



Biota Holdings Limited (BTA)

Speculative Buy

HRV Phase 2a Challenge Study Success

\$1.27

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Key Points

Phase 2a challenge study of BTA798 in Human Rhinovirus (HRV) shown to reduce incidence and severity of infection.

Highest dose demonstrated statistical significance in peak viral level reduction ($p=0.03$) and total viral load ($p=0.02$).

Trial stopped at 41 patients versus 240 under original trial design, capping trial costs at approx. \$4.0m, well below estimates.

Biota confirmed intention to license global rights, and is seeking commercial partners while continuing to plan for new treatment trials.

Summary

Market Capitalisation (M)	\$221.7
Share Price	\$1.27
Shares on Issue (M)	174.6
Av. Monthly Volume (Yr Rolling)(M)	14.4
52 Week High	\$1.79
52 Week Low	\$0.29
Valuation Per Share (fully diluted)	\$1.80
Cash (M) as at 31/12/08	\$55.4

Our View

- Biota has again shown its internal drug development capacity is capable of delivering compounds that show excellent anti-viral properties. The current Phase 2a challenge study with BTA798 revealed very significant inhibition of viral replication, with statistical significance achieved at the highest (undisclosed) dose. Given each treatment arm was ~10 patients and ~10 patients in the placebo arm, the significance of this result should not be underestimated. Given the effects seen with a small number of patients, the trial was concluded early, resulting in potential savings of up to \$11m based on expectations for costs with 240 patients. Investors need to be cognisant that this prophylaxis challenge study was designed to show a drug effect on the virus and reduction in incidence and severity in artificial HRV infection conditions (i.e. infect otherwise healthy patients pre-treated with BTA798 for two days). We believe a single dose, Phase 2b treatment study in naturally acquired HRV infections for patients likely to have pre-existing lung conditions (asthma, COPD, CF) will be designed during 2H CY09 to determine if BTA798 can reduce disease symptoms in a statistically significant manner.

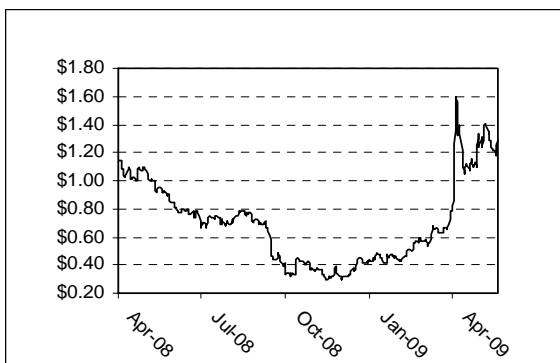
Key Financials (A\$'000)

Year End	FY08 Actual	FY09 Est.	FY10 Est.
Relenza Royalties	20,544	45,610	32,784
Partnering Income*	5,871	4,069	23,410
Total Revenue	44,989	64,815	60,990
Total Op. Expenses	(41,397)	(20,868)	(13,119)
R&D Expenses	(10,287)	(14,171)	(11,274)
EBITDA	(9,897)	39,667	33,510
Normalised NPAT	10,735	17,285	27,901
Adj. NPAT	(6,489)	37,429	27,901
Adj. EPS (c)	(3.5)	21.4	16.0
Adj. PE Ratio (x)	n/a	5.9	7.9

* Upfront/Milestones only (ex-R&D income)

- Though the Phase 2a trial has shown some clinical effects, we have not reduced our risk-adjustment (20%) for BTA798 in HRV, believing a Phase 2b treatment trial under natural conditions will present a somewhat higher hurdle for Biota to maintain the efficacy effect. This, coupled with a further determination of the exact reproductive/developmental safety of BTA798, in light of previous regulatory roadblocks for HRV capsid inhibitors +/- potential resistance issues has seen us maintain our BTA798 valuation at \$41.8m (\$0.24 per share). However, we have increased our FY09 NPAT estimates by 16.2% to \$37.4m due to the lower than expected clinical trial spend on BTA798 in HRV (\$4.0m versus TC estimates of \$7.5m). Our FY10, FY11 NPAT estimates remain largely unchanged. On this basis, Biota currently trades on a FY09 PE multiple of 5.9x with material upside on better than anticipated 4Q GSK Relenza™ sales due July 22nd. We have upgraded our price target by 2.9% to \$1.80. We maintain our Speculative Buy recommendation.

Share Price Graph (A\$)



BTA798 Phase 2a Synopsis

BTA798 is a potent inhibitor of HRV spread.

