BTG

CytoFab study failure

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Look beyond the short-term shock

Biotech & pharma

AstraZeneca's discontinuation of AZD9773/CytoFab after the failure of a Phase IIb study in severe sepsis/septic shock has a material impact on BTG's valuation, but given the larger recent share price movement, the investment case remains strong. Removing CytoFab's contribution and making certain other changes reduces our valuation from 430p to 398p per share. This suggests there is an almost 15% upside to a valuation that is largely underpinned by the DCF value of a solid revenue-generating business while, by biotech standards, BTG has a low risk profile.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
03/11	111.4	16.6	13.6	0.0	25.2	N/A
03/12	197.0	57.2	14.9	0.0	23.0	N/A
03/13e	201.0	49.4	12.5	0.0	27.4	N/A
03/14e	223.5	53.5	12.0	0.0	28.3	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation and exceptional items.

CytoFab fails in the challenging sepsis indication

AstraZeneca has discontinued AZD9773/CytoFab after the failure of its 300-patient Phase IIb study in severe sepsis/septic shock. Although disappointing, the outcome of the study is a reflection of the challenging nature of the sepsis indication. CytoFab was carried at a low probability in our model, although the attractive economics of the licensing deal meant it still made a material contribution (£136m) to the valuation.

Benefix windfall, Zytiga sales tracking $1.2bn/year

BTG recently disclosed a further windfall royalty on Benefix, which added c £10m to its FY13 revenue guidance to £190-200m; Edison's model suggests revenues may come in slightly higher at £201m. Furthermore, reported sales of Zytiga by Johnson & Johnson suggest this product is on track to achieve $1.2bn sales this year. It thus has the potential to make a significant (and probably under-appreciated) contribution to BTG's FY13 revenues.

Core business performing well

BTG's core direct sales operations (CroFab, DigiFab and Bead products) continue to perform well. The next key milestone is likely to be the planned filing of Varisolve, due in Q412.

Valuation: Fair value now 398p per share

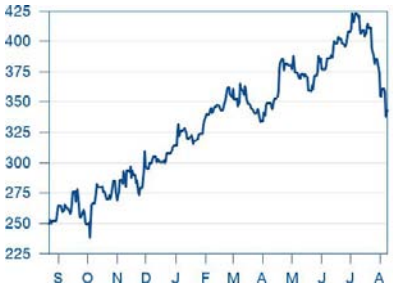
Removing the CytoFab contribution and updating the valuation to reflect the Benefix windfall and using FY13 year-end cash (£144m) suggests a valuation of £1.3bn or 398p per share. This compares with the previously published £1.4bn or 440p/share. Thus we consider BTG offers an attractive investment proposition, with the current share price offering 14% upside to a valuation that is supported by the DCF value of its core business activities and a low risk profile by biotech standards.

9 August 2012

Price	343p
Market cap	£1,125m

Shares in issue	328.1
Free float	100%
Code	BTG
Primary exchange	LSE
Other exchanges	N/A

Share price performance



%	1m	3m	12m
Abs	(18.9)	(7.3)	41.2
Rel (local)	(21.4)	(11.8)	22.5
52-week high/low	423.0p		236.8p

Business description

BTG is a UK-based biopharmaceutical company with a direct commercial presence in US acute care medicine and interventional oncology. It has a number of internal and partnered R&D programmes.

Next events

Varisolve filing	Q412

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BTG datasheet

Exhibit 1: Divisional profile/principal products

Business unit	Product	Indication	Notes
Specialty pharma	CroFab	Antivenom	Approved in US.
	DigiFab	Digoxin antidote	Approved (US, Switzerland, Canada and UK).
	Voraxaze (glucarpidase)	Treatment for MTX toxicity	Approved US/available elsewhere under named-patient/compassionate use protocols. Licensed to Ohara Pharmaceutical (Japan).
	Uridine triacetate	5-FU toxicity	NDA filing expected H113. US and EU named-patient rights licensed from Wellstat.
Interventional medicine	LC/DC beads	Embolization/ TACE	Sold direct in US, via distributors elsewhere: Termuno (EU), Transmedic (SE Asia); Eisai (Japan, filed), Device Technologies (Aus/NZ); SciClone (China, filing in preparation). Humanitarian use device designation granted US for Precision Bead for uveal melanoma with hypervascularised hepatic metastases. Phase II study planned of DEBIRI in liver metastases from colorectal cancer and DEBIRI/DEBDOX in cholangiocarcinoma and metastatic ocular carcinoma.
	Brachytherapy	Prostate cancer	Radioactive seed implants. Various devices (AnchorSeed, EchoStrand, VariStrand) and radio-isotope (Iodine-125, Palladium-103, Cesium-131) combinations.
	Varisolve	Varicose veins	Phase III programme completed, US filing due at end of 2012.
Licensing and biotech	Zytiga	mCRPC	Approved US/EU. Partner: Johnson & Johnson.
	Lemtrada	MS	Filed June 2012. Partner: Sanofi.

