax rate (%)	0.0%	0.0%	6.1%	71.2%	15.6%
Significant items (after tax)	0.0	-1.3	0.0	0.0	0.0	EBITDA growth (%)	-20.0%	-16.0%	118.3%	51.8%	-432.1%
Reported NPAT	-4.1	-4.8	-7.0	-3.1	34.1	EBIT growth (%)	-22.4%	-15.6%	116.8%	53.3%	-427.1%
Cash NPAT	-4.1	-4.8	-7.0	-3.1	34.1	NPAT growth (%)	-5.5%	16.7%	46.7%	-55.3%	-1183.5%
Cashflows (A\$m)	FY12	FY13	FY14	FY15F	FY16F	Cash Flow Ratios	FY12	FY13	FY14	FY15F	FY16F
Operating cashflows	-3.3	-2.9	-9.6	-3.6	32.0	FCF (OC - CAPEX)	-3.3	-2.9	-9.6	-3.7	29.0
Investing cashflows	0.1	0.3	0.3	1.0	-1.8	FCF (growth pcp %)	-9.5%	-13.9%	234.7%	-62.0%	-892.7%
Financing cashflows	-0.4	1.1	39.1	0.0	0.0	Total CAPEX spend	0.0	0.0	0.0	-0.1	-3.0
Net increase in cash	-3.6	-1.5	29.8	-2.6	30.2	Net borrowings	-0.6	0.0	0.0	0.0	0.0
Cash at end of the year	3.1	1.6	31.4	28.8	59.0						
	-	-	-	-	-						
Balance Sheet (A\$m)	FY12	FY13	FY14	FY15F	FY16F	Balance Sheet Ratios	FY12	FY13	FY14	FY15F	FY16F
Cash	3.1	1.6	31.4	28.8	59.0	Period end shares	37.1	46.1	90.4	115.2	115.2
Receivables	0.1	0.1	0.1	0.1	6.6	NAV per share	0.1	0.0	0.3	0.2	0.5
Inventories	0.0	0.0	0.0	0.0	0.0	ROE (%)	-309%	-211%	-41%	-9%	102%
Plant & equipment	0.3	0.0	0.0	0.4	3.4	P / NAV (P/BV)	11.8x	78.9x	2.6x	3.2x	1.4x
Deferred tax assets	0.0	0.0	0.0	0.0	0.0	NTA per share	0.1	0.0	0.3	0.2	0.5
Intangibles	0.0	0.0	0.0	0.0	0.0	ROTE (%)	-337%	-226%	-41%	-10%	76%
Other assets	0.0	0.0	3.0	0.0	0.0	P / NTA (x)	11.8x	78.9x	2.6x	3.2x	1.4x
Assets	3.5	1.8	34.5	29.3	69.0	Gearing	FY12	FY13	FY14	FY15F	FY16F
	-	-	-	-	-	Net Debt	Net Cash	Net Cash	Net Cash	Net Cash	Net Cash
Payables	0.5	1.0	0.8	1.7	7.1	Net Debt / Equity	Net Cash	Net Cash	Net Cash	Net Cash	Net Cash
Provisions	0.6	0.1	0.2	0.2	0.2	Net Debt / (ND+E)	Net Cash	Net Cash	Net Cash	Net Cash	Net Cash
Tax liabilities	0.0	0.0	0.0	0.0	0.0	Int cover (x) (EBITDA)	N/A	N/A	N/A	N/A	N/A
Borrowings	0.0	0.0	0.0	0.0	0.0	Int cover (x) (EBIT)	N/A	N/A	N/A	N/A	N/A
Other liabilities	0.0	0.0	0.0	0.0	0.0						
Liabilities	1.1	1.1	1.0	1.8	7.3						
	-	-	-	-	-						
Net Assets	2.4	0.6	33.5	27.5	61.7						
Net Tangible Assets	2.4	0.6	33.5	27.5	61.7						

Source: Shaw Stockbroking

Mode of action defined

Researchers at the UNSW have shown that the beta III-tubulin gene has a significant role in modulating the PTEN/AKT signalling pathway in non-small cell lung cancer (NSCLC) cells. These findings were published in the international peer-reviewed journal Cancer Research on 20 November 2014 online. The title of the paper is “TUBB3/ β III-tubulin acts through the PTEN/AKT signalling axis to promote tumorigenesis and anoikis resistance in non-small cell lung cancer”.

The UNSW findings were that the “Suppression of beta III-tubulin using RNA interference dampens the AKT survival pathway in NSCLC cells, thus pointing to the potential mechanism by which beta III-tubulin expression affects tumour growth and resistance to chemotherapy drugs”.

Non Small Cell Lung Cancer

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer accounting for 85% to 90% of lung cancers. NSCLC usually grows and spreads more slowly than small cell lung cancer, however the rapid emergence of drug resistance is a major challenge. Drug resistance results in a high and rapid mortality, and a significant need exists for a therapy capable of restoring and/or improving the effect of therapeutic drugs in resistant tumours.

Benitec’s Drug Candidate - Tribetarna™

Benitec is not attempting to use ddRNAi to cure NSCLC. Rather, it is targeting a gene that is associated with the development of resistance to chemotherapy. Several research groups have demonstrated that resistance to chemotherapy is strongly associated with overexpression of β III-tubulin, (encoded by the TUBB3 gene). Inactivation of TUBB3 using RNA interference has been shown to restore chemosensitivity. Two separate experiments, each comprising six control-treated mice and six Tribetarna™-treated mice with human lung tumours has shown that an intravenous administration of Tribetarna™ is very efficiently taken up by lung tumours and results in significant silencing of the target gene in those tumours. This resulted in the reduction of tumour resistance to chemotherapy drugs, and doubling of survival in animals with Tribetarna™ who were administered the chemotherapy drug cisplatin.

Trial Plan

Benitec has contracted European-based clinical research organisation Clinical Trials Group (CTGCRO) to manage the initial clinical development of Tribetarna™. BLT is also undertaking biodistribution and toxicology studies in animal models prior to commencing a clinical trial. In parallel with these studies BLT is developing a companion diagnostic to stratify patients prior to human trials.

Global Market

Lung cancer is the leading cause of cancer-related deaths worldwide with 1.3 mn deaths p.a. Industry sources estimate the global NSCLC drug market to increase from US \$4.3 bn in 2009 to US\$ 6.9 bn in 2019 and the market is growing with a CAGR of 4.8% during 2009 to 2019. The high growth forecast is primarily attributed to the strong pipeline landscape, population growth and release of new first-in-class drugs with better safety and efficacy profiles.



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Rating Classification

Buy	Expected to outperform the overall market
Hold	Expected to perform in line with the overall market
Sell	Expected to underperform the overall market
Not Rated	Shaw has issued a factual note on the company but does not have a recommendation

Risk Rating

High	Higher risk than the overall market – investors should be aware this stock may be speculative
Medium	Risk broadly in line with the overall market
Low	Lower risk than the overall market.

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