In the Phase 2a trial, Biota utilised an undisclosed inoculum of a single strain of HRV for which patients had not been previously exposed to (i.e. no immunity – which could have skewed the results to the negative) and for which was known to be sensitive to BTA798. The Phase 2a trial was in healthy male volunteers. As a refresher, BTA798 is a potent inhibitor of the HRV VP1 capsid protein, present on the outer surface of the virus. VP1 is crucial to the HRV virus in releasing its genetic material (RNA) into the target cell, facilitating viral replication and thereafter release from infected cells.

Very significant reduction in viral load and total virus a key Phase 2a benefit.

While the data is convincing from a preventative perspective (to obtain a statistically significant result in terms of load reduction and total virus in such a small patient cohort v placebo is remarkable), we believe the take home message from the study is BTA798 is very effective at **preventing** viral replication when sufficient plasma quantities of the drug exist and when using a single viral strain known to be sensitive to BTA798.

Next clinical trial will be a treatment trial in patients with compromised lung function.

We do not however know whether BTA798 will demonstrate in a statistical manner, a reduction in overall disease symptoms/duration in a naturally acquired cohort **treated** with BTA798. Biota will not seek a preventative indication for BTA798 in our view, given the difficulty of demonstrating a pharmacoeconomic benefit of such a label in patients without an acquired infection (i.e. rhinovirus free). We believe the Company will take a single dose into its treatment trials (whether partnered or not), more than likely at the highest dose. The cohort of patients targeted for treatment are likely to be those with a pre-existing pulmonary condition, such as asthma, cystic fibrosis or chronic obstructive pulmonary disease (COPD), where HRV exacerbates and quite often causes serious complications.

Can we take anything from the Phase 2a study into the Phase 2b treatment trials?

We believe yes. While the disclosure of clinical information was on the light side for Biota (dose, dosing schedule, PK, infectious units of virus administered, disease duration effects and adverse events were not disclosed), certain aspects proved interesting. On the positive, the inoculum of virus administered to patients under the Phase 2b trial conditions was at a much higher dose of virus than would be acquired naturally – and as such, given the anti-viral effect, one could rationally argue the inhibitory effects of the drug will be superior in a treatment trial with a lower viral load.

Limited disclosure from the Phase 2a makes interpretation more challenging.

On the negative, as the Phase 2b trial will be treating a pre-existing infection, there is a risk such an infection, if well established, may result in viral titres in excess of that under trial conditions in Phase 2a. This will also depend on the pharmacokinetics (PK) of the drug (also thus far undisclosed) and how quickly it reaches the maximum concentration (C_{Max}) (or inhibitory concentration) in the blood. We also note a field study will involve patients with varying stages of infection (and potentially different lung diseases) and different viral strains, some of which may be less susceptible to BTA798.

Phase 2a study highlights strong specificity for reducing viral replication, in challenged patients.

In short, we draw the conclusion that the Phase 2a challenge study does provide evidence that BTA798 can inhibit viral replication and therefore reduce disease incidence and severity but its success in a treatment trial will depend on whether this can be achieved with a pre-existing infection, rather than simply inoculating a single virus type with known sensitivity to BTA798 into the nasopharynx with an existing concentration of drug in the blood.

With this in mind, an examination of the HRV family reveals some interesting insights. There are two genetic sub-groups, namely HRV-A and HRV-B (with a third recently discovered). At least 100 different strains of HRV have been genetically sequenced, adding significant diversity to overcome any targeted drug strategies drug. Moreover, HRV has recently been shown to recombine to create new viral strains. The direct and indirect and indirect cost of common colds in the US annually is estimated to be as high as US\$60b.

We have not increased our risk-adjustment (20%) on BTA798 as a result of this challenge study because we feel that while the drug has been shown to statistically knock down viral load and reduce incidence and severity of infection, it was a prophylaxis trial under

No change to risk-adjusted NPV of \$41.8m.

We believe the Company can execute a license deal worth \$120m for BTA798.

Pleconaril is a HRV drug also targeting VP1 and was rejected by the FDA for approval in 2002 on safety concerns.

Undesirable effects in females.....which Biota need to sort out for BTA798.

Pleconaril also displayed some resistance issues, up to 23.7% in Phase 3.

controlled conditions. The real test will come from Phase 2b studies in naturally acquired rhinovirus infections, where treatment effects are required and a far more heterogeneous population of individuals will arise and multiple strains of HRV potentially present. We maintain our risk-adjusted valuation of **\$41.8m (\$0.24 per share)** for this program, which assumes the company can execute a Phase 2a license deal worth \$120m, with a 15% royalty rate – consistent with historic deals in the space (see below).