Source: Edison Investment Research

Exhibit 2: Licensing and biotechnology programmes

Drug/indication	Licensee	Development/notes
Zytiga (abiraterone)	J&J	Approved for mCRPC (post-docetaxel) in US/EU. Filing expected for pre-chemo use in H212, based on positive outcome in a 1,000-pt Phase III study. Data presented at ASCO 2012.
Campath/Lemtrada (alemtuzumab)	Sanofi (Genzyme)	Approved as Campath for B-CLL. Filed for MS, with approval possible in Q213. Positive results in two Phase III studies for MS (CARE-MS I and CARE-MS II). Patent to 2017.
Two-part hip cup	Various	Prosthetic hip that allows an improved range of motion that helps to avoid dislocation. Licensees include Zimmer, Stryker, Smith & Nephew and Biomet. Patent to 2019.
MRC IP	Various	Multiple partners. Patents (on antibody humanisation) to 2015.
ONYX 0801	Onyx	60-pt Phase I study in pts with advanced solid tumours (completed).
Otelixizumab/ GSK2136525	GSK	Phase II for myasthenia gravis (no details); 40-pt Phase I study in rheumatoid arthritis (results: Jul 2014). Reported to be in Phase I for Grave's disease and Type I diabetes (sc formulation).
Nexvax2	ImmusanT	34-pt Phase I study in coeliac disease completed.

Source: Edison Investment Research

Exhibit 3: Key catalysts (including competitor products)

Date	Event/product	Comment
Sept 12	Potential US approval of Aubagio	Potential competitor to Lemtrada, to be marketed by Sanofi. PDUFA date: 12 Sept. Pricing, given desire for differentiation from Lemtrada, will be of relevance.
H212	Zytiga pre-chemo mCRPC filing	Approval, possibly very quickly (eg in <6 mths). Anecdotal reports of off-label use in pre-chemo mCRPC setting, ahead of approval.
H212	Sprycel Phase III data in mCRPC.	Potential broader competitor to Zytiga in mCRPC (although study tests use in combination with docetaxel).Already available for other cancer indications.
Q412	Varisolve filing	BTG will file regulatory submissions once 12-month follow-up data are available. Approval expected in c 12 months, perhaps late 2013, allowing launch in early 2014.
Nov 12	Enzalutamide US approval decision	Potential competitor to Zytiga filed in US in May 12 (EU in June) for post-chemo mCRPC. PDUFA date: 22 Nov.
Q113	BG-12 approval.	Potential competitor to Lemtrada. Filed Feb 12, granted standard review.
Q213	Lemtrada approval and launch	Filing in Jun 12, approval expected in Q2 13; launch mid 13.
2013	Filing of uridine triacetate.	Filing targeted in 2013; launch possible in 2014.
2013/14	Enzalutamide pre-chemo data	Potential competitor to Zytiga. Study may be render an early result, if positive, may lead to off-label use in this setting, ahead of approval.

Source: Edison Investment Research

Update: CytoFab shock creates buying opportunity

AstraZeneca has discontinued AZD9773/CytoFab after the failure of its 300-patient Phase IIb study in severe sepsis/septic shock. Although disappointing, the outcome of the study is a reflection of the peculiarly challenging nature of the sepsis indication. This was well known and reflected in the fact that CytoFab was carried at a low probability (relative to its development stage) in our valuation model. However, the attractive economics of the licensing agreement meant that it still made a material (c £136m) contribution to the valuation. Adjusting our model to remove this and making certain other minor changes produces a new valuation of £1.31bn or 398p per share (versus the previously published £1.41bn or 430p per share).

BTG does not intend to develop CytoFab further and will record a £28m impairment charge, of which £25m is non-cash write downs of intangible and tangible fixed assets. The remaining £3m (cash) element reflects costs incurred associated in R&D. These are now reflected in our financial model.

BTG recently boosted its revenue guidance for FY13 to £190-£200m (from £180-£190m previously) as a result of windfall royalty on BeneFIX of c £14m. We forecast revenues slightly above guidance at £201m.