Human Rhinovirus (HRV) – Pleconaril and BTA798

There are currently no approved drugs to treat Human Rhinovirus infections. One drug, pleconaril, which is also an HRV capsid inhibitor (and has activity against other picornaviruses) was rejected by the FDA in March 2002 on the basis that the safety effects outweighed the clinical benefits observed. Pleconaril was shown in two pivotal Phase 3 trials to show some treatment effects with a net 0.5 day reduction in symptoms for all randomised patients and 1.0 day in patients confirmed by a technique known as PCR to have viral infection. The drug was not efficacious for smokers. Both pleconaril and BTA798 bind to a key part of the VP1 protein on the viral surface to inhibit viral replication.

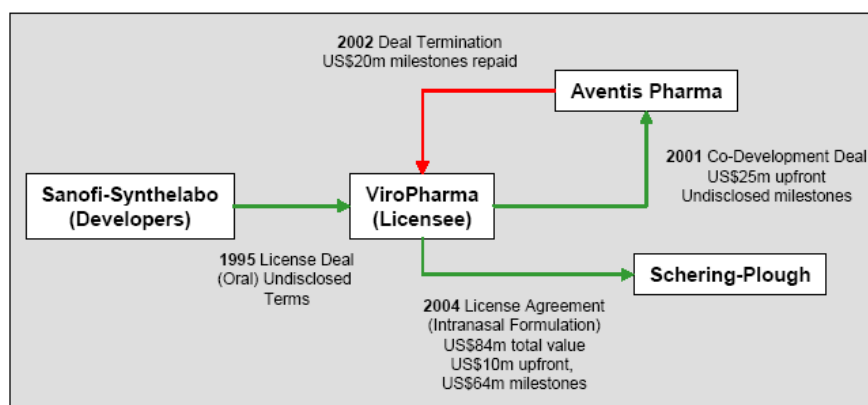
The undesirable safety effects of pleconaril were increased menstrual abnormalities in female patients and gastrointestinal side effects including vomiting diarrhoea and nausea. The female effects were via CYP3A4 induction, which has been shown to result in menstrual disorders, unintended pregnancies and potential for interactions with other drugs. In short, the drug interfered with female contraception strategies. We understand that while Biota has examined effects of BTA798 on CYP3A4 *in vitro*, there is further work to be done to completely rule out induction of this protein by BTA798 *in vivo* via reproductive toxicology studies.

The FDA also commented on resistance issues in the pivotal phase 3 studies (23.7% overall). 13% of viruses assayed showed a lack of susceptibility to pleconaril on a baseline basis, while 10.7% resulted from a loss of susceptibility – due to treatment. In other words, the use of pleconaril drove the emergence of drug resistant mutant strains. The FDA noted ¾ with the baseline lack of susceptibility had a single amino acid change at position 98 of the VP1 capsid protein.

We understand from Biota management that BTA798 has not been tested *in vitro* against this particular mutant strain, however, we note a number of virus variants with reduced susceptibilities to pleconaril have been shown to pre-exist at very low levels in susceptible virus populations and can be isolated in cell culture under drug selection pressure. Indeed, subsequent scientific analysis of the Phase 3 pleconaril trials also suggested the emergence of viruses with reduced drug susceptibility did not affect the clinical outcome in pleconaril-treated adults with colds caused by rhinoviruses.

The interest for pleconaril has provided for an interesting commercial history, as shown below. At present, the drug has completed a Phase 2 study sponsored by Schering-Plough.

Pleconaril has seen a number of commercial deals, and has completed another Phase 2 trial via Schering-Plough.



Source: Recap

New intranasal form of pleconaril developed.

The Schering-Plough clinical study does not utilise an oral form of pleconaril, but instead the study will examine the efficacy of the drug via intranasal administration of pleconaril over 7 days (14 doses) versus placebo. The intranasal form was developed to deliver significantly more drug to the site of active common cold infection than the oral formulation, while limiting its systemic exposure and thus minimising the risk of drug interactions.

The study is examining the effects of pleconaril nasal spray on common cold symptoms and asthma exacerbations following HRV exposure. Interestingly, the specific exclusion criteria include active smokers and breast feeding, pregnant or intending to become pregnant women. We understand Schering-Plough may report its Phase 2 pleconaril data later in the year at an international conference.