Zytiga sales continue to grow

Meanwhile Zytiga, in which BTG holds a 6% gross (c 3% net) royalty interest, continues to enjoy one of the most successful launches ever seen in oncology. [1] Johnson & Johnson (J&J) reported Q2 sales of $232m, up 16% sequentially from the $200m for Q112, which suggest Zytiga sales could reach at least $1.2bn in 2012, its first full year on the market. Our financial model for BTG currently assumes sales of $1bn (and thus royalties of £40m to BTG); hence there is potential for upgrade.

However, we also assume Zytiga sales will level off in 2013 at c $1.5bn/year, although this figure could prove to be conservative. This is based on the likely introduction of competing agents for metastatic castration-resistant prostate cancer (mCRPC), principally Medivation/Astellas's enzalutamide, which has a 22 November PDUFA date. J&J will shortly file Zytiga for pre-chemotherapy use in mCRPC and could see its first approvals in this setting towards the end of this year.

Other Phase III studies in mCRPC may also shortly read out including those of Bristol-Myers Squibb's Sprycel (dasatinib), which is approved in other cancer indications, and Takeda's ortoronel, both in the chemo-naïve setting. An updated list of studies with competing agents is shown in Exhibit 4 overleaf, with a comparison on the efficacy data from controlled studies in mCRPC in Exhibit 5.

BTG receives a 6% royalty on worldwide Zytiga sales for as long as a licensed patent remains in force. The licensed patents include ones covering processes that extend to 2025. There is a patent on abiraterone listed in the FDA orange book that expires in 2014, but we assume J&J will enjoy a longer period of exclusivity in the US, probably into the 2020s. In the EU, abiraterone has exclusivity via data protection to 2022.

[1] Zytiga sales in H112 ($432m) were roughly three times those of Sanofi's Jevtana (€119m or $147m), which is indicated for post docetaxel mCRPC.

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Exhibit 4: Competing Phase III programmes for mCRPC

Compound	Company	Setting(s)	Notes
Sprycel (dasatinib)	BMS	chemo-naïve	1,500-pt Phase III study (READY) of docetaxel ± dasatinib (fully-recruited, results: Aug 2012).
Orteronel	Takeda	chemo-naïve	1,454-pt Phase III study of ortoronel vs placebo (results: Jan 2013). Primary endpoint: PFS.
		post-docetaxel	1,083-pt Phase III study of ortoronel vs placebo (results: Sep 2013).
enzalutamide (MDV3100)	Medivation/ Astellas	chemo-naïve	1,680 pt Phase III study (PREVAIL) of enzalutamide vs placebo (results: Sep 2014). Co-Primary endpoints: OS and PFS.
tasquinomod	Active Biotech/Ipsen	chemo-naïve	1,200-pt Phase III study of tasquinomod vs placebo (results: Jan 2016). Primary endpoint: PFS.
Jevtana (cabazitaxel)	Sanofi	chemo-naïve	1,170-pt Phase III study (FIRSTANA) of cabazitaxel at 20mg/m^2 and 25mg/m^2 vs docetaxel (results: Jan 2016).
		post-docetaxel	1,200-pt Phase III study (PROSELICA) of cabazitaxel at 25 vs 20mg/m^2 (results: Sep 2017). 1,000-pt Phase III study early access (results: Dec 2015).
Yervoy (ipilimumab)	BMS	chemo-naïve	630-pt Phase III study of cabazitaxel ± custirsen (results: Feb 2015).
		post-docetaxel	800-pt Phase III study, monotherapy vs placebo (results: Dec 2012).
Custirsen	Teva/ OncoGenex	first-line combo with chemo	1,000-pt Phase III study (SYNERGY) of docetaxel ± custirsen (results: Dec 2013).
		post-docetaxel	630-pt Phase III study (AFFINITY) of cabazitaxel ± custirsen (results: Dec 2015).
Prostvac	Bavarian Nordic	chemo-naïve	1,200-pt Phase III study of Prostvac ± GM-CSF vs placebo (results: Dec 2014).
Cabozantinib	Exelixis	post docetaxel	960-pt Phase III study (COMET-1) of cabozantinib vs prednisone (2:1) (results: Mar 2014). 587 events for primary analysis, interim at 387 events.
		post docetaxel/ abiraterone/ cabazitaxel	246-pt Phase III study (COMET-2) of cabozantinib vs mitoxantrone in pts with mod to severe pain (BPI>4) despite optimised narcotic therapy (results Jun 2013) Primary endpoint is alleviation of pain. Secondary endpoints: OS and rPFS.

Source: Edison Investment Research. Note: Primary endpoint is OS, unless shown otherwise.