Though Biota acknowledge the future clinical plans for BTA798 have not been finalised, it is not unreasonable, in our view, to assume that if the pleconaril study proves effective and the trial largely accepted by clinicians and regulators that this may form the basis of Biota's next clinical trial (partnered or unpartnered).

Changes to Forecasts

We have increased our FY09 NPAT estimates by 16.2% to \$37.4m due to the lower than expected clinical trial spend on BTA798 in HRV (\$4.0m versus TC estimates of \$7.5m). We have maintained our FY10 estimates on the basis that Biota will continue to spend money on HRV clinical planning and development in the absence of partnering in the near/medium term. For FY10, we have assumed \$5.7m in this regard. Naturally, a partnering deal with extinguish part of this expected cost and drive the top/bottom line commensurate with the upfront licence fee received. Our view is that the efficacy data will provide Biota with a greater ability to secure a licence deal (pleconaril may also prove a positive), but we do not expect this to be consummated during CY09. Our FY11 estimates remain unchanged.

Changes to Forecasts

	FY09E			FY10E			FY11E		
	Previous	Revised	Change	Previous	Revised	Change	Previous	Revised	Change
Relenza Volumes (m)	26.1	26.1	0.0%	18.7	18.7	0.0%	19.8	19.8	0.0%
Relenza Royalties (A\$m)	45.6	45.6	0.0%	32.8	32.8	0.0%	34.6	34.6	0.0%
EBITDA	36.1	39.7	9.9%	33.5	33.5	0.0%	21.9	21.9	0.0%
Adj. NPAT	33.9	37.4	10.4%	27.8	27.9	0.4%	18.2	18.2	0.5%
Adj. EPS (c)	19.4	21.4	10.5%	15.9	16.0	0.4%	10.4	10.5	0.5%

Source: Taylor Collison estimates

Biota Holdings Limited - Summary of Forecasts

BTA \$1.27

PROFIT & LOSS SUMMARY (A\$'000)

	FY07A	FY08A	FY09E	FY10E	FY11E
Relenza Royalties	39,789	20,544	45,610	32,784	34,629
Partnering (Licence) Income	5,726	5,871	4,069	23,410	10,000
Research income (inc Grants)	8,740	15,042	12,171	1,624	700
Total Revenue	57,300	44,989	64,815	60,990	50,041
<i>Growth (ppp)</i>	282.8%	-21.5%	44.1%	-5.9%	-18.0%
Net Gain on GSK Settlement	0	0	12,736	0	0
Net Operating Revenue	27,576	3,592	56,683	47,871	37,754
R&D Expenses	(8,198)	(10,287)	(14,171)	(11,274)	(11,903)
EBITDA	16,871	(9,897)	39,667	33,510	21,895
Depreciation	(1,228)	(933)	(1,207)	(1,254)	(1,616)
Amortisation	(317)	(1,681)	(3,877)	(2,787)	(2,943)
EBIT	15,326	(12,511)	34,584	29,470	17,335
Net Interest	2,507	3,202	2,845	3,087	3,957
Pre-Tax Profit	17,833	(9,309)	37,429	32,556	21,292
Tax Expense	2,347	2,820	0	(4,656)	(3,045)
Minorities	0	0	0	0	0
NPAT Normalised *	21,424	10,735	17,285	27,901	18,247
NPAT Adj.	20,180	(6,489)	37,429	27,901	18,247
<i>Growth (ppp)</i>	n/a	n/a	n/a	-25.5%	-34.6%
Net Adjustments	0	0	0	0	0
Reported Profit	20,180	(6,489)	37,429	27,901	18,247

PER SHARE DATA

Period	FY07A	FY08A	FY09E	FY10E	FY11E
Adjusted EPS (c)	11.2	(3.5)	21.4	16.0	10.5
<i>Growth (ppp)</i>	n/a	n/a	n/a	-25.5%	-34.6%
Reported EPS (c)	11.2	(3.5)	21.4	16.0	10.5
<i>Growth (ppp)</i>	n/a	n/a	n/a	-25.5%	-34.6%
Dividend (c)	0.0	0.0	0.0	0.0	0.0
Franking	0%	0%	0%	0%	0%
Gross CF per Share (c)	6.9	2.4	14.9	78.5	30.7
NTA per share (c)	32.2	28.0	82.7	157.6	187.1

VALUATION MULTIPLES

Period	FY07A	FY08A	FY09E	FY10E	FY11E
Adjusted PE Ratio (x)	11.3	n/a	5.9	7.9	12.1
PE Ratio (x)	11.3	n/a	5.9	7.9	12.1
Dividend Yield (%)	n/a	n/a	0.0%	0.0%	0.0%
EV/EBITDA (x)	9.5	n/a	3.4	3.1	3.7
EV/EBIT (x)	10.4	n/a	3.9	3.6	4.7

CAPITAL RAISING ASSUMPTIONS

Period	FY07A	FY08A	FY09E	FY10E	FY11E
Shares Issued (m)	0.0	0.0	0.0	0.0	0.0
Issue Price (A\$)	0.0	0.0	0.0	0.0	0.0
Cash Raised (A\$m)	0.0	0.0	0.0	0.0	0.0

KEY RATIOS

Period	FY07A	FY08A	FY09E	FY10E	FY11E
EBITDA/Sales Margin %	29.4%	-22.0%	61.2%	54.9%	43.8%
EBIT/Sales Margin %	26.7%	-27.8%	53.4%	48.3%	34.6%
Current ratio (x)	5.3	3.4	5.4	12.4	13.5
Net Debt : Equity (%)	-86.9%	-94.8%	-87.1%	-90.3%	-95.8%
ROE (%)	34.1%	-9.6%	45.6%	24.3%	13.2%
Dividend Payout Ratio (%)	n/a	n/a	0.0%	0.0%	0.0%

*Excluding litigation expense and settlement, tax effected at 30%

BALANCE SHEET SUMMARY (A\$'000)

Period	FY07A	FY08A	FY09E	FY10E	FY11E
Cash	62,156	60,164	87,756	116,182	140,765
Receivables	9,350	4,270	16,204	11,588	9,508
Inventories	0	0	0	0	0
Other	0	0	0	0	0
Total Current Assets	71,506	64,434	103,960	127,770	150,273
Inventories	0	0	0	0	0
Property Plant & Equip	5,152	7,543	7,836	8,082	7,966
Intangibles	13,447	12,113	8,236	5,450	2,506
Other	2,349	5,168	6,888	5,168	5,168
Total Non-Current Assets	20,948	24,824	22,960	18,700	15,640
TOTAL ASSETS	92,454	89,258	126,920	146,470	165,913
Accounts Payable	6,004	12,023	14,908	9,148	7,506
Borrowings	0	0	0	0	0
Provisions	1,097	1,122	1,122	1,122	921
Other (inc Def Rev)	6,457	6,059	3,125	0	2,733
Total Current Liab	13,558	19,204	19,155	10,270	11,160
Borrowings	0	132	0	0	0
Provisions	6,339	6,622	6,991	7,524	7,830
Other (inc Def Rev)	1,022	0	0	0	0
Total Non-Current Liab	7,361	6,754	6,991	7,524	7,830
TOTAL LIABILITIES	20,919	25,958	26,146	17,795	18,990
TOTAL EQUITY	71,535	63,300	100,775	128,675	146,923

CASH FLOW SUMMARY (A\$'000)

Period	FY07A	FY08A	FY09E	FY10E	FY11E
EBIT (excl Abs/Extr)	15,326	(12,511)	34,584	29,470	17,335
Add: Depreciation	1,228	933	1,207	1,254	1,616
Amortisation	317	1,681	3,877	2,787	2,943
Change in Pay.	1,970	6,019	2,885	(5,759)	(1,642)
Less: Tax paid	2,347	2,820	0	(4,656)	(3,045)
Net Interest	2,507	3,202	2,845	3,087	3,957
Change in Rec.	(3,486)	5,080	(11,934)	4,616	2,080
Change in Prov.	(6,820)	(308)	(369)	(533)	(105)
Change in Def Tax Assets	(2,349)	(2,819)	0	0	0
Change in Inv.	0	0	0	0	0
Change in Def. Rev.	1,468	(1,420)	(2,934)	(3,125)	0
Gross Cashflows	12,508	4,358	34,037	29,926	26,083
Capex	(893)	(3,785)	(1,500)	(1,500)	(1,500)
Free Cashflows	11,615	573	32,537	28,426	24,583
Re-Purchase of Shares**	0	(3,020)	(4,945)	0	0
Net Cash Flow	11,615	(2,447)	27,592	28,426	24,583

** Biota bought back 9.17m shares, or 5% of its issued capital, ending 7th Oct 2008

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