Exhibit 5: Comparison of controlled survival studies in mCRPC

Drug, company	N	Comparator	Study (year)	Setting	Hazard ratio for OS (95% CI)	p value	Increase in OS	Median OS improvement, absolute (%)
Zytiga (abiraterone), **J&J**	1,088	placebo/ prednisone	COU-AA-302 (2012)	chemo-naïve	0.75 (0.61-0.93)	0.0097	33.3%	Not reached, vs 27.2 mth (N/A)
Zytiga (abiraterone), **J&J**	1,195	placebo/ prednisone	COU-AA-301 (2010)	post-docetaxel	0.740 (0.638-0.859)	<0.0001	35.1%	4.6 mth, 15.8 vs 11.2 (41.1%)
Alpharadin (Ra-223), **Algeta/Bayer**	921	placebo	ALSYMPCA (2011)	pre-/post docetaxel	0.695 (0.581-0.832)	0.00007	43.9%	3.6 mth, 14.9 vs 11.3 (31.8%)
Alpharadin, **Algeta/Bayer**	526	placebo	ALSYMPCA (2011)	post-docetaxel sub-group	0.710 (0.565-0.891)	0.00307	40.8%	3.1 mth, 14.4 vs 11.3 (27.4%)
Alpharadin, **Algeta/Bayer**	395	placebo	ALSYMPCA (2011)	chemo-naïve, sub-group	0.745 (0.562-0.897)	0.03932	34.2%	4.6 mth.16.1 vs 11.5 (40.0%)
Jevtana (cabazitaxel), **Sanofi**	755	mitoxantrone/ prednisone	TROPIC (2010)	post-docetaxel	0.70 (0.59-0.83)	<0.0001	42.8%	2.4 mth, 15.1 vs 12.7 (18.9%)
Enzalutamide, **Medivation/ Astellas**	1,199	placebo	AFFIRM (2011)	post-docetaxel	0.631	<0.0001	58.4%	4.8 mth, 18.4 vs 13.6 (35.2%)
Taxotere (docetaxel), **Sanofi**	1,006	mitoxantrone/ prednisone	TAX327 (2004)	chemo-naïve	0.76 (0.62-0.94)	0.009	31.5%	2.4 mth, 18.9 vs 16.5 (14.5%)
Prostvac (Tricom), **Bavarian Nordic**	125	placebo	NCI multicentre*	chemo-naïve	0.56 (0.37-0.85)	0.006	78.5%	8.5 mth, 25.1 vs 16.6 (51.2%)
Provenge (sipuleucel-T), **Dendreon**	512	placebo	IMPACT (2010)	chemo-naïve	0.759	0.032	31.8%	4.1 mth**, 25.8 vs 21.7 (18.9%)

Source: Edison Investment Research. Notes: * Phase II study; ** Median overall survival would be 7.8 months and HR=0.60 (95% CI: 0.41, 0.95) if adjusted for known biasing factor of the cross-over to APC8015F in this study. N/A = not available.

Valuation

We have removed CytoFab's contribution from our valuation and also revised for certain other minor changes, including using FY13 year-end cash of £144m (versus the £112m in at the end of FY12). This suggests a new valuation for BTG of £1.31bn or 398p per share, compared with the previously published £1.41bn or 430p/share. Thus we consider BTG to offer an attractive investment proposition, with the current share price offering 14% upside to a valuation that is largely supported by the DCF value of its core business activities and a low risk profile by biotech standards.

Exhibit 6: BTG valuation summary

Component	Value (£m)	Notes
Core business (speciality pharma/int oncology, royalties)	737	DCF value with explicit forecast to 2016, terminal value based on 2017. 10% WACC, long-term growth 2%.
Varisolve	270	Assumes a 90% probability.
Lemtrada	147	Assumes 90% probability, peak sales of $1.25bn, 3% net royalty to 2017.
Otelixizumab	9	
Cash	144	Net figure forecast for 31 March 2013.
Total	**1,305**	

Source: Edison Investment Research

Sensitivities

BTG derives revenue principally from direct product sales and royalty interests in marketed products, sold by third parties. Directly marketed products are primarily used in emergencies and are subject to little actual, or potential, competition. CroFab may face competition at some point and Varisolve, if approved, will have to compete with RF or laser ablation. Zytiga and, if approved, Lemtrada, are both competing in highly dynamic markets that make forecasting sales longer term more uncertain. We have modelled what we consider to be a cautious base case, leaving significant potential for upside surprise. Principal risks relate to the success of commercialisation of products, both directly and by partners. The company is exposed to the normal drug development risks (ie the success or failure of clinical trials including those of competitors), regulatory risk and commercial decisions by partners and potential partners, although by biotech standards, we consider these to be low.

Financials

Our financial model has been updated and suggests revenues for the current year ending March 2013 will be £201m, just ahead of the guided range (£190-200m), with a pre-tax profit of £2m (£49m profit normalised). Year-end cash is shown at £144m.

Exhibit 7: Financial summary

£m	2011	2012	2013e	2014e
Year end 31 March	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	**111.4**	**197.0**	**201.0**	**223.5**
COGS/revenue sharing	(34.1)	(56.3)	(61.3)	(73.2)
Gross profit	77.3	140.7	139.7	150.4
EBITDA	**16.0**	**57.3**	**49.4**	**53.0**
Op Profit (before amortisation and except)	13.6	54.1	46.4	50.0
Amortisation of Patents	(19.6)	(30.7)	(45.0)	(17.0)
Profit on disposals	1.5	0.2	0.0	0.0
Write-offs	(1.4)	(0.2)	0.0	0.0
Restructuring costs	(7.3)	(1.1)	0.0	0.0
Share based payments	(0.6)	(2.4)	(2.4)	(2.4)
Operating Profit	**(13.8)**	**19.9**	**(1.0)**	**30.6**
Net Interest	3.0	3.1	3.0	3.5
Profit Before Tax (norm)	**16.6**	**57.2**	**49.4**	**53.5**
Profit Before Tax (reported)	**(10.8)**	**23.0**	**2.0**	**34.1**
Tax	20.0	(8.4)	(8.4)	(14.0)
Profit After Tax (norm)	**36.6**	**48.8**	**41.0**	**39.5**
Profit After Tax (reported)	**9.2**	**14.6**	**(6.4)**	**20.1**
Average Number of Shares Outstanding (m)	269.0	327.0	328.1	328.1
EPS - normalised (p)	13.6	14.9	12.5	12.0
EPS - reported (p)	3.4	4.5	(1.9)	6.1
Dividend per share (p)	0.0	0.0	0.0	0.0
Gross Margin (%)	69.4	71.4	69.5	67.3
EBITDA Margin (%)	14.4	29.1	24.6	23.7
Operating Margin (before GW and except.) (%)	12.2	27.5	23.1	22.4
BALANCE SHEET				
Fixed assets	**358.9**	**331.5**	**288.0**	**272.5**
Intangible assets	271.0	246.0	201.8	185.6
Goodwill	59.2	59.2	59.2	59.2
Tangible assets	24.8	22.0	22.7	23.4
Investment in associates	3.9	4.3	4.3	4.3
Current assets	**129.6**	**174.3**	**208.6**	**250.8**
Stocks	20.0	21.8	23.2	24.8
Debtors	32.7	40.1	40.9	45.5
Cash	73.9	112.4	144.5	180.5
Other	3.0	0.0	0.0	0.0
Current liabilities	**(52.3)**	**(58.3)**	**(63.0)**	**(68.0)**
Creditors	(32.2)	(37.4)	(45.0)	(50.0)
Accruals/deferred income	(18.0)	(18.0)	(18.0)	(18.0)
Employees/provs/tax	(2.1)	(2.9)	(0.8)	(0.8)
Derivative instruments	0.0	0.0	0.0	0.0
Short-term borrowings	0.0	0.0	0.0	0.0
Long-term liabilities	**(43.9)**	**(41.3)**	**(28.7)**	**(23.9)**
Long-term borrowings	(2.9)	0.0	0.0	0.0
Other long-term liabilities	(41.0)	(41.3)	(28.7)	(5.1)
Net assets	**392.3**	**406.2**	**404.9**	**431.4**
CASH FLOW				
Operating cash flow	**(10.7)**	**48.3**	**33.7**	**40.4**
Net interest	0.4	0.6	3.0	3.5
Tax	(1.3)	(1.1)	(0.1)	(3.4)
Acquisition/disposal of intangibles	0.2	(6.0)	(0.8)	(0.8)
Capital expenditure	(10.2)	(3.7)	(3.7)	(3.7)
Acquisitions/disposals	14.4	0.0	0.0	0.0
Financing	0.0	0.1	0.0	0.0
Dividends	0.0	0.0	0.0	0.0
Other	(4.0)	0.0	0.0	0.0
Net cash flow	(11.2)	38.2	32.1	36.0
Opening net debt/(cash)	**(81.9)**	**(71.0)**	**(112.6)**	**(144.5)**
HP finance leases initiated	0.0	0.0	0.0	0.0
Other	0.3	3.4	(0.2)	0.1
Closing net debt/(cash)	**(71.0)**	**(112.6)**	**(144.5)**	**(180.6)**

Source: Edison Investment Research